WATCH YOUR STEP!

TOWARDS PREDICTING OSTEOARTHRITIS ONSET

BASED ON SIDE-TO-SIDE IMBALANCES

By

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Abstract: Osteoarthritis (OA) is a debilitating disease characterized by the erosion of articular cartilage at the extremity of bones. OA contributes to economic burdens, pain, and abnormal locomotion to accommodate for loss of protective cartilage. Since there is no cure for OA, mitigating disease onset can relieve the lives of millions of people who are at higher risk of OA such as females and overweight people.

The progressive disappearance of protective cartilage leads to bone-on-bone contact at the joints, which is aggravated by higher-than-normal joint contact forces. Although OA can affect any joint, the primary weight-bearing joints of the lower body, *i.e.* hip, knee, and ankle, suffer the most impairment. Thus, investigating walking behavior can aid in detecting abnormal locomotion that may lead to OA.

The objectives of this study were (1) to investigate a simple mechanical model's ability to accurately reproduce measured gait kinetics and (2) to propose and evaluate novel parameters to supplement current noninvasive clinical tools for gait analysis.

For a total of forty healthy subjects, kinematic and kinetic parameters were optimized for 300 consecutive steps to fit experimental vertical ground reaction force data measured during treadmill walking. Using an existing inverted spring-loaded pendulum with a spring-loaded ankle, we assessed the variations in leg and ankle stiffnesses during gait. We quantified bilateral lower limb symmetry, gait regularity, and gait variability based on the optimized stiffness values, which highlighted gait disparities between males and females, and between different body mass index categories.

Our results confirmed that all subjects exhibited a certain amount of side-to-side asymmetry, irregularity, and variability in their leg and ankle stiffnesses during walking. Furthermore, large inter-subject variability indicated that our simple model could detect idiosyncratic gait patterns and therefore estimate potential imbalances in gait patterns. Future studies to test these walking assessments with accelerations as input parameters, which are easier to measure in a clinical setting, can improve current screenings for OA.

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CHAPTER I

INTRODUCTION

1.1. Motivation and objectives

Osteoarthritis (OA) is a disease distinguished by the progressive degeneration of articular cartilage at the joints causing pain, discomfort, and economic burdens due to debilitation (Das & Farooqi, 2008) (Woolf & Pfleger, 2003). OA is prevalent in over 528 million people globally and is projected to persist, especially in populations with longer living expectancies and higher obesity rates (Zhang & Jordan, 2010) (Leifer, 2022). It is the most common form of arthritis, and the most common joint disorder in the United States. Among adults 30 years old and older, 6% experience pathological symptoms in the knee (Felson, 2000). Females experience greater burdens due to OA (O'Connor, 2007) (Felson, 1988). The weight-bearing joints of the lower extremity are most affected by OA (Fowler-Brown, 2015). There is no current cure for OA, so once disease onset occurs, treatment options are limited to surgical procedures and physical therapy which may only provide temporary relief (Hawker, 2000) (Roos & Juhl, 2012). Thus, mitigating disease-driven tendencies is necessary to improve the quality of life of millions of people.

This work focuses on the development of a noninvasive clinical tool that can assess the risk of osteoarthritis in the lower body by recognizing biomechanical symptoms indicating disease. Current imaging for pre-OA biomarkers have been suggested to mitigate disease onset

(Chu, 2012). However, they require expensive equipment, and with disease prevalence rapidly growing, availability for screening may be challenged.

Mechanical overload of the joints that increase contact forces and other joint injuries have been shown to increase OA incidence (Andriacchi, 2004) (Kaufman, 2001) (Chu, 2012). Although risk factors such as innate gender and inevitable aging cannot be avoided, modifying locomotion behavior during everyday tasks can attenuate degeneration.

One of the most common and assessable methods of transportation among healthy bipeds is walking. Gait has been a metric utilized by clinicians to categorize pathological tendencies (Shi, 2018) (Sangeux, 2015). Since humans walk differently based on gender (Kerrigan, 1998) (Smith, 2002) (Bruening, 2015) (Toda, 2015) and body mass index (BMI) (Browning & Kram, 2007) (Cimolin, 2017) (Adhikary & Ghosh, 2022), it is useful to assess the effects of these parameters on locomotion behaviors.

Our first objective is to implement an assessable approach by selecting a gait model that is accurate, requires noninvasive input parameters, and is of course capable of producing reasonable estimations for vertical ground reaction forces that have been notoriously challenging to simulate (Cavagna, 1976) (Mochon & McMahon, 1980) (Pandy, 2003) (Buczek, 2006) (McGrath, 2015). Human balance and posture described as an inverted pendulum can be used to identify gravitational and acceleration perturbations and pinpoint the motor mechanisms that can defend against any perturbation when appropriate versions of the model are utilized (Winter, 1995) (Anderson & Pandy, 2003). Ameliorating gait analysis with simple models as a methodology to recognize abnormal gait behavior can offer more accessible resources to clinically assess unfavorable movement tendencies prone to disease. Previous studies usually utilize mean values of gait parameters to investigate variables despite the characteristic variability of biological systems. Indeed, many studies consider the average of ground reaction force data (Antoniak, 2019). Thus, we implemented our method with 300 individual consecutive steps of data from able-bodied participants to assess leg and ankle stiffnesses.

Normal gait yields a deterministic pattern that describes itself as chaotic. However, the pathogenesis of movement inhibiting diseases or lower limb surgery can disturb such cohesion (Stergiou, 2004) (Hausdorff, 2005) (Kobsar, 2019). Variability in walking patterns and bilateral limb asymmetry of the lower extremity muscles contribute to conflicting perspectives for effective rehabilitation strategies. For example, anterior cruciate ligament reconstruction patients often experience limb stiffness of the surgical leg that results in disproportionate contralateral quadriceps, causing strength weaknesses associated with decreased knee cartilage which can contribute to the development of osteoarthritis (OA) (Shi, 2018). Knee OA patients exhibit kinematic and kinetic gait pattern deviations from the progressive erosion of articular cartilage (Deluzio, 1997) (Kobsar, 2019), so recognizing prevailing deviances in leg and ankle stiffness strategies can provide an early indicator of disease onset. However, suggesting perfect performance symmetry may be further categorized as abnormal gait (Stergiou, 2006), and with some reinjury rates surpassing risk of initial injury occurrence (Shi, 2018), further investigation of biomechanical parameters in healthy walking subjects can reveal thresholds for clinical applications. Our next goal is to assess levels of symmetry, regularity, and variability among healthy young males and females with distinguishable categorical BMI (> 25 kg/m^2 and ≥ 25 kg/m^2) to investigate any disparities or parameter interactions.

Since forces are related to accelerations, a smart phone can be attached to a person's belt as they walk, and its built-in accelerometer can be used to estimate forces that show side-to-side discrepancies, detrimental variability, and abnormal chaos. For example, Mohamed Refai et al. (2020) found that a single pelvis inertial measurement unit (IMU) that measures accelerations at the hips could estimate 3D ground reaction forces with just over-ground walking. Similar procedures have been evaluated for efficient methods to predict the risk of joint issues (Kobayashi, 2014) (Cimolin, 2017). We hope to contribute to studies on gait performance that can suggest preliminary clinical assessments by estimating thresholds for healthy walking performance with an overarching goal to develop noninvasive clinical tools that can evaluate large joint contact forces and thus predict potential joint health issues.

1.2. Parameters studied

The parameters investigated in this research are the leg stiffness and the ankle stiffness based on vertical ground reaction forces and fit to a parametric curve with differential equations of a simple gait model available in the literature.

Dynamic leg movements exhibit compressive behavior similar to springs when a limb responds to its interactions with the ground (Hong, 2013). The leg stiffness describes a relationship between the deformation of muscles and connective tissues with the ground reaction forces. Simple walking models add springs to an inverted pendulum to represent the leg stiffness as a spring suspended from a pivot that represents a person's center of mass (Figure 1) (Dutto & Smith 2002) (Geyer 2006) (Hong, 2013) (Jung & Park, 2014).

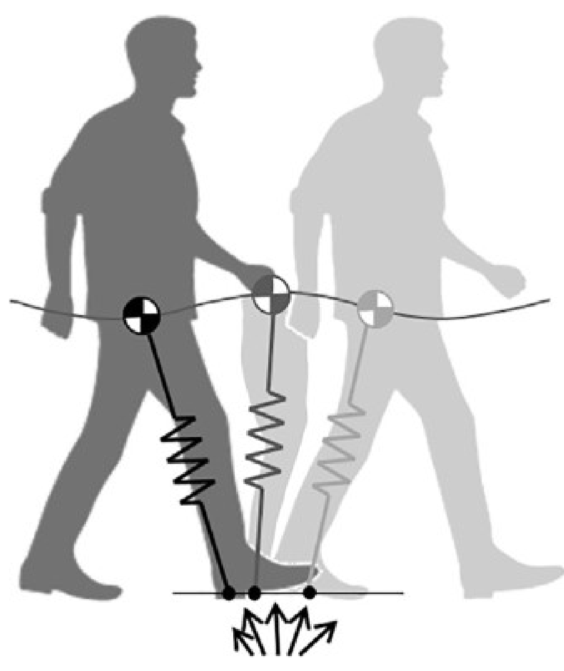

Figure 1. Leg stiffness represented by suspended springs (Ryu & Park, 2018).

A linear torsional spring represents the behavior of an ankle (Figure 2) (Shamaei, 2011). The ankle stiffness describes a relationship between the ankle moment and its angular displacement during plantarflexion and dorsiflexion, resisting motion away from the vertical of the leg (Antoniak, 2019).

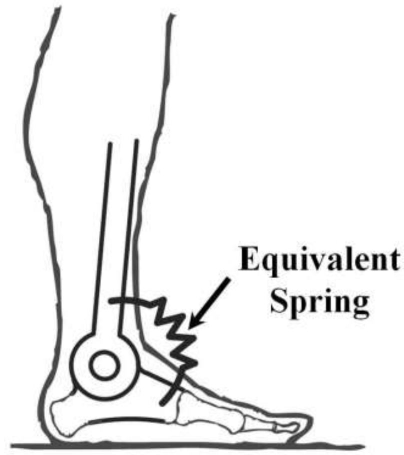

Figure 2. Ankle stiffness represented by linear torsional spring (Shamaei, 2011).

1.3. Hypotheses

This research sought to investigate the efficacy of utilizing a simple mechanical model to produce the behavior of vertical ground reaction forces recorded from experimental human gait. We hypothesize that:

1. a gait model with minimal input parameters can provide adequate qualities of walking dynamics
2. optimized values of leg and ankle stiffnesses can help assess the severity of bilateral lower limb asymmetry, gait irregularity, and variability
3. this model can evaluate existing gender-related disparities between young healthy males' and females' gait
4. this model can evaluate existing disparities between low (< 25 kg/m^2) and high (≥ 25 kg/m^2) BMI subjects' gait walking

CHAPTER II

LITERATURE REVIEW

2.1. Osteoarthritis: an ongoing worldwide issue

Osteoarthritis (OA) is a musculoskeletal disorder characterized by the thinning of articular cartilage, causing pain in affected joints and less effective postural stability (Das & Farooqi, 2008). With pain and impaired musculoskeletal functioning, OA contributes to qualms due to the economic burden for treatment management and debilitating cases that compromise job employments (Woolf & Pfleger, 2003). OA is the most common form of arthritis and joint disease worldwide and superlatively leads as a global cause for disability (Peat, 2020). In the United States, OA affects over 32.5 million adults (CDC, 2021) and is more prevalent among females than males, with the former exhibiting higher rates of disease severity (Safiri, 2020). Females are also less likely to undergo joint replacement surgery as a treatment intervention (Hawker, 2000). Additionally, joint replacement surgery such as knee arthroplasty can be ineffective in improving acute OA symptoms, and more attainable, non-invasive regimens including exercise therapy may provide only temporary relief (Roos & Juhl, 2012), but more severe disease stages impose irremediable lifestyle burdens among affected individuals (Loeser, 2017). Since there is no current cure for OA, mitigating disease onset can improve the quality of life of millions of people.

As of December 2021, the Centers for Disease Control and Prevention recommends weight loss for disease management. OA is related to higher-than-normal joint contact forces that erode articular cartilage with repetitive subjection to loading (Andriacchi, 2004). Although OA can affect any joint, the primary weight-bearing joints, *i.e.* ankles, knees, and hips, tend to be most compromised (Fowler-Brown, 2015). A random-effect meta-analysis from Zheng & Chen (2015) combined literature data of the relative risks of OA with 5 kg/m^2 increases in body mass index (BMI). Increased BMI was found to increase the risk of OA by 35%, highlighting the relationship between weight and potential cartilage degradation (Zheng & Chen, 2015). One of the largest studies was The Framingham Study cohort, which included radiographs of 1420 subjects with compartmentalized Metropolitan Relative Weight that quantifies body weight relative to a person's height (Felson, 1988). The results showed greater OA incidence in overweight and obese subjects.

Weight and the risk of knee OA show a stronger association in women than in men (Felson, 1988). Overall, females are more affected by the burdens of lower limb OA than their male counterparts (O'Connor, 2007) (Felson, 1988); thus, gender characteristics are assessed to speculate disparities that increase the risk of disease. For example, a potentially limiting protective apparatus at the joint contact surfaces, females have been found to have thinner articular cartilage at the distal femur and less cartilage volume at knee joints in comparison to males (Faber, 2001). However, it is unclear whether gender-specific anatomy solely contributes to the vulnerability of cartilage degradation (O'Connor, 2007). A study by Fowler-Brown et al. (2014) with 653 participants found hormonal connections between elevated BMI and knee OA, suggesting greater complexity when investigating gender effects.

The prevalence of OA is comparable between males and females up to 50 years of age and becomes disproportionate in succeeding years (Oliveria, 1995), further reinforcing the associations of hormonal influences since female menopausal transitioning starts and physiological impediments alter with chronic disease and age (Felson & Zhang, 1998). Studies have repeatedly shown that lower limb OA strongly correlates with increasing age (Felson, 1987) (Oliveria, 1995) (Felson & Zhang, 1998). The Framingham Study investigated radiographs of subjects aged 28 to 58 years old in an initial evaluation at the commencement of the study and approximately 36 years after the first assessment for possible diagnosis of definite joint space narrowing or present osteophytes indicating decreased bone cushioning; over one-third of the subjects showed evidence of radiographic knee OA (Felson, 1988), associating age with OA pathogenesis. Aged joints can experience elevated shear stress at that basal cartilage layers (Felson & Zhang, 1998), suggesting investigations in dynamic biomechanical models for early indicators of disease-driven tendencies.

2.2. Clinical use of gait and relationship with OA

One of the most common forms of daily transportation among able-bodied bipeds requires the support and propulsion coordinated between two legs, called walking or gait. Assessing anomalies in gait performance could potentially indicate behaviors that increase the risk of OA and possible, early rehabilitation interventions to delay disease pathogenesis (Chu, 2012). Existing arthritic joints can affect walking tendencies due to pain, swelling, muscle stiffness, and overall lower limb weakness. Thus, gait will be altered to mitigate discomfort during locomotion. For example, studies have shown multivariate gait deviations in patients experiencing symptomatic effects of OA (Kobsar, 2019) (Naili, 2017).

Assessing thresholds for normal dynamic ranges during walking can improve the accuracy of methods for clinical pathology detections. For example, a study investigating the effectiveness of the plantarflexor–knee extension index for classifying physical anomalies based on the distance between a mid-stance ankle and knee referenced clinically normative alignment values for expected lower extremity kinematic responses (Sangeux, 2015). Tingley et al. (2002) relied on empirical data of normal gait patterns in children to describe the inversely proportional relationship between the decline of unusual toddler walking behavior with age. The reliability of the normalcy index in a clinical setting was evaluated with subjects exhibiting disordered gait behavior in comparison to the average performance of able-bodied subjects (Romei, 2004). In assessing the reliability of the Gillette Gait Index as a tool to quantify pathological gait severity, the control group consisted of able-bodied individuals for a measurable comparison between disordered locomotion (McMulkin & MacWilliams, 2008). In recognizing the vast tendencies of healthy bipeds, characteristics of disease-driven movement can be more efficiently monitored.

With applications of gait analysis being utilized in clinical settings, variables are being investigated to conclusively define acceptable parameters that professionals can prescribe as normal human movement. From some of the earliest investigations of human locomotion instigating in Classical Ancient Greece and the Renaissance, mechanical movement studies in living creatures and excelling accuracy of anatomical human drawings inspired photography as a method to evaluate gait mechanics by offering consecutive depictions of the anthropomorphic structure's two-dimensional movements that defined lower limb positioning (Baker, 2007) (Al-Zahrani & Bakheit, 2008), and primitive observations of bipedal motion in the sagittal plane were augmented by studies that distinguished the universal gait cycle.

A single gait cycle describes the general position, timing, and behavior of a single limb during a stride of normative walking. Furthermore, the gait cycle constitutes a single-legged support phase that comprises over half of the time of a single stride. The single-legged support during the stance phase of gait is the primary experimental focus of this work, so it is relevant to study mechanisms that imperil the stance phase during locomotion. The multi-joint interaction can characterize healthy gait habits when considering muscle activation patterns that contribute to stabilization and forward motion. The heel strike initiates a loading response as a person's body weight is gradually bearing on the single-supporting limb once the contralateral leg elevates off the contact surface. Muscles of the ipsilateral limb are tasked to lift the body's mass by pushing against gravity and coordinating muscular activity, facilitating the forward progression of walking (Anderson & Pandy, 2003) (Bartlett, 2014) (Freddolini, 2017). Each lower body muscle of the effective leg contributes to various functions in locomotion such as forward propulsion, joint preservation, and trunk stability (Zajac, 2003) (Anderson & Pandy, 2003). Musculoskeletal mechanics of healthy single-legged supported gait events have been useful in categorizing abnormal gait since the ipsilateral limb experiences maximal compression when maintaining the integrity of the torso's weight (Figure 3). Altered intensity and activations of lower extremity muscle activity are suggested to be indicators of compensated joint stabilizing mechanisms (Freddolini, 2017) (Childs, 2004). Additionally, in response to the condition of the joints' protective articular cartilage, excessive versus limited joint ranges of motion can reveal underlying conditions (Wei, 2009) (Gillam, 2013) (Mills, 2013) (Akl, 2020).

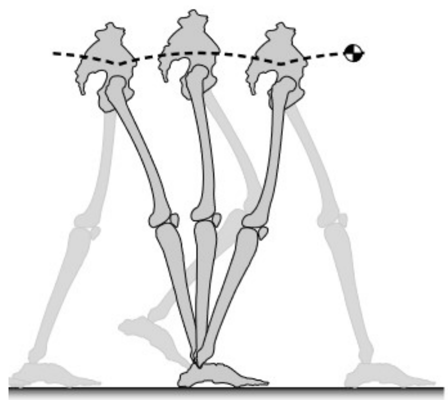

Figure 3. Description of the single-legged support phase and the associated motion of the center of mass (Kuo, 2007).

Causes and consequences of OA on gait biomechanics may be indistinct (Guilak, 2011), so OA symptoms may not be known until initial disease onset. Kinematic deviations during gait can foreshadow degenerative changes in joints that can lead to OA development or progression. Since OA is a multifactorial condition that is incompatible with a single universal prescription (Felson & Zhang, 1998) (Fowler-Brown, 2015) (Loeser, 2017), recognizing dynamic biomechanical factors contributing to the pathogenesis of OA are heeded. Thus, gait analysis tools supplement as an accessible approach in detecting OA onset.

2.3. Relevant gait characteristics

2.3.a. Center of mass trajectory

The center of mass dynamics highlight complex details regarding biped locomotion. Kinematic variables are also considered when assessing disordered gait (Lee & Chou, 2006). Merited "The Father of Biomechanics" (Pope, 2005), Giovanni Alfonso Borelli pioneered one of the earliest distinctions for bipedal locomotion studies: the human center of mass (Baker, 2007) (Provencher & Abdu, 2000). Borelli investigated the human body's frontal plane location of equilibrium with vulgar tools that instigated Renaissance gait analysis, identifying a common anthropomorphic center of mass (COM) existence to be superior to the hip bones (Provencher & Abdu, 2000). Succeeding experiments with complex technology validated Borelli's geometric deduction and further distinguished the criterion with qualities of gender and limb proportions (Smith, 2002) (Lee & Chou, 2006) (Virmavirta & Isolehto, 2014). With the development of experimental tools necessary to assess the location of the COM (Saini, 1998) (Virmavirta & Isolehto, 2014), these static bipedal investigations warranted a milestone in biomechanical analysis.

An early intention to distinguish normal and pathological gait with the COM was with the six determinants of gait: pelvic rotation, pelvic tilt, single-limb support knee flexion, foot and knee mechanics, and lateral displacement of the pelvis (Saunders, 1953). Saunders et al. (1953) hypothesized that the body minimizes its vertical COM trajectory through exaggeratedly heightened knee flexion, pelvic rotation, and pelvic tilt during gait. The idea of reducing the COM displacement and indicating the influencing parameters intended to classify anomalies during walking. The determinants of gait orchestrate to flatten the COM trajectory and suggest that a flat COM trajectory gait reduces muscular work necessary to lift the body to improve energy economy (Saunders, 1953). Although some determinants have been found to reduce the vertical movements of the human body COM (Ortega & Farley, 2005) and have all been utilized as a foundation for modeling gait (Mochon & McMahon, 1980), lowering of the pelvis ipsilateral to the swing leg is trifling to the trunk's locomotion (Gard & Childress, 1997) (Pandy, 2003), and the stance-phase knee flexion does not significantly reduce the COM's vertical displacement to flatten its trajectory as hypothesized (Gard & Childress, 1999). The vertical COM trajectory as a person walks forward is of interest since it can expose potential implications in relation to abnormal gait (Ortega & Farley, 2005) (Kuo, 2007) and can be easily calculated (Saini, 1998).

Furthermore, Saunders et al. (1953) suggested that metabolically efficient forward locomotion for the cycloid shape of the COM trajectory would be to approach a sinusoidal pathway with a vanishingly low amplitude. Some clinical interventions aim to reduce the COM vertical motion since it is a placid metric for physical recovery.

However, studies disprove the prediction that energy needs diminish in a reduced COM vertical displacement since the net metabolic rate required by the lower limbs to maintain a nearly linear translation, as also acknowledged by Saunders et al. (1953), is greater than twice the empirically found value (Kuo, 2007) (Ortega & Farley, 2005). This model also fails to resemble habitual human walking when modeled since the COM produces a greater vertical displacement in healthy bipedal locomotion, thus, an ineffective evaluation for dichotomizing gait tendencies. Despite the faults of defining the six determinants of gait for diagnosing gait behavior, the prominent hypothesis of reducing the COM displacement during walking has been seen as a rehabilitative objective and remains controversial.

2.3.b. Bilateral limb symmetry

Healthy biped gait is traditionally expected to perform symmetrically throughout consecutive steps between the left and right limbs to achieve optimal stability. Gait symmetry can be defined as identical behavior and performance between limbs (Sadeghi, 2000). The effectiveness of therapeutic interventions has relied on the reduction of asymmetry following the categorization of functional inefficiency in the lower body (Becker, 1995) (Hesse, 1997) (Patterson, 2012) (Pirker & Katzenschlager, 2017) (Shi, 2018). Since side-to-side gait imbalances are associated with disease (Kaufman, 2001), lower limb injury (Stergiou, 2004) and surgery (Shakoor, 2002), and neurological conditions (Nasirzadeh, 2017) (Shi, 2018), interventions have been suggested to reduce locomotion asymmetry (Durham, 2004) (Hodt-Billington, 2012) (Renner, 2018). For example, in association with lower body OA onset, imbalances during pathological gait can increase joint contact forces (Kaufman, 2001), and unilateral joint replacement surgery elevates the risk of OA progression in the contralateral limb (Shakoor, 2002). A longitudinal study done by Metcalfe et al. (2012) focused on 140 middle-aged patients with knee pain to assess the potential progression of unilateral knee OA developing into bilateral disease. Results suggested that lower body OA onset is asymmetrical but will be present in the contralateral limbs over time, even without previous lower limb injuries. Al-Juaid & Al-Amri (2020) assessed walking performance of able-bodied men and found that vertical ground reaction forces exhibit the most symmetrical performance bilaterally to promote postural steadiness, but they were considered detrimental during walking while performing a cognitive task. Furthermore, subjects with an ACL rupture exhibit less sensitivity to small perturbations in the deficient knee during treadmill walking, causing imbalanced stability strategies during locomotion and increased risk for lower limb pathologies (Stergiou, 2004). However, this study excluded control participants without ACL rupture, neglecting a comparative analysis between the functional amounts of bilateral symmetry between groups. Additionally, weaker adaptive strategies when encountering external disturbances of motion are associated with the reduction of afferent proprioceptive input from the ACL injury.

In contrast to this perspective, the literature has challenged the inclination for perfect symmetry. The idea of such harmony aimed in physiotherapy strategies has been criticized since the conceptual simplicity contradicts the complexity of gait performance (Nasirzadeh, 2017). Various literature suggests that there is a permissible threshold of violating gait symmetry acceptable and necessary for adaptable movement from ubiquitous kinetic perturbations (Sadeghi, 1997) (Sadeghi, 2003) (Al-Juaid & Al-Amri, 2020). In a review by Nasirzadeh et al. 2017, nearly ten studies found healthy subjects exhibiting asymmetrical gait. Since interactions require volatile reactions, variability theories suggest that optimal dynamic movement of biological systems must be capable of performing the same task repeatedly, utilizing a multitude of diverse strategies to function (Stergiou, 2006). Therefore, it may be necessary to exhibit limited asymmetry to permit adaptability during walking.

2.3.c. Leg and ankle stiffness

Leg dynamics during walking have been found to be spring-like (Hong, 2013). Thus, studies have utilized Hooke's Law when describing anatomical components that determine the overall leg stiffness, such as muscles and connective tissues (Geyer, 2006) (Whittington & Thelen, 2009) (Antoniak, 2019). Kim & Park (2011) suggested that springy dynamics of muscular activity offer optimal leg stiffness with maximum elastic energy stored in the stance leg. In a drop landing study, muscular activity was detected prior to the touchdown, suggesting that the human central nervous system estimates some necessary force to protect the joints in preparation for weight acceptance during locomotion (Gambelli, 2016).

During walking, the quadriceps, hamstrings, and gastrocnemii muscles of the legs are dominant contributors to the knee joint loading (Kumar, 2013) (Pandy & Anderson, 2010), so leg stiffness is associated with joint contact forces and thus potentially OA onset and progression (Andriacchi, 2004). In post-traumatic OA, imbalances can cause leg stiffness during gait, and since increased quadriceps strength is associated with greater cartilage cross-sectional area, asymmetrical lower limb muscle weakness can increase the risk of OA onset (Shi, 2018).

Furthermore, the planterflextors and dorsiflexors have been suggested to control the anterior-posterior direction by resisting motion from small perturbations directed away from the leg's vertical orientation, achieving postural balance in upright positions (Winter, 1995) (Gatev, 1999) (Antoniak, 2019). In the sagittal plane, the ankle control is largely responsible for balance during the stance phase (Gatev, 1999).

2.3.d. Variability

A prominent characteristic of human movement is its variability, although it may appear as a purely cyclic activity. During gait, the average performance of the motion was traditionally considered to consist of random noise that minimally contributed to walking deviations (Hausdorf, 2005). As a multi-joint movement that requires the coordination of several muscle forces, joint motions, and physiological feedback (Socie & Sosnoff, 2013), healthy walking exhibits a deterministic pattern among strides that yields long-range correlations with fractal properties in fluctuations (Hausdorff, 1995) (Stergiou, 2006). Variability in gait patterns is crucial for healthy locomotion adaptability strategies (Hausdorf, 1995) and is inherent in biological functioning, yet thresholds must exist for establishing adequate ranges of distinguishable noise. For example, in patients with multiple sclerosis, gait variability increases with increasing Expanded Disability Status Scale scores (Socie & Sosnoff, 2013) which positively correlates with impairment severity. Fickle movement patterns could indicate less behavioral control between the coordination of the musculoskeletal and nervous systems, while less chaos may restrict physical resilience capabilities in opposing external perturbations. Both extremes led to poor adaptation capabilities and ultimately potential health issues (Brach, 2005) (O'Connor, 2012). Barrett et al. (2008) suggests that lower variability can increase localized mechanical stress on anatomical structures, causing more susceptibility to injury due to overuse degeneration.

For its ease of use and reliability in studying variability of time series, the coefficient of variation (CV) has been used in several studies as a measure of the natural fluctuations of gait during locomotion (Hausdorff, 1995) (Hausdorff, 2001) (Masani, 2002) (Wang, 2003) (Hausdorff, 2005) (Lamoth, 2010) (Lamoth, 2011). The CV is a ratio of the standard deviation to the mean value of the data set to quantify the relative dispersion of a series with respect to the average. While standard deviation (SD) is useful in interpreting the spread of solitude data, the CV offers a metric for comparison among an assortment of information, and for allowing inter-subject comparisons. For example, Ortega & Farley (2005) investigated inconsistencies in human COM vertical trajectories by computing the SD of the COM displacement while using strategies to minimize vertical movement. Although the units for the parameter of interest remain the same among each experiment, the relative magnitude of the SD, or the CV, would have effectively normalized the variability to aid in comparison. Nevertheless, SD and CV are both valuable measures that describe data concentrations with respect to the mean

From clinical cases, Stergiou et al. (2006) proposed that fostering an optimal amount of movement variability improves locomotion strategies by renewing pathological tendencies unique to the individual that are too unpredictable or rigid. However, in addition to this theory, the authors suggest the mere importance of utilizing the amount of chaos in the dynamics of the system as a metric for physical health and motor skill evaluations.

2.3.e. Regularity / complexity

Sample Entropy (SampEn) is a common nonlinear method for assessing the complexity of biological data. Its measure is the negative natural logarithm of the conditional probability that two sequences similar of simultaneous data points of their particular lengths and constrained with a specified distance less than the tolerance will remain similar at the next vector. Thus, patterns of time series are completely predictable when SampEn is zero, while larger values are associated with a more chaotic system. Contrasting from other entropy statistics, the development of SampEn eliminates the comparison of self-matching patterns to relieve bias of self-similarities and intended to improve the accuracy of shorter physiological time-series, simplify implementation, and evaluate relative consistency (Richman & Moorman, 2000). Yentes et al. (2013) investigated the usage of SampEn for shorter data sets and found it to be less sensitive to data length changes and validated that relative consistency was improved in comparison to former methodology.

SampEn has been used to assess the predictability and regularity of gait parameters (Lamoth, 2010) (Yentes, 2013). Larger SampEn values in postural walking studies have been associated with impaired balance in dual-task conditions (Lamoth, 2010) (Lamoth, 2011) and post-stroke (Roerdink, 2006) which suggest a greater risk of falling. Segal et al. (2018) suggests assessing gait complexity to evaluate human physical functioning since poorer performance correlated with less chaotic gait can be associated with the risk for knee OA. Therefore, quantifying the complexity of gait parameters with SampEn is pertinent towards disease preventative measures.

2.4. Gender and BMI effects

2.4.a. Gender effect

Males and females each possess unique anatomical characteristics that affect their walking strategies. In healthy young subjects, females exhibit greater pelvic obliquity during walking, and this trend increases among elderly participants (Smith, 2002) (Bruening, 2015). Smith et al. (2002) suggest that such a strategy may be compensating for the reduced COM vertical displacement females also demonstrate which overall might contribute metabolic efficiency as opposed to the COM vertical trajectory mechanisms found in Ortega & Farley (2005) that increased energy economy. However, Smith et al. (2002) also suggest social and cultural expectations for female posture that impact gait performance since increased pelvic obliquity causes maladaptively for the lumbosacral spine during locomotion, which they suggest further dichotomizes movement by gender since women have elevated motions of the lumbar spinal region. Furthermore, contemporary gender stereotypes for attire may expect females to wear high-heeled shoes which have been shown alter ankle functioning, increase compressive forces at the knee joint, and cause compensatory torque at the hips and knees to maintain stability when worn (Kerrigan, 1998). These behaviors require more activation of the quadricep muscles when performing the stance phase of walking, increasing leg stiffness and potentially offsetting gait performance when barefoot. Exaggerated joint motions while wearing high-heeled shoes has not been directly related to OA onset despite females exhibiting greater knee flexions and extensor moments in prevalent OA (Kaufman, 2001). However, it may suggest a cause for deficiencies in walking characteristics discriminated by gender.

Males and females also exhibit significantly different peak joint moments when reacting to loads. Toda et al. (2015) suggest that strategies adapting knee joint moments control the ground reaction forces produced during gait. Females implemented more reliance on their quadriceps muscles despite reduced muscular strength, which may cause abrupt limb stiffening upon ground contact (Lephart, 2002). In a drop landing study, females were found to land with increased knee and hip extension, suggesting a different strategy for maximizing energy absorption since the ankle muscles were the secondary shock absorbers in landing (Decker, 2003), potentially impacting anterior tibial shear forces during knee extension that can lead to ACL strain (Hirokawa, 1992). Since females show higher rates of injury and OA prevalence, assessing gait differences between genders can reveal locomotive strategies that increase the risk of disordered walking.

2.4.b. BMI effect

The World Health Organization defines adults as overweight when their BMI (mass/height^2 [kg/m2]) is greater than 25 kg/m^2, and obese when their BMI is greater than 30 kg/m^2. In this study, we investigated two categories of BMI: lower and higher than 25 kg/m^2 (WHO, 2021).

Postural strategies alter based on load distributions. For example, distinct vertical movement patterns are recognizable in regards to subjects' categorical BMI classification of underweight, normal weight, and overweight or obese (Adhikary & Ghosh, 2022). Obese adults spend more time in stance phase during walking and take wider strides than their low-weight counterparts (Browning & Kram, 2007) (Cimolin, 2017) potentially due to deceased strength challenging their abilities to accelerate their COM (Dufek, 2012). They also may reduce walking speeds to minimize mechanical work associated with locomotion (Malatesta, 2009). Additionally, their vertical accelerations do not oscillate as frequently as underweight subjects since they may perform more complete absorption upon foot-to-ground contact impact impulse (Adhikary & Ghosh, 2022).

A BMI greater than 25 kg/m^2 increases the risk of OA (Zheng, 2015). Obese subjects produce significantly larger ground reaction forces (Browning & Kram, 2007), resulting in increased joint contact forces that contribute to the onset of OA. Professionals suggest weight loss as a treatment to reduce joint aggravation in overweight OA patients since in most patients, BMI is considerably modifiable (Zheng, 2015). Since excessive fat distributions near anatomical landmarks can challenge traditional methods of gait analysis involving marker placement, studies have utilized accelerometers to measure spatiotemporal parameters during gait (Cimolin, 2017) (Adhikary & Ghosh, 2022). Advancing such mechanisms can suggest biomechanical efforts that higher BMI persons utilize for moderating dynamic balance and potential contributions those strategies have on joint loads.

2.5. Simple *in silico* gait models

One of the objectives of this study was to harvest the low computational cost of simple gait models for real-time clinical use. Therefore, the advantages and disadvantages of various gait models must be evaluated.

Despite the intricate qualities of gait, decomposing the mechanical movement during walking into familiar components can support observational interpretations of human locomotion (Alexander, 1995) (Whittlesey, 2000). Applying less complexity to a walking model and gradually modifying parameters of a minimal system can provide an easier method of analysis to gain insightful fundamentals of the motion's mechanisms (Alexander, 1995) (Zajac, 2003) (McGrath, 2015). An elementary perspective of biped walking can be described as a "stick-figure" consisting of two straight legs attached to a torso that is teetering for forward locomotion.

This illustration offers boundless potential for gradually enhancing with more anatomically accurate components. Thus, validating the experimental accuracy of an efficiently simple simulation can encourage further investigations that supplement more physiologically distinct features (Pandy, 2003).

The Weber brother's seventeenth-century suggestive modeling of a simple pendulum to describe the repetitive oscillations of the lower limbs attracted investigations to evaluate its anatomical and functional accuracy (Baker, 2007). Starting with the location of the body's COM at its apex, potential energy is converted to kinetic energy for forward progression. Thus, it is agreed upon that the COM moves in a pendular direction in the sagittal plane during gait, and its trajectory contributes to an extensive number of methods for gait modeling and empirical interpretations of human physiology (Hausdorff, 1995) (Cavagna, 1976) (Dutto & Smith, 2002) (Pandy, 2003) (Geyer, 2006) (Whittington & Thelen, 2009) (Antoniak, 2019).

2.5.a. Stiff-legged inverted pendulum

Coining the Inverted Pendulum (IP) as a trajectory strategy of the human body's COM, Cavagna et al. (1976) found familiar conversions between potential and kinetic energy existing during single-limb support in walking at speeds up to 7 km/h. Similar to pendular dynamics, kinetic energy during the initial duration of the stance phase is converted into gravitational potential energy as the COM approaches a height extremum in the sagittal plane during its trajectory (Cavagna, 1976). This potential energy is then exchanged for kinetic energy before the transition to the double support phase. This discovery of a predictable mechanical energy-conserving system correlating with the physiological metabolic cost validated the use of IP dynamics to emulate bipedal gait. The human body can then be modeled as a point mass equivalent to the body's total mass, standing atop a massless supporting stance leg, which is itself connected to the ground via a pivot point representing the foot (Figure 4). During gait, the human COM slowly rises at the initiation of the first half of the stance phase and begins to accelerate at its descent during the second half of the phase (Thorstensson, 1984), emulating the kinematic behavior of an IP. With the pendular model's gait resemblance and ability to predict fluctuations between kinetic and potential energy during the single-support phases of gait (Cavagna, 1976), its performance as a minimal biped has been compared with experimental data to evaluate potential correlations for accurate walking predictions (Whittlesey, 2000) (Buczek, 2006) (McGrath, 2015), and has inspired other simple models to replicate human gait for clinical applications.

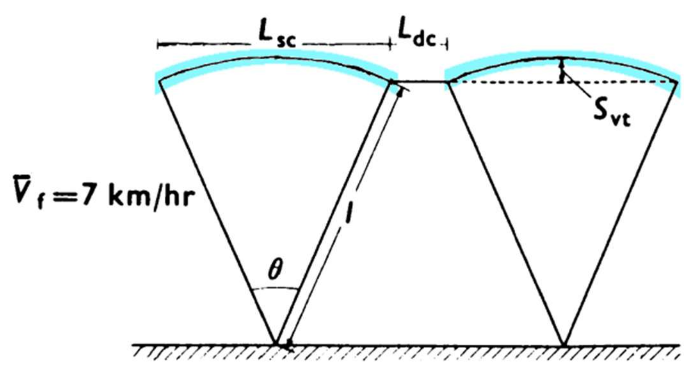

Figure 4. Stiff-legged inverted pendulum (Cavagna, 1976). The blue curve indicates the proposed trajectory for the center of mass.

However, simplifying gait mechanics has its limitations. One of the obvious weaknesses of the IP model is the exclusion of the swing leg and its possible contributions in the contralateral limb's vertical ground reaction forces (GRF). Additionally, stiff-legged mechanics fails to mimic the natural behavior of multi-joint human walking since it negates the contribution of joints and behavioral characteristics of muscles performing the motion. Multi-linked legs was a potential solution to addressing the shortcomings of the IP.

To this end, Mochon & McMahon (1980) developed an extension of the pioneering model with a double IP including the knee flexion that occurs during the contralateral leg swing to potentially describe a force lifting the COM in its pendular trajectory. Accompanying the stance leg and a point mass at the hip joint that represents the trunk, head, and arms of the body, this variation includes a compounded IP suspended from the hip to pivot at the knee and a second one attaching the foot from the knee, and the system is actuated by torques instead of muscles (Figure 5.a.). Additionally, Mochon & McMahon (1980) revised their model by replicating the swing leg to also encompass two links in the stance leg (Figure 5.b.). Supplementing the knee flexion attempts to explain an upward force that lifts the COM against gravity to revise the vertical GRF simulated by the IP (Mochon & McMahon, 1980). This model was used to describe the swing phase of gait as "ballistic," similar to a projectile motion, and highlighted that the dynamics of the swing leg under the influence of gravity was the missing culprit for improving kinematic simulations of gait (Mochon & McMahon, 1980). Despite addressing several of the IP's weaknesses, the double IP proposed by Mochon & McMahon (1980) was unable to reproduce realistic vertical GRF. Later studies that simulated normal walking with a simple IP model found that the contralateral leg muscles contribute less than 15% of the effective limb's vertical GRF, suggesting that the primary mechanism driving vertical movements is the single-supporting leg (Anderson & Pandy, 2003). Thus, the inclusion of the swing leg in the double IP failed to ameliorate vertical GRF gait simulations.

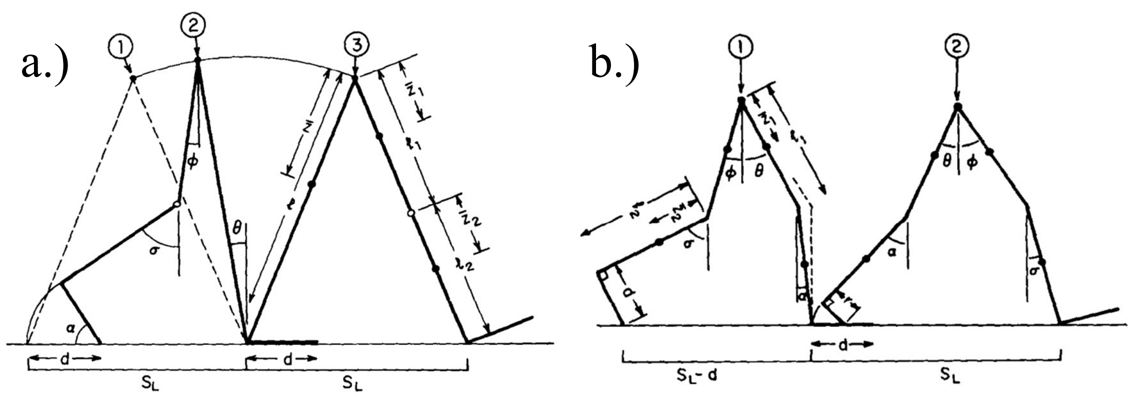

Figure 5. Double inverted pendulums with segments for knee flexion and swing leg. (Mochon & Mahon 1980).

The pendulum analogy describing human walking originated upon the assumption that the leg swing during walking is unforced (Baker, 2007), which motivated the two-legged model from Mochon & McMahon (1980). This suggestion generalized the swing-phase joint moments to be negligible (Whittlesey, 2000) (Baker, 2007), and early electromyographic lower limb data suggests that minimal muscular activity occurs during the swing phase (Alexander, 1995) (McGeer, 1990). Due to the body's tendency to adapt with efficient metabolic physiology, the IP predicts no energy expenditure or necessary net mechanical work to perform the motion under the assumption that muscular activity is negligible. However, assuming a passive movement negates muscular control and contradicts the metabolic demands found in empirical walking (Endo, 2014), and the fact that substantial energy is necessary to lift the body's COM against gravity (Neptune, 2004). Anderson & Pandy (2003) utilized the IP model to investigate muscle contributions during walking and managed to produce vertical GRF that showed some resemblance with empirical force data. Muscles are expected to generate a force that can maintain a straight leg during the single support phase, so the simple gait models exploiting stiff-legged mechanics are insufficient.

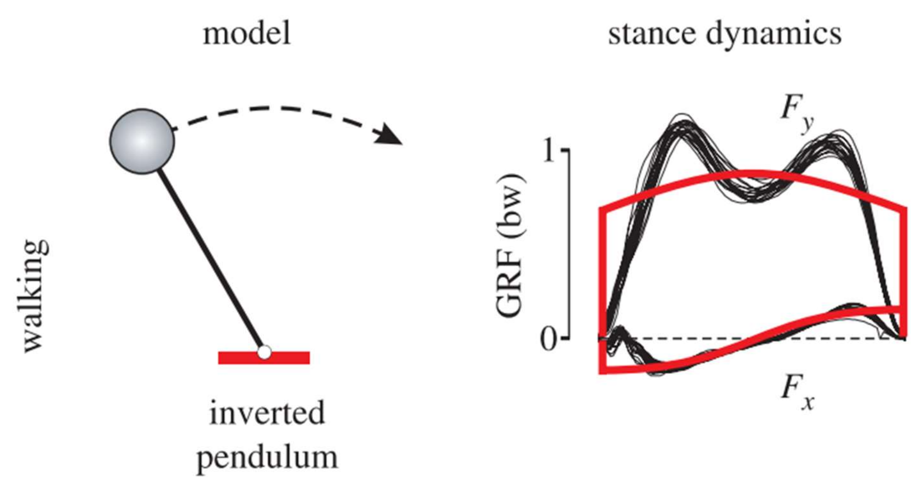

Figure 6. Vertical GRF graph produced by inverted pendulum models. (Geyer, 2006).

The IP model produced a force curve with two minima (Mochon & McMahon, 1980) (Buczek, 2006) (Pandy, 2003) (McGrath, 2015), thus failing to predict the characteristic double maxima pattern of measured vertical GRF (Figure 6) (Pandy, 2003) (McGrath, 2015).

2.5.b. Spring-loaded inverted pendulum

Mochon & McMahon (1980) proposed that the stiff-legged IP model is missing a component that drives human gait mechanics, and Anderson & Pandy (2003) revealed that muscles generating forces drive the vertical movements during walking and supplement the deficient forces that the stiff-legged model is unable to detect. Muscle contributions in walking have been suggested to account for 50-95% of the vertical GRF generated during the stance phase (Anderson & Pandy, 2003). However, muscle-based models are highly multivariate, complicate causation relations between parameters, and require optimizations that are often computationally expensive (Pandy, 2003). Including the range of motion of joints caused by muscle-tendon contraction relations in modeling has been shown to improve simulations of vertical kinematics (Pandy, 2003) (Endo, 2014), and studies have found that compliant legs explain the rebounding that follows the lower limb vaulting motion during running and walking (Buczek, 2006) (Geyer, 2006) (Jung & Park, 2014). To achieve similar mechanics while maintaining simplicity, a massless spring is portrayed at the knee joint to supplement the stiff leg (Figure 7) (Geyer, 2006) (Whittington & Thelen, 2009) (Antoniak, 2019). This spring-loaded model was originally only applied to running, but since the contraction of the quadriceps exhibit the same concentric and eccentric behavior in walking (Alexander, 1995), and the knee exhibits a slight bend that changes the initial length of the leg (Minetti & Alexander, 1997), the spring analogy has been widely used for simulating gait.

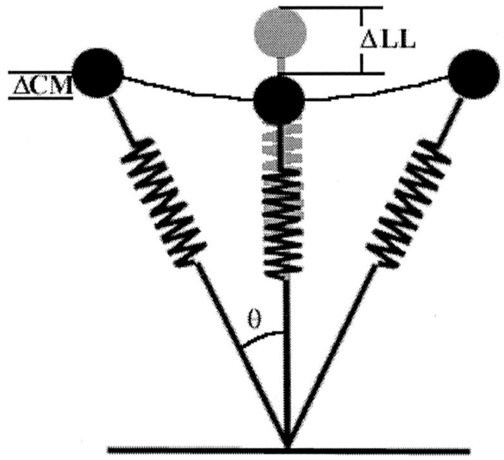

Figure 7. Spring-loaded inverted pendulum (Dutto & Smith, 2002).

The spring-loaded inverted pendulum (SLIP) model demonstrates the oscillatory behavior of a biped COM and reproduces a mechanism that suggests an altered leg length during the single support phase (Geyer 2006) (Hong, 2013) (Jung & Park, 2014). The success of SLIP models to emulate the effective leg during the single support phase of gait (Dutto & Smith 2002) inspired the development of a double SLIP (DSLIP) model to address the double support phases and step-to-step transitioning during gait (Whittington & Thelen, 2009) (Jung & Park, 2014) (Ryu & Park, 2018). However, only limited locomotion speed ranges are feasible to yield quantitative results, and the duration of the stance phase that constitutes to the ipsilateral vertical GRF is inaccurately simulated in comparison to empirically observed data (Geyer, 2006). Additionally, demonstrating both legs as springs with the GRF directly pointing at the COM has been shown to be deficient, and gravitational force further needs an opposing component, so the addition of tangential forces with the torque at a modeled is used to improve simulated features of locomotion (Figure 8) (Biswas, 2018).

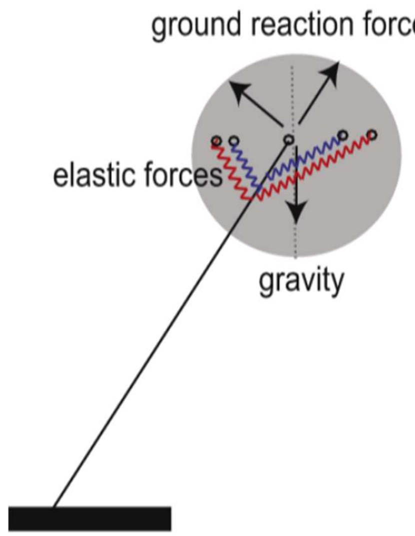

Figure 8. Angular spring-modulated inverted pendulum (Biswas, 2002). Model includes forces tangent to the center of mass trajectory.

This study utilizes the angular radial spring-loaded inverted pendulum (ARSLIP) model (Figure 9) developed to improve the accuracy of dynamic ground reaction forces by accounting for angular kinematics of the lower extremity during gait (Antoniak, 2019). The ARSLIP model intends to include restorative forces during single-limb support to allow for directional changes at midstance. Antoniak et al. (2019) found that the stance leg performs a contraction-expansion-contraction-expansion cycle during single-support, which increases the phase duration and resolves the deficiencies from traditional SLIP-inspired models. The leg angle and position dynamics of the ARSLIP model are similar to the SLIP model but with the inclusion of the angular spring stiffness (k_a) of the leg that resists motion away from the neutral vertical position (Antoniak, 2019).

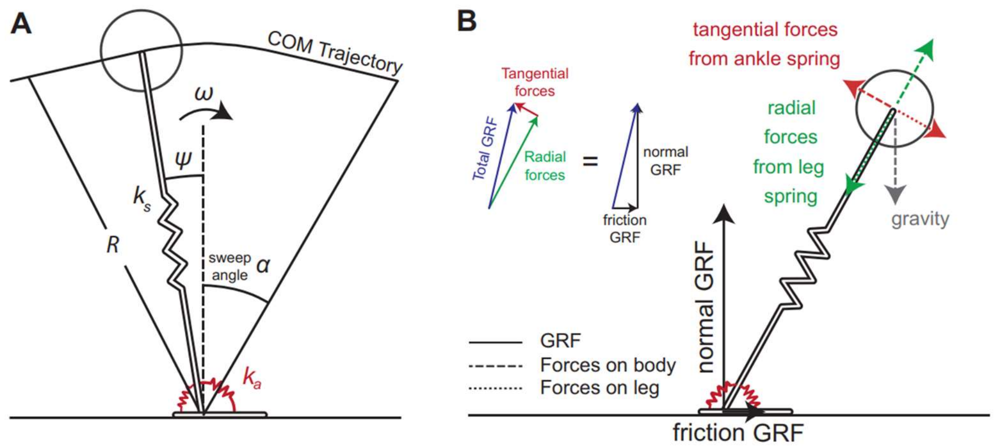

Figure 9. Angular radial spring-loaded inverted pendulum (Antoniak, 2019).

Although both the SLIP and ARSLIP models can predict the characteristic double maxima curve of experimental vertical GRF, the latter improves the root mean square error of the median data by a factor of 2.4 (Antoniak, 2019). Thus, the ARSLIP model is a simple model that yields accurate-enough vertical GRF for this study.

CHAPTER III

METHODS

3.1. Experimental data

Experimental data were collected during a previous study (Ekanayake, 2019), which included twenty males (age: 21.9 ± 1.8 years) and 20 females (age: 21.9 ± 1.2 years) without a previous diagnosis of OA, history of any lower limb surgeries, and existing cardiac conditions. Subjects were instrumented with twenty-six motion analysis markers and walked barefoot at a self-selected speed on an instrumented treadmill (Noraxon, Scottsdale, AZ, USA) for ten minutes, while plantar pressure distributions and kinematics were recorded. The variables used for the current study were the left and right vertical ground reaction forces (vGRF). Forces were filtered using a 5^{th} order Butterworth filter with a cut-off frequency of 20 Hz (Ryu 2018) and were then used to define the single stance phase of each step (starting with a right step) and compute single stance intervals (Figure 10). For each step, the corresponding vGRF curve was cropped to the single stance phase and linearly interpolated between 0 and 100% of this phase. Thus, for each step, the inputs used in the simulations were the interpolated vGRF curve (101 data points) and the single stance interval (1 data point).

In addition, the simulations required the subject's height ($height\ [m]$), mass ($mass\ [kg]$), and the self-selected gait speed ($speed\ [\frac{m}{s}]$).

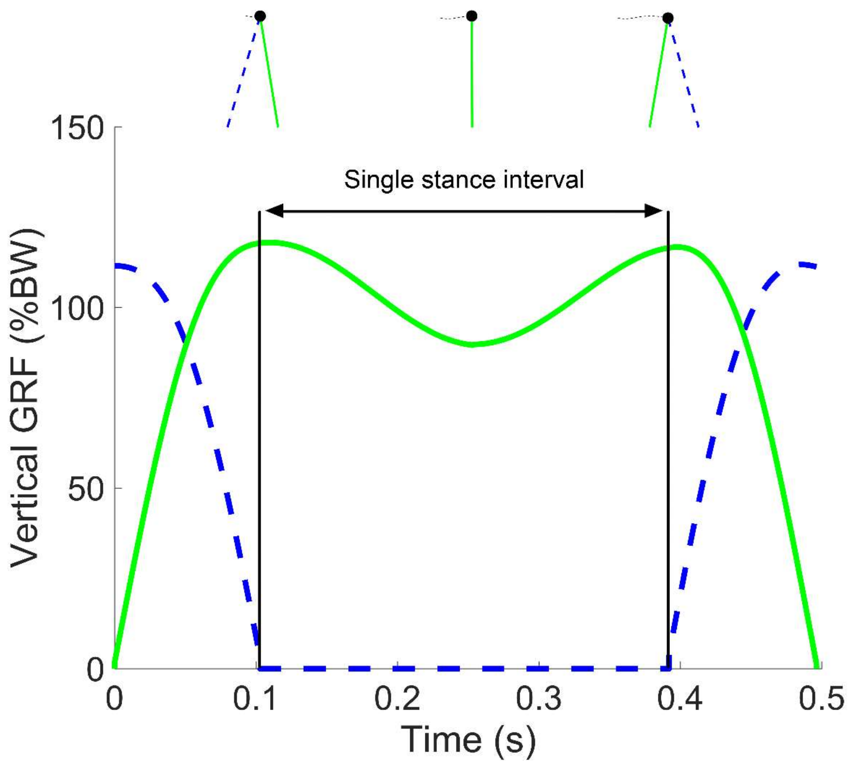

Figure 10. Single stance phase definition based on the vertical GRF measured, expressed as a percentage of the body weight (%BW).

3.2. Spring-mass model

Since the angular and radial spring-loaded pendulum (ARSLIP) model can simulate the characteristic double maxima of expected vGRF (Antoniak, 2019), the corresponding equations were implemented in MATLAB (MathWorks, Natick MA, USA) for the single-support phase modeled by ARSLIP; the differential equations are defined as:

$$\ddot{\psi} = \frac{g}{L}\sin\psi - \frac{k_a}{mL^2}\psi - 2\frac{\dot{L}\dot{\psi}}{L}$$

$$\ddot{L} = L\dot{\psi}^2 - \mathrm{g}\cos\psi + \frac{k}{m}(L_0 - L)$$

where $\psi(t)$ $[rad]$ is the angle of the stance leg from the vertical, L_0 $[m]$ is the uncompressed leg length (resting spring length), and $L(t)[m]$ is the instantaneous effective leg length, m $[kg]$ is the mass of the subject , k_a $[\frac{Nm}{rad}]$ is the angular spring stiffness, k $[\frac{N}{m}]$ is the leg spring stiffness, and $g = 9.807$ $\left[\frac{m}{s^2}\right]$ is the constant acceleration of gravity (Figure 11).

The initial conditions $L(0)$, $\dot{L}(0)$, $\psi(0)$, and $\dot{\psi}(0)$ at the beginning of the single stance (t = 0) are unknown.

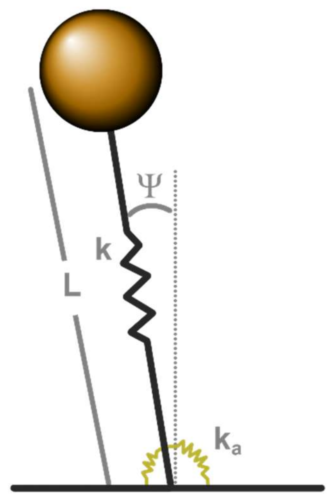

Figure 11. ARSLIP model with linear and angular springs, representing the leg and ankle actions, respectively.

The vertical ground reaction force F_y is then computed based on the force developed in the linear and rotational springs:

$$F_y = k(L - L_0)\cos\psi + k_a \frac{\psi}{L} \sin\psi$$

3.3. Optimizations

The approach implemented is outlined in Figure 12 for each step. Six parameters were optimized: the four initial conditions ($L(0)$, $\dot{L}(0)$, $\psi(0)$, and $\dot{\psi}(0)$), and the two spring stiffnesses

(k and k_a). The goal of the optimization was to fit the experimental vGRF curve during the single stance phase.

The parameters were optimized using MATLAB's patternsearch algorithm (MathWorks, Natick MA, USA). Ranges for each parameter are given in Table 1.

Table 1. Parameter ranges used for optimization. The theoretical leg length was defined as: $l_0 = 0.57 * height$ (Ryu 2018) and the theoretical leg stiffness was defined as $k_0 = 40 * mass * \frac{g}{heigh} * speed$.

Name	Range	Unit
Initial leg length $L(0)$	$[0.7\ 1.0] * l_0$	m
Initial leg velocity $\dot{L}(0)$	$[-1.0\ 1.0] * speed$	m/s
Initial leg angle $\psi(0)$	$[-0.7854 \quad -0.0873]$	rad
Initial leg angle velocity $\dot{\psi}(0)$	$[0\ 5] * speed/l_0$	rad/s
Leg stiffness k	$[0\ 5.0] * k_0$	N/m
Ankle stiffness k_a	$[0\ 0.5] * k_0$	Nm/rad

The objective function defining the fitness F of a potential solution was defined as the root mean square error between the simulated (F_y) and measured ($vGRF$) vGRF curves, after linearly interpolating F_y between 0 and 100% of the single stance phase to match the input vGRF format (101 data points):

$$F = \sqrt{\frac{1}{101}\sum_{n=1}^{101}\left(F_{y,n} - vGRF_n\right)^2}$$

The "patternsearch" algorithm increments each initial input parameter individually by a mesh size of 1 and then increases by a multiple of 2 with each successful iteration; the algorithm seeks the smallest objective value from a predefined function to proceed to the subsequent iteration with the new parameters at the next intended mesh size (Figure 13). If an iteration fails to yield a fitness value that is smaller than the previous, then the previous parameters that generated the current lowest objective function value will be used and the mesh size will be halved for the next iteration.

The “patternsearch” algorithm will advance until ending conditions are satisfied, as this will be the least summed error between the experimental force data points and the ARSLIP model produced vGRF at the respective percent of the gait cycle. Constraints for the mesh tolerance, number of iterations, and number of times the function is called were established to be 10^{-6}, 10^{3} x initial leg length, and 36000 respectively. If any ending conditions are met, then the algorithm is complete and returns the optimized output parameters with its respective input.

A minimized fitness value will indicate that the given parameters following an optimization cycle have computed parametric vGRF comparable to the experimental data.

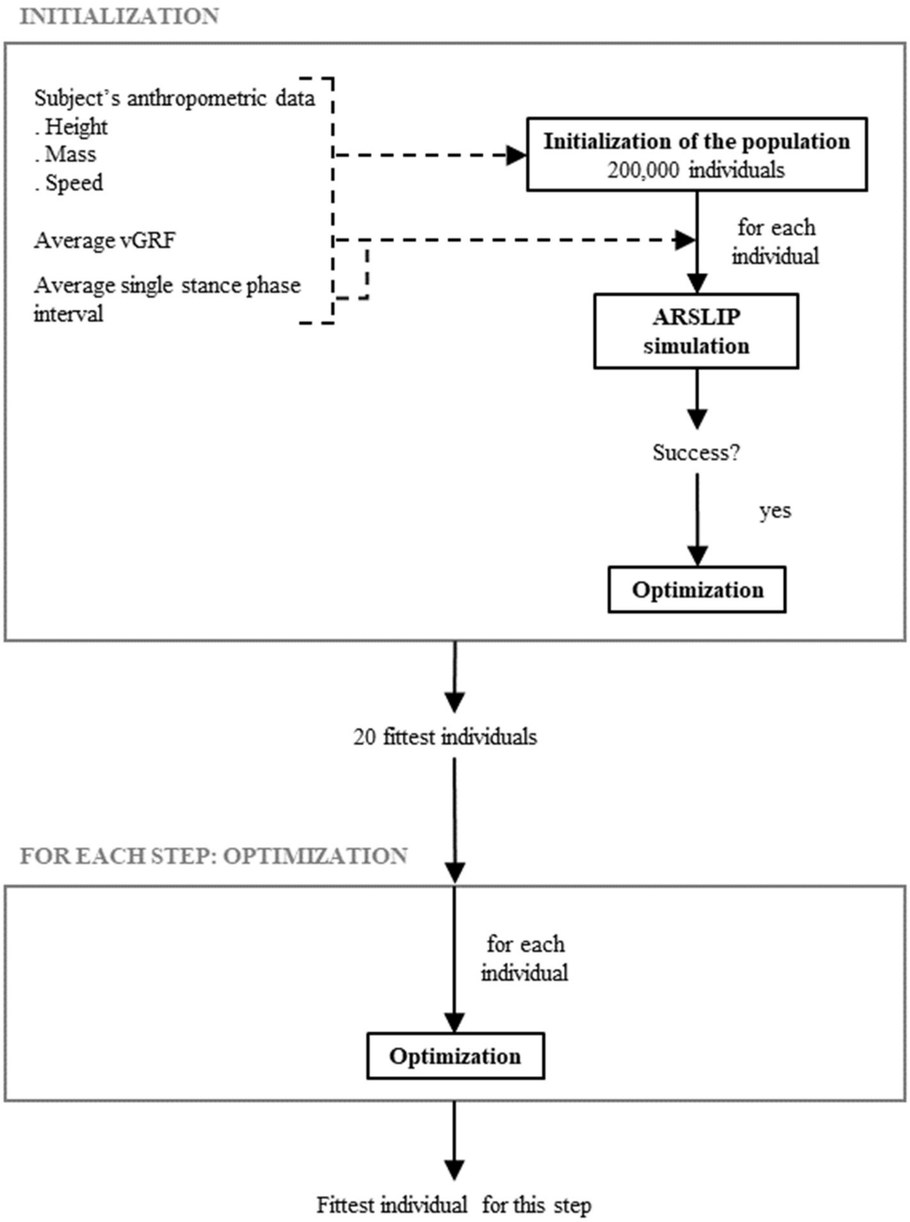

Figure 12. Overall approach implemented to optimize the leg and ankle stiffnesses of the ARSLIP model (Antoniak, 2019) for each step.

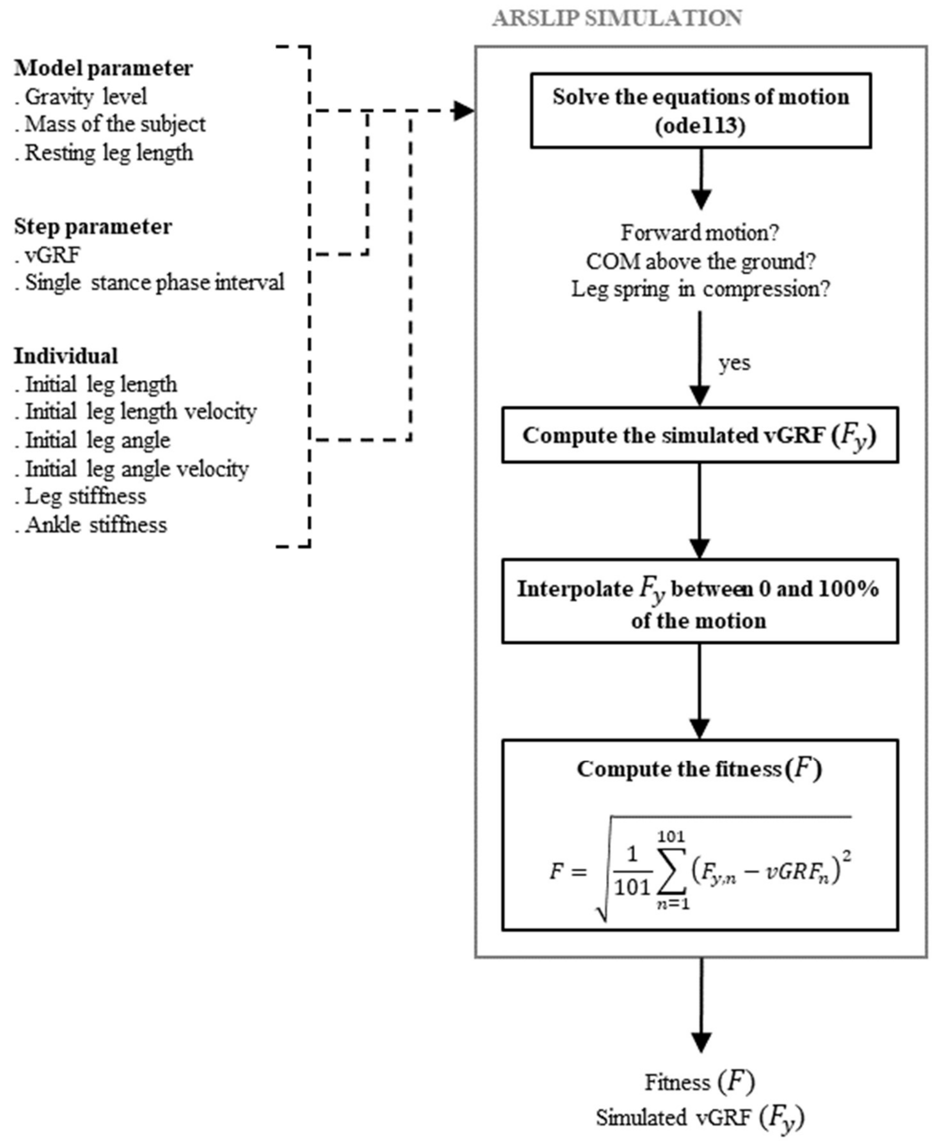

Figure 13. Schematic of the ARSLIP simulation for each step, leading to the assessment of the fitness value.

3.4. Post processing

For each subject, the 300 consecutive steps leading to the lowest average fitness value were selected for further analysis.

3.4.a. Speed correlations

Linear regression was performed between speed with the average leg and ankle stiffnesses in JMP Pro 15 (JMP®, Version 15. SAS Institute Inc., Cary, NC, 1989–2021) to assess relations and trends between variables and plotted in MATLAB (MathWorks, Natick MA, USA).

3.4.b. Gait symmetry

Gait symmetry was assessed using the averaged Normalized Symmetry Index (NSI) (Queen 2000), where a low NSI represents a more symmetrical gait. Given two time series $\{X_{n,right}\ and\ X_{n,left} \quad n = 1, \dots, 150\}$ of 300 consecutive right and left steps, the averaged NSI is computed as:

$$NSI = \frac{1}{150} * \sum_{n=1}^{150} \frac{X_{n,right} - X_{n,left}}{max_{n=1:150}\left(max\ (0, X_{n,right}\ , X_{n,left}\right) - min_{n=1:150}\left(min\ (0, X_{n,right}\ , X_{n,left}\right)} * 100$$

3.4.c. Gait regularity

Gait regularity was assessed using Sample Entropy (SampEn) (Richman & Moorman, 2000), where a low value shows that a parameter has a high degree of regularity and a large SampEn per respective variable will indicate a small chance of similar data within the set being repeated. With $m = 2$ as the embedding dimension, tolerance $r = 0.2$, and N as the total number of points in the time series, SampEn can be calculated as:

$$SampEn(m, r, N) = -\ln\left(\frac{\sum_{i=1}^{N-m} A_i}{\sum_{i=1}^{N-m} B_i}\right)$$

where A is the number of matches of length $(m + 1)$ and B is the number of matches of length m.

3.4.d. Gait variability

Gait variability was assessed using the coefficient of variation (CV) of the leg and ankle stiffnesses calculated as:

$$CV = \frac{s}{\bar{x}} * 100$$

where s is the standard deviation of the sample data and $\bar{x}$ is the sample average.

3.5. Statistical analysis

Statistical analysis was performed in JMP Pro 15 (JMP®, Version 15. SAS Institute Inc., Cary, NC, 1989–2021) and used to determine the effects of BMI and gender on gait symmetry, regularity, and variability. It was also used to assess differences in BMI between categories and genders. Two sample t-tests or pooled two-sample t-tests were used to determine statistically significant averages in BMI between genders and BMI categories (BMI < 25 and BMI ≥ 25) depending on if they had unequal variances since all of those distributions met normality assumptions. All comparison groups were independent samples. To test for differences between average values, two sample t-tests were used depending on assumptions of normality in data distribution and unequal variances, Wilcoxon Man Whitney test was used upon nonparametric data distributions with equal variances, and pooled two-sample t-tests were used for data with drastically dissimilar sample sizes with normally distributed data and equal variances. The level of significance was set to $p < 0.05$.

CHAPTER IV

RESULTS

4.1. Optimization results

Optimizing the six parameters specified in 3.3. to be implemented in the ARSLIP model (Antoniak, 2019), described in 3.2., produced individual vGRF per each step of subjects with fitness values 1-50% of the experimental data (Figure 14). The leg stiffness and ankle stiffness values averaged to be 11.28 ± 6.73 kN/m and 0.70 ± 0.35 kNm/rad, respectively (Table 2).

Table 2. Average leg and ankle stiffnesses. n represents the number of subjects considered.

Name	n	Average ± Standard deviation	Unit
Leg stiffness	40	11.28 ± 6.73	kN/m
Ankle stiffness	40	0.70 ± 0.35	kNm/rad

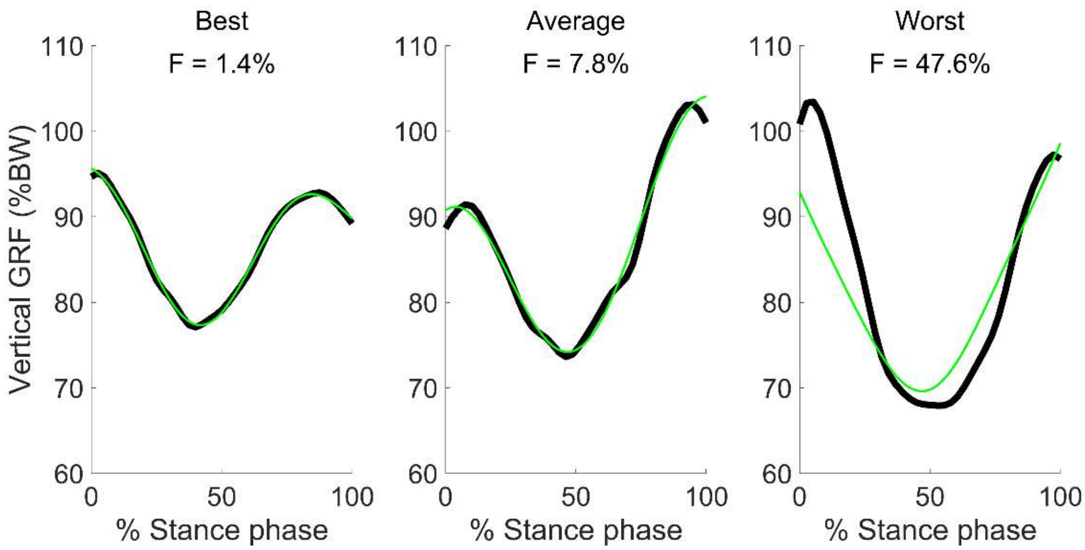

Figure 14. The best, average, and worst curve fits (green) of the experimental vGRF (black), where F is the corresponding fitness value.

4.2. Subjects

4.2.a. BMI

BMI averages among subjects per each comparative group have been assessed for significant differences as described in 3.5. Overall results are summarized in Table 3.

Table 3. Average BMI of subjects in each comparative category. n represents the number of subjects considered.

Gender	BMI	n	Average BMI ± Standard deviation (kg/m^2)
-	<25	26	22.03 ± 2.00
-	≥25	14	27.99 ± 3.05
F	<25	15	21.73 ± 2.20
F	≥25	5	26.62 ± 0.96
M	<25	11	22.45 ± 1.72
M	≥25	9	28.74 ± 3.58

The twenty-six subjects with a BMI less than 25 kg/m^2 had an average BMI of 22.03 ± 2.00 kg/m^2, and the fourteen subjects with a BMI of at least 25 kg/m^2 or greater had an average

BMI of 27.99 ± 3.05 kg/m^2. There was a significant difference of the average BMI values between the two BMI groups (p = <0.0001).

Fifteen female subjects with a BMI less than 25 kg/m^2 had an average BMI of 21.73 ± 2.20 kg/m^2. Five female subjects with a BMI of at least 25 kg/m^2 or greater had an average BMI of 26.62 ± 0.96 kg/m^2. There was a significant difference of the average BMI values between the two female BMI groups (p = <0.0001).

Eleven male subjects with a BMI less than 25 kg/m^2 had an average BMI of 22.45 ± 1.72 kg/m^2. Nine male subjects with a BMI of at least 25 kg/m^2 or greater had an average BMI of 28.74 ± 3.58 kg/m^2. There was a significant difference of the average BMI values between the two female BMI groups (p = <0.0005).

There were no significant differences in average BMI between males and females of the less than 25 kg/m^2 BMI group nor with the 25 kg/m^2 or larger BMI group.

4.3. Speed effects

Effects of subjects' self-selected walking speed and with their BMI were plotted to assess potential correlations (Figure 15). R^2 for the data was 0.0.

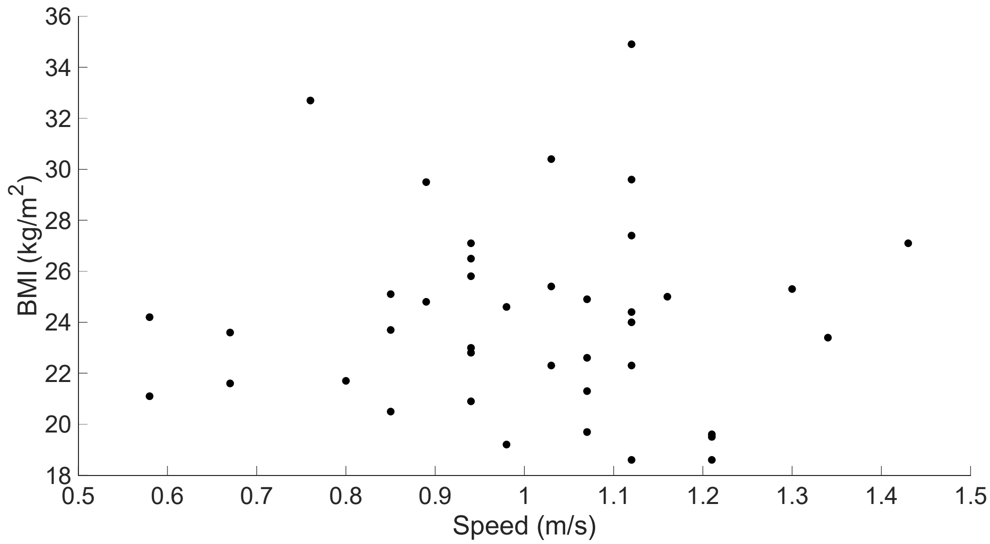

Figure 15. BMI versus gait speed for each subject.

Effects of subjects' self-selected walking speed and their heights were plotted to assess potential correlations (Figure 16). The correlation coefficient (R^2) between height and speed was 0.009, highlighting there was no correlation between these two parameters.

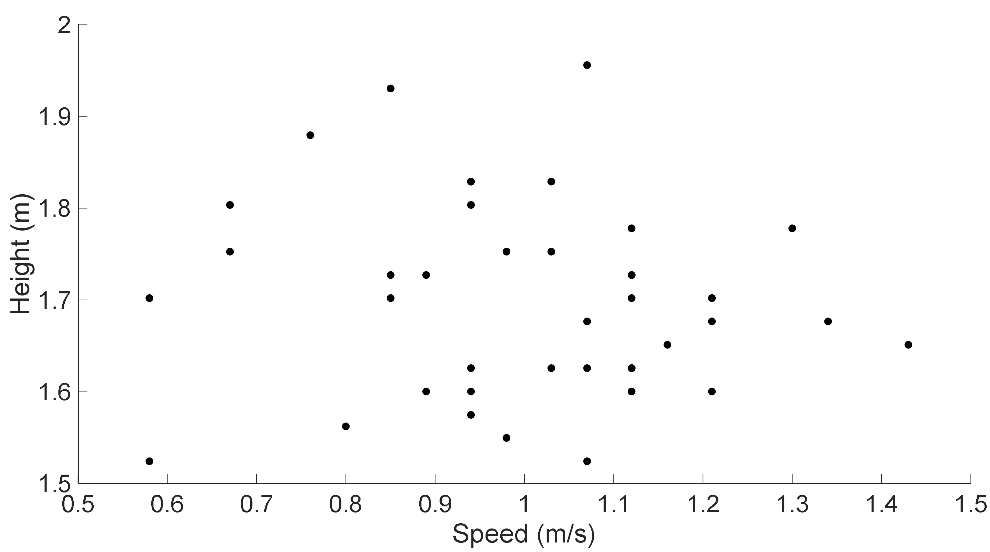

Figure 16. Height versus gait speed for each subject.

Effects of speed on the leg and ankle stiffnesses were plotted to assess potential relationships (Figure 17). The correlation coefficient (R^2) between average leg and ankle stiffnesses with speed was less than 0.2, highlighting there was no correlation between these parameters.

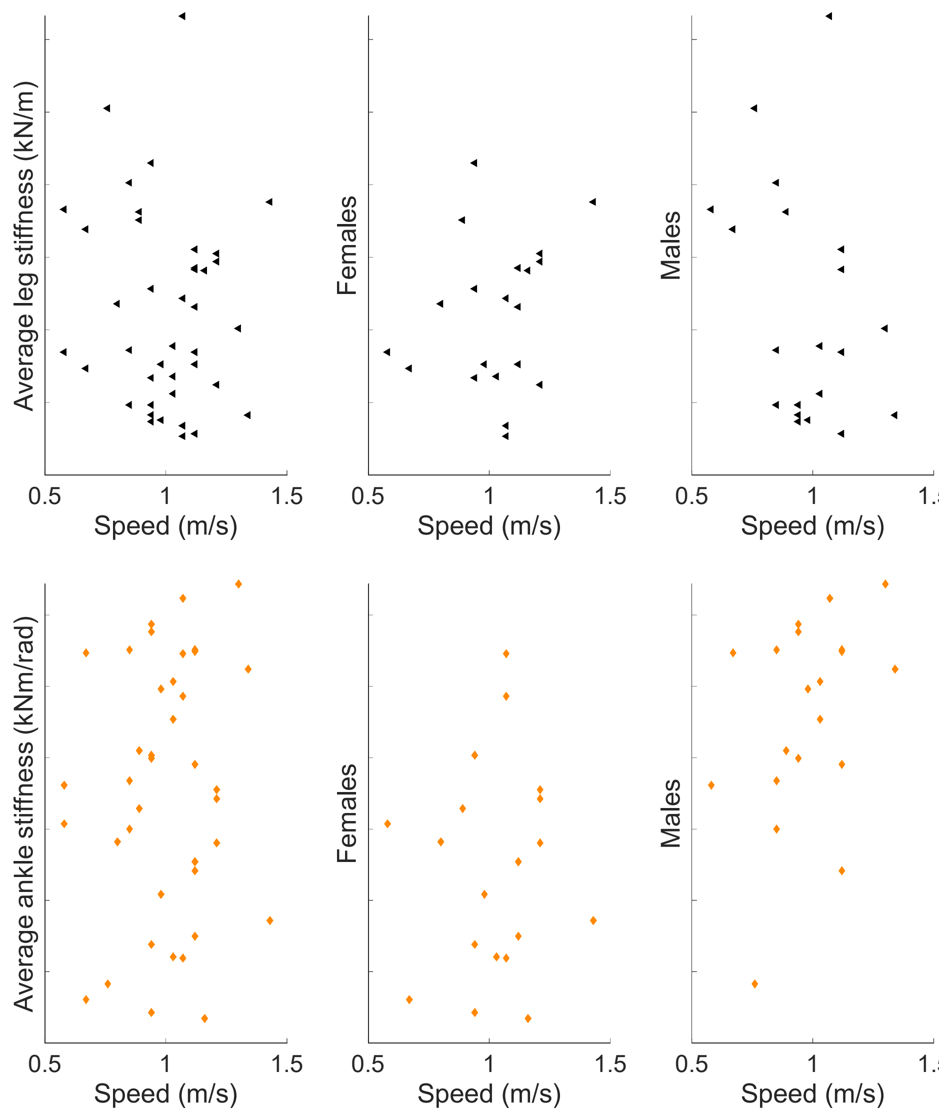

Figure 17. Average leg stiffness versus gait speed (top) and average ankle stiffness versus walking speed (bottom): all participants (left), females (middle), males (right).

Effects of speed on the NSI of the leg and ankle stiffnesses were plotted to assess potential relationships (Figure 18). The correlation coefficient (R^2) between the NSI of the leg and ankle stiffnesses with speed was less than 0.075, highlighting there was no correlation between these parameters.

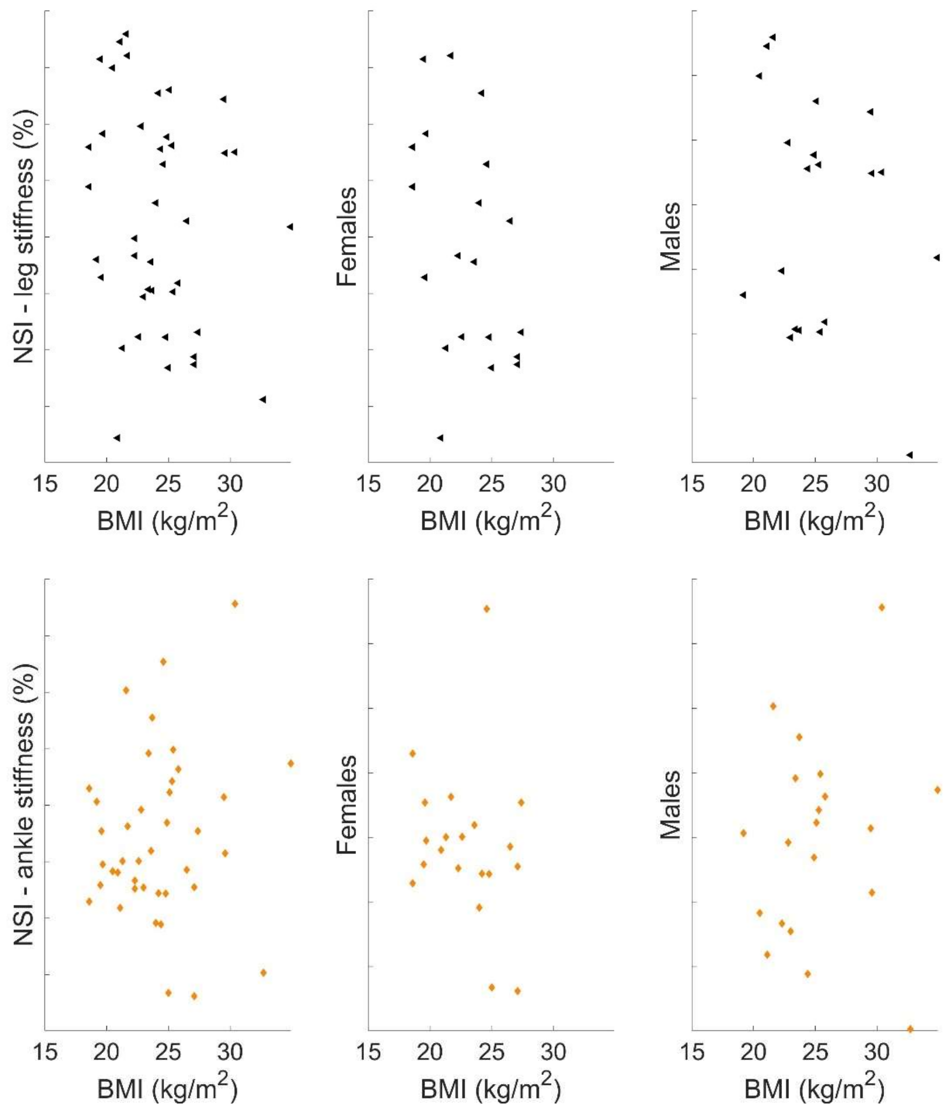

Figure 18. NSI of the leg stiffness versus gait speed (top) and NSI of the ankle stiffness versus walking speed (bottom): all participants (left), females (middle), males (right).

Effects of speed on the SampEn of the leg and ankle stiffnesses were plotted to assess potential relationships (Figure 19). The correlation coefficient (R^2) between the SampEn of the leg and ankle stiffnesses with speed was less than 0.1, highlighting there was no correlation between these parameters.

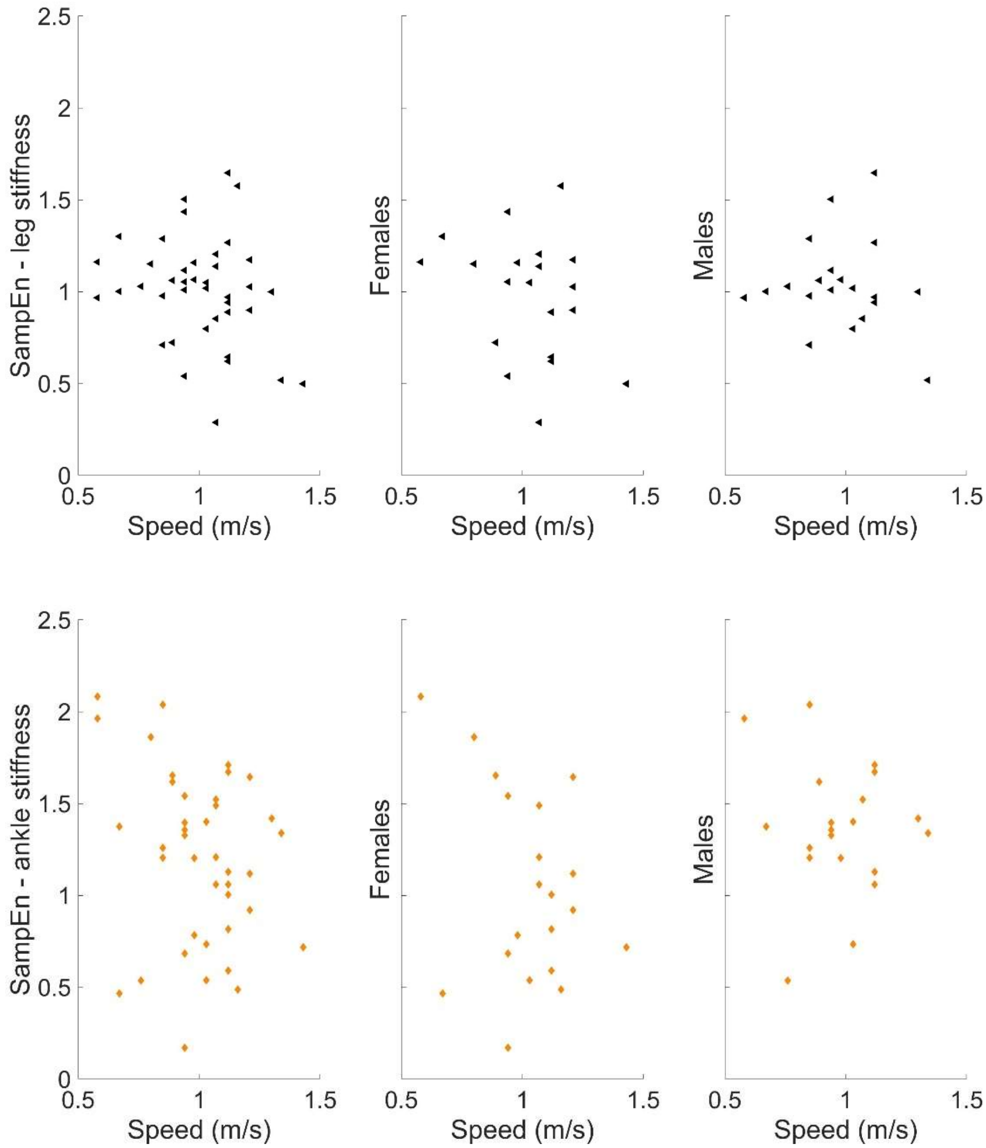

Figure 19. SampEn of the leg stiffness versus gait speed (top) and SampEn of the ankle stiffness versus walking speed (bottom): all participants (left), females (middle), males (right).

Effects of speed on the CV of the leg and ankle stiffnesses were plotted to assess potential relationships (Figure 20). The correlation coefficient (R^2) between the CV of the leg and ankle stiffnesses with speed was less than 0.2, highlighting there was no correlation between these parameters.

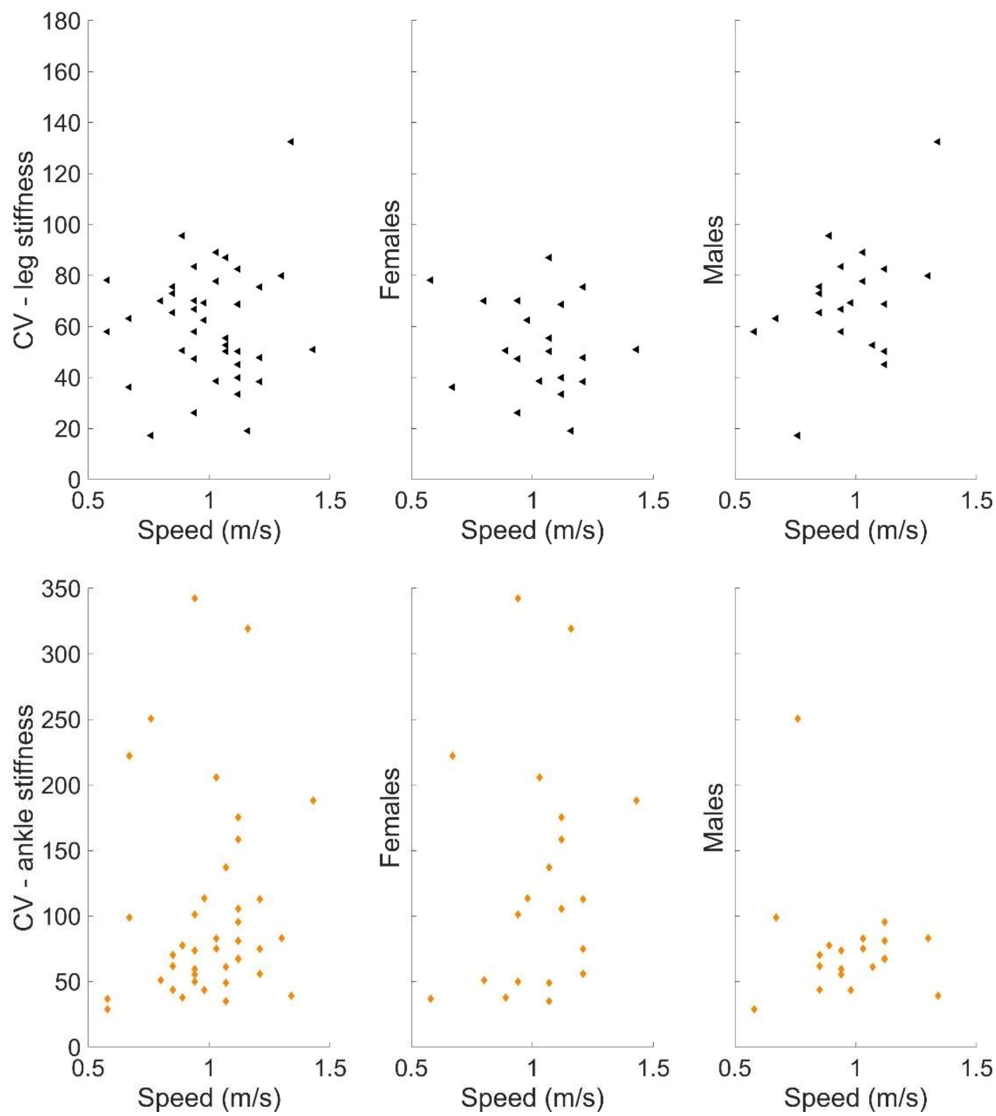

Figure 20. CV of the leg stiffness versus gait speed (top) and CV of the ankle stiffness versus walking speed (bottom): all participants (left), females (middle), males (right).

4.4. Gait symmetry

Gait symmetry for the leg and ankle stiffnesses among subjects has been assessed using the Normalized Symmetry Index (NSI) as described in 3.4.b. Overall results are summarized in Tables 4 and 5.

Table 4. Normalized Symmetry Index (NSI) for leg stiffness. n represents the number of subjects for each category considered.

Gender	BMI	n	Average NSI ± Standard deviation (%)
-	-	40	26.69 ± 9.76
F	-	20	24.10 ± 10.03
M	-	20	29.28 ± 8.99
-	<25	26	28.17 ± 9.74
-	≥25	14	23.94 ± 9.52
F	<25	15	26.51 ± 10.15
F	≥25	5	16.88 ± 5.46
M	<25	11	30.44 ± 9.12
M	≥25	9	27.86 ± 9.15

Table 5. Normalized Symmetry Index (NSI) for ankle stiffness. n represents the number of subjects for each category considered.

Gender	BMI	n	Average NSI ± Standard deviation (%)
-	-	40	22.06 ± 7.42
F	-	20	19.34 ± 6.18
M	-	20	24.79 ± 7.69
-	<25	26	21.81 ± 6.20
-	≥25	14	22.54 ± 9.53
F	<25	15	20.71 ± 5.58
F	≥25	5	15.23 ± 6.65
M	<25	11	23.03 ± 6.95
M	≥25	9	26.60 ± 8.57

4.4.a. Gender effect

Female subjects had an average NSI for leg stiffness of 24.10 ± 10.03 % and an average NSI for ankle stiffness of 19.34 ± 6.18 %. Male subjects had an average NSI for leg stiffness of 29.28 ± 8.99 % and an average NSI for ankle stiffness of 24.79 ± 7.69 % (Figure 18). Males had a significantly higher average NSI for leg stiffness (p = 0.047) and for ankle stiffness (p = 0.016) in comparison to females.

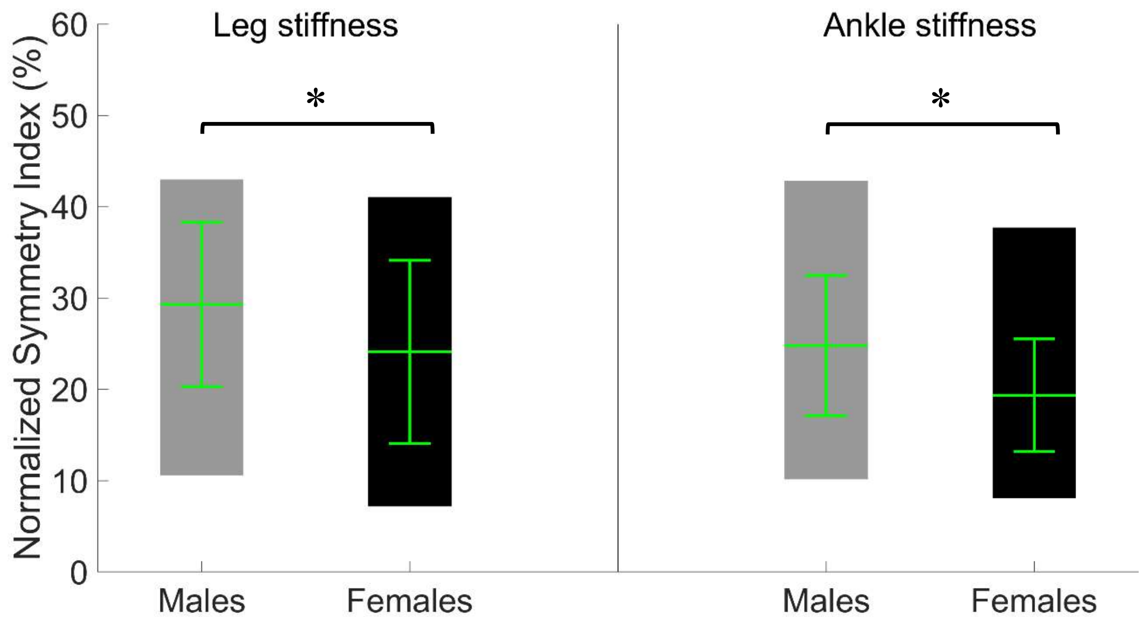

Figure 18. NSI for the leg and ankle stiffnesses for males and females. The filled areas represent the range, the horizontal green lines represent the average, and the whiskers represent one standard deviation. An asterisk highlights a significant difference.

4.4.b. BMI effect

Results are shown on Figures 19 and 20. Overall, twenty-six subjects with a BMI less than 25 kg/m^2 had an average NSI for leg stiffness of 28.17 ± 9.74 % and an average NSI for ankle stiffness of 21.81 ± 6.20 %. Fourteen subjects with a BMI of at least 25 kg/m^2 or greater had an average NSI for leg stiffness of 23.94 ± 9.52 % and an average NSI for ankle stiffness of

22.54 ± 9.53 %. There was no significant difference of the average NSI values between the two BMI groups.

Fifteen female subjects with a BMI less than 25 kg/m^2 had an average NSI for leg stiffness of 26.51 ± 10.15 % and an average NSI for ankle stiffness of 20.71 ± 5.58 %. Five female subjects with a BMI of at least 25 kg/m^2 or greater had an average NSI for leg stiffness of 16.88 ± 5.46 % and an average NSI for ankle stiffness of 15.23 ± 6.65 %. Females with a BMI less than 25 kg/m^2 had a significantly larger average NSI for leg stiffness ($p = 0.031$) in comparison to females with a higher BMI, and there was no significant difference in average NSI for ankle stiffness between the BMI groups of females.

Eleven male subjects with a BMI less than 25 kg/m^2 had an average NSI for leg stiffness of 30.44 ± 9.12 % and an average NSI for the ankle stiffness of 23.03 ± 6.95 %. Nine male subjects with a BMI of at least 25 kg/m^2 or greater had an average NSI for leg stiffness of 27.86 ± 9.15 % and an average NSI for ankle stiffness of 26.60 ± 8.57 %. There was no statistically significant difference in average NSI for leg stiffness and for ankle stiffness among males between the BMI groups.

Males with a BMI of at least 25 kg/m2 or greater had a higher average NSI for the leg stiffness than their female counterparts ($p = 0.016$), but there was no significant difference between the two groups for the average NSI for ankle stiffness. In subjects with a BMI less than 25 kg/m^2, there was no significant difference in the average NSI for leg stiffness and for ankle stiffness between males and females of the

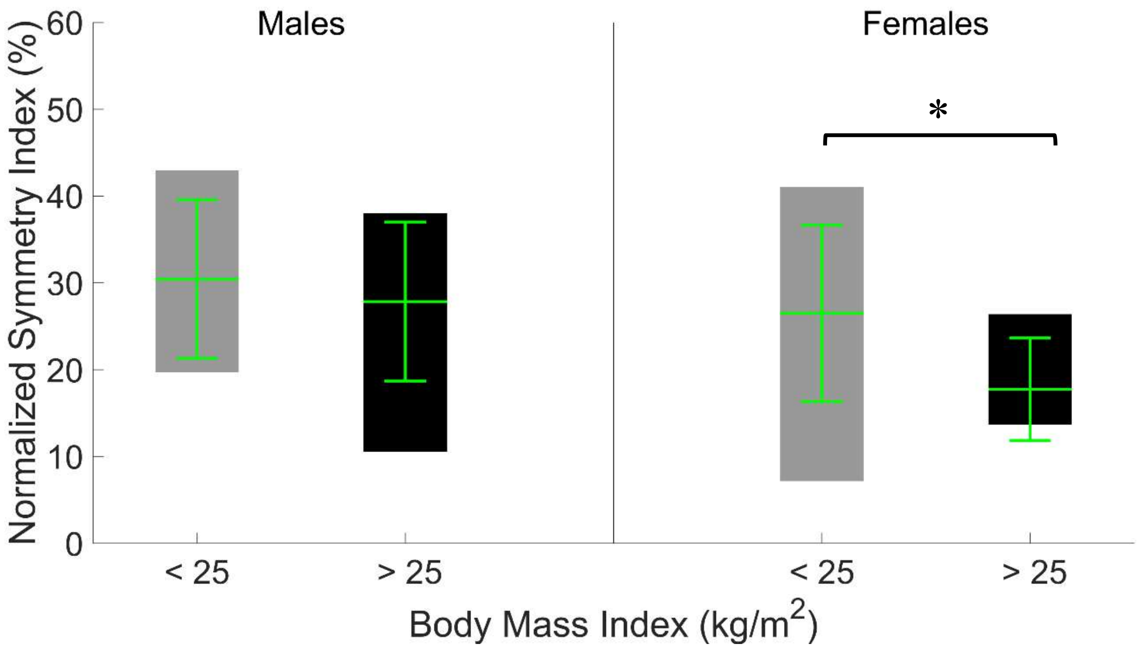

Figure 19. NSI for the leg stiffness for males and females and two BMI categories. The filled areas represent the range, the horizontal green lines represent the average, and the whiskers represent one standard deviation. An asterisk highlights a significant difference.

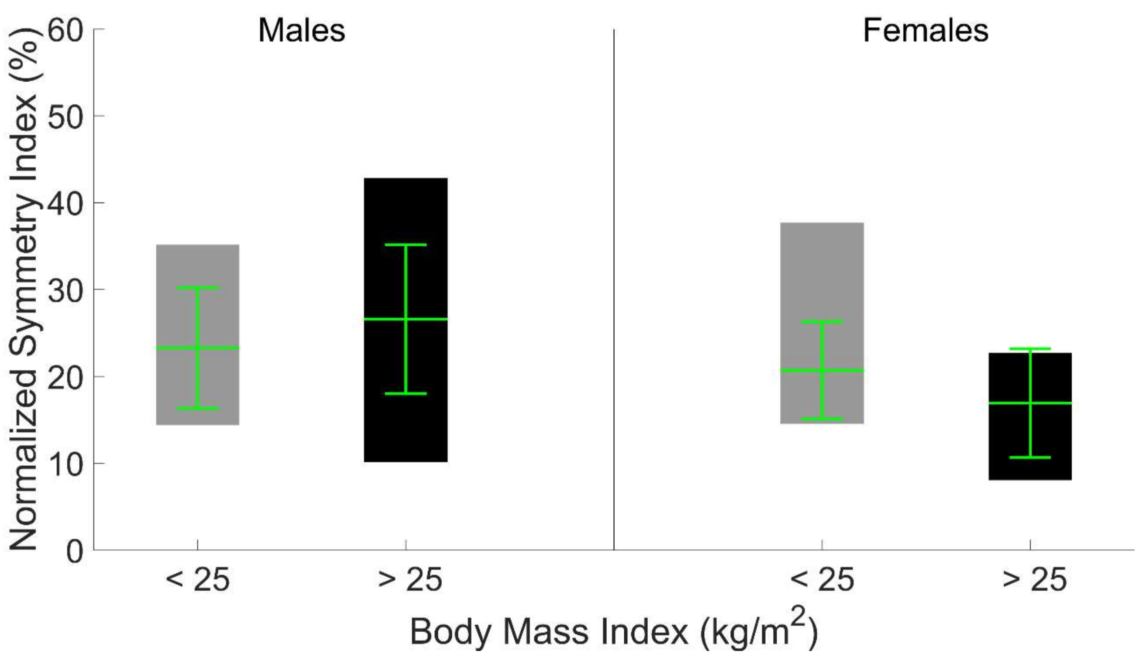

Figure 20. NSI for the ankle stiffness for males and females and two BMI categories. The filled areas represent the range, the horizontal green lines represent the average, and the whiskers represent one standard deviation.

4.4.c. Combined BMI and gender effect

There was no significant difference of the average NSI for leg stiffness between males and females with a BMI less than 25 kg/m^2. In subjects with a BMI of at least 25 kg/m^2 or greater, males had a significantly higher average NSI for the leg stiffness than females (p = 0.016).

4.5. Gait regularity/complexity

Gait regularity for the leg and ankle stiffnesses among subjects has been assessed using Sample Entropy as described in 3.4.c. Overall results are summarized in Tables 6 and 7.

Table 6. Sample Entropy (SampEn) for leg stiffness. n represents the number of subjects for each category considered.

Gender	BMI	n	Average SampEn ± Standard deviation (%)
-	-	40	1.01 ± 0.29
F	-	20	0.98 ± 0.33
M	-	20	1.04 ± 0.25
-	<25	26	1.01 ± 0.28
-	≥25	14	1.00 ± 0.33
F	<25	15	1.02 ± 0.29
F	≥25	5	0.86 ± 0.46
M	<25	11	1.01 ± 0.27
M	≥25	9	1.07 ± 0.23

Table 7. Sample Entropy (SampEn) for ankle stiffness. n represents the number of subjects for each category considered.

Gender	BMI	n	Average SampEn ± Standard deviation (%)
-	-	40	1.20 ± 0.47
F	-	20	1.04 ± 0.52
M	-	20	1.36 ± 0.36
-	<25	26	1.33 ± 0.43
-	≥25	14	0.98 ± 0.48
F	<25	15	1.21 ± 0.48
F	≥25	5	0.53 ± 0.22
M	<25	11	1.48 ± 0.30
M	≥25	9	1.22 ± 0.39

4.5.a. Gender effect

Female subjects had an average Sample Entropy for the leg stiffness of 0.98 ± 0.33 and an average Sample Entropy for ankle stiffness of 1.04 ± 0.52. Male subjects had an average Sample Entropy for leg stiffness of 1.04 ± 0.25 and an average Sample Entropy for ankle stiffness of 1.36 ± 0.36 (Figure 21). There was no significant difference between the average Sample Entropy for the leg stiffness between genders, but males had a significantly higher average Sample Entropy for ankle stiffness ($p = 0.039$) in comparison to females.

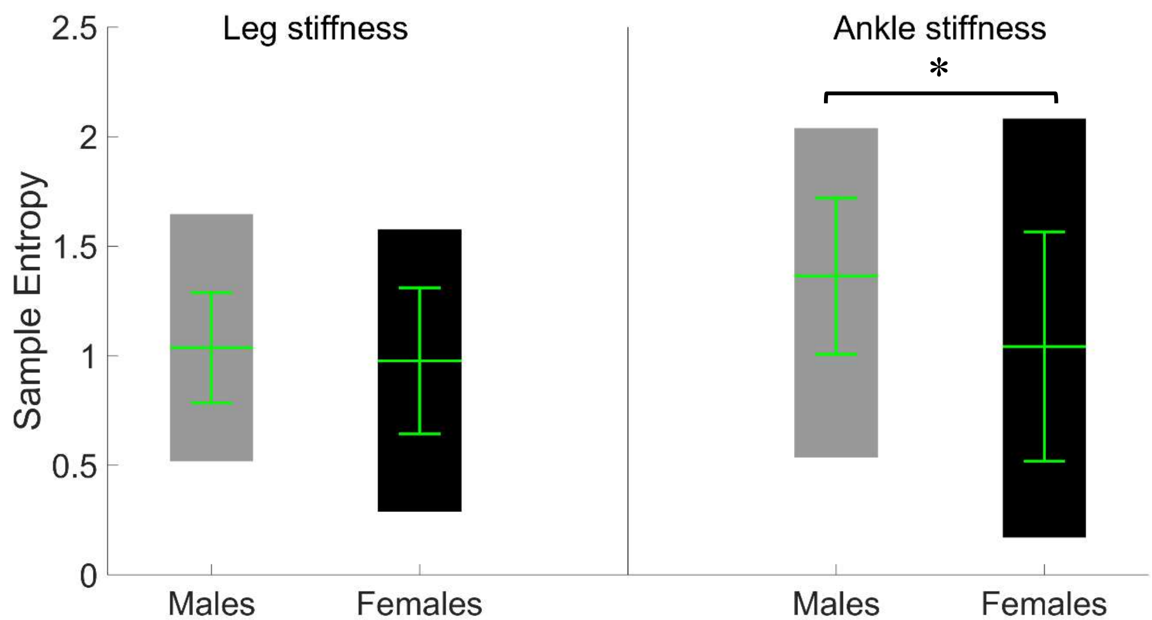

Figure 21. Sample Entropy for the leg and ankle stiffnesses for males and females. The filled areas represent the range, the horizontal green lines represent the average, and the whiskers represent one standard deviation. An asterisk highlights a significant difference.

4.5.b. BMI effect

Results are shown on Figures 22 and 23. Overall, twenty-six subjects with a BMI less than 25 kg/m^2 had an average Sample Entropy for the leg stiffness of 1.01 ± 0.28 and an average Sample Entropy for the ankle stiffness of 1.33 ± 0.43. Fourteen subjects with a BMI of at least 25 kg/m^2 or greater had an average Sample Entropy for the leg stiffness of 1.00 ± 0.33 and an average Sample Entropy for the ankle stiffness of 0.98 ± 0.48. There was no significant difference between the BMI groups of the average Sample Entropy for the leg stiffness, but subjects with a BMI less than 25 kg/m^2 had a significantly higher average Sample Entropy for the ankle stiffness (p = 0.0156) in comparison to the larger BMI group.

Fifteen female subjects with a BMI less than 25 kg/m^2 had an average Sample Entropy for the leg stiffness of 1.02 ± 0.29. Five female subjects with a BMI of at least 25 kg/m^2 or greater had an average Sample Entropy for the leg stiffness of 0.86 ± 0.46. There was no statistically significant difference in Sample Entropy for the leg stiffness between the BMI groups of females.

Eleven male subjects with a BMI less than 25 kg/m^2 had an average Sample Entropy for the leg stiffness of 1.01 ± 0.27. Nine male subjects with a BMI of at least 25 kg/m^2 or greater had an average Sample Entropy for the leg stiffness of 1.07 ± 0.23. There was no statistically significant difference in Sample Entropy for the leg stiffness between the BMI groups of males.

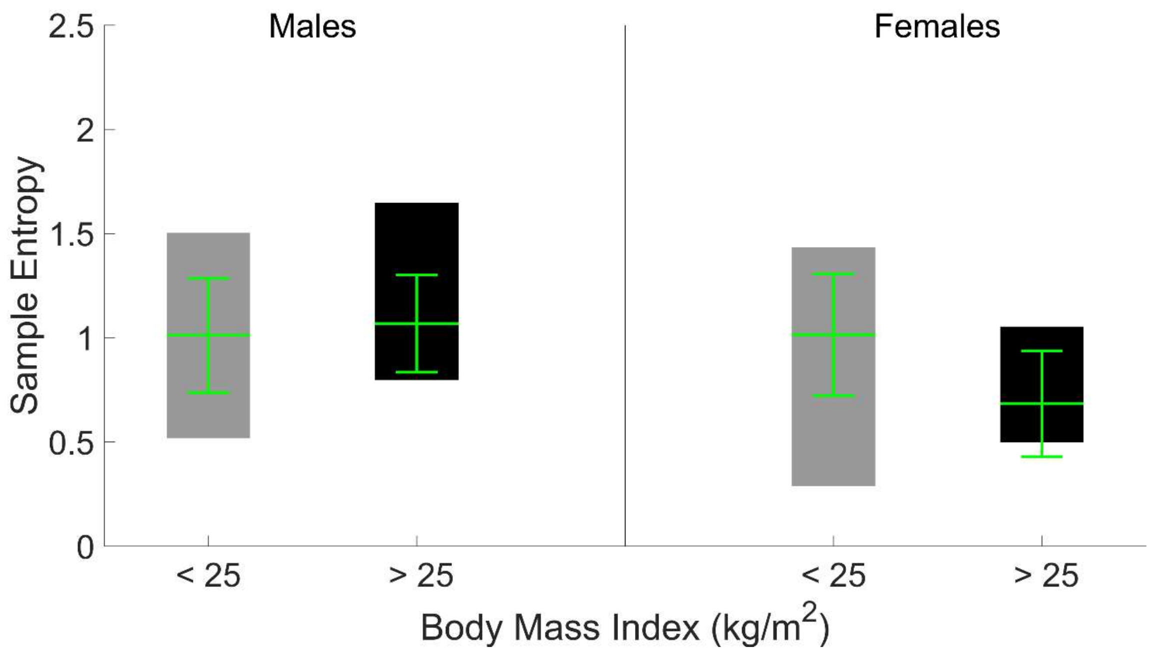

Figure 22. Sample Entropy for the leg stiffness for males and females and two BMI categories. The filled areas represent the range, the horizontal green lines represent the average, and the whiskers represent one standard deviation.

Fifteen female subjects with a BMI less than 25 kg/m^2 had an average Sample Entropy for the ankle stiffness of 1.21 ± 0.48. Five female subjects with a BMI of at least 25 kg/m^2 or greater had an average Sample Entropy for the ankle stiffness of 0.53 ± 0.22. Females with a BMI less than 25 kg/m^2 had a significantly higher average Sample Entropy for the ankle stiffness (p = 0.0003).

Eleven male subjects with a BMI less than 25 kg/m^2 had an average Sample Entropy for the ankle stiffness of 1.48 ± 0.30. Nine male subjects with a BMI of at least 25 kg/m^2 or greater had an average Sample Entropy for the leg stiffness of 1.22 ± 0.39. There was no statistically significant difference in average Sample Entropy for the ankle stiffness between the BMI groups of males.

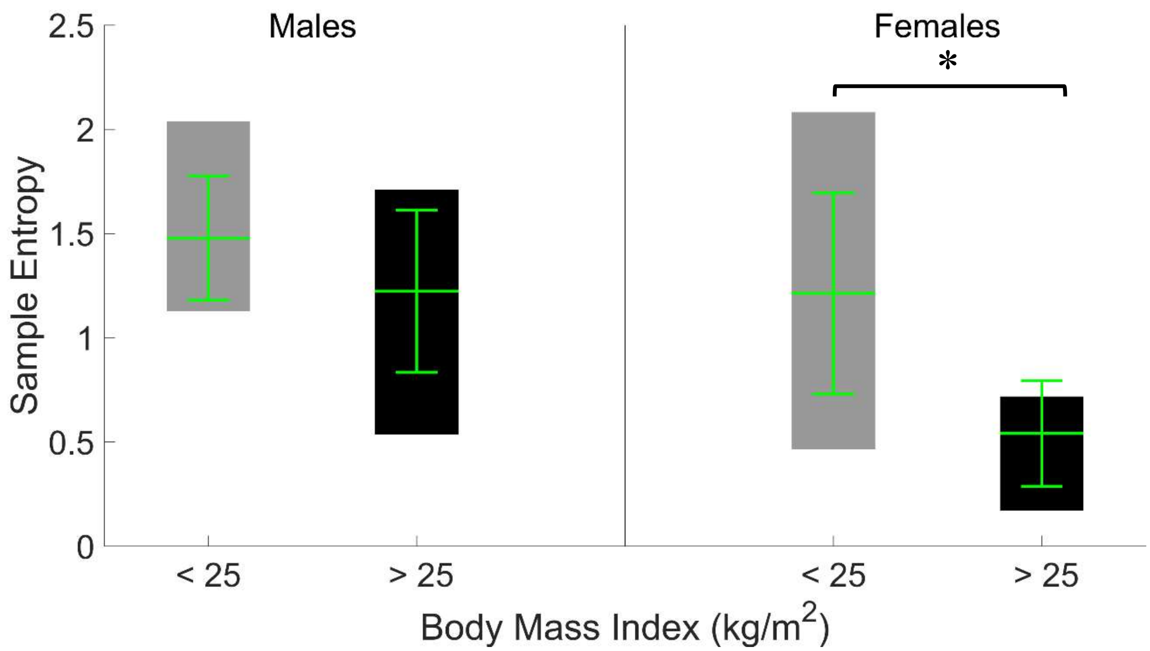

Figure 23. Sample Entropy for the ankle stiffness for males and females and two BMI categories. The filled areas represent the range, the horizontal green lines represent the average, and the whiskers represent one standard deviation. An asterisk highlights a significant difference.

4.5.c. Combined BMI and gender effect

There was no significant difference in average Sample Entropy for the leg stiffness between males and females with BMI less than 25 kg/m^2 nor with subjects with a BMI of at least 25 kg/m^2 or greater. There was no significant difference in average Sample Entropy for the ankle stiffness between males and females with BMI less than 25 kg/m^2, but with subjects who had a BMI of at least 25 kg/m^2 or greater, males had a significantly higher average Sample Entropy for the ankle stiffness (p = 0.0006) in comparison to females.

4.6. Gait variability

Gait variability for the leg and ankle stiffnesses among subjects has been assessed using the coefficient of variation (CV) and standard deviation as described in 3.4.d. Overall results are summarized in Tables 8 and 9.

Table 8. Coefficient of variation (CV) for leg stiffness. n represents the number of subjects for each category considered.

Gender	BMI	n	Average CV± Standard deviation
-	-	40	61.26 ± 22.39
F	-	20	52.31 ± 18.38
M	-	20	70.21 ± 22.85
-	<25	26	63.30 ± 20.15
-	≥25	14	57.47 ± 26.44
F	<25	15	57.95 ± 16.41
F	≥25	5	35.39 ± 13.60
M	<25	11	70.60 ± 23.16
M	≥25	9	69.73 ± 23.87

Table 9. Coefficient of variation (CV) for ankle stiffness. n represents the number of subjects for each category considered.

Gender	BMI	n	Average CV± Standard deviation
-	-	40	102.26 ± 75.72
F	-	20	128.64 ± 91.00
M	-	20	75.87 ± 44.99
-	<25	26	83.33 ± 51.20
-	≥25	14	137.39 ± 100.58
F	<25	15	99.83 ± 60.32
F	≥25	5	215.04 ± 118.99
M	<25	11	60.84 ± 22.25
M	≥25	9	94.25 ± 59.13

4.6.a. Gender effect

Twenty female subjects had an average CV for leg stiffness of 52.31 ± 18.38 and an average CV for ankle stiffness of 128.64 ± 91.00. Twenty male subjects had an average CV for leg stiffness of 70.21 ± 22.85 and an average CV for ankle stiffness of 75.87 ± 42.99 (Figure 24). Males had a significantly higher average CV for leg stiffness ($p = 0.0049$) in comparison to females, but there was no significant difference between genders in average CV for ankle stiffness.

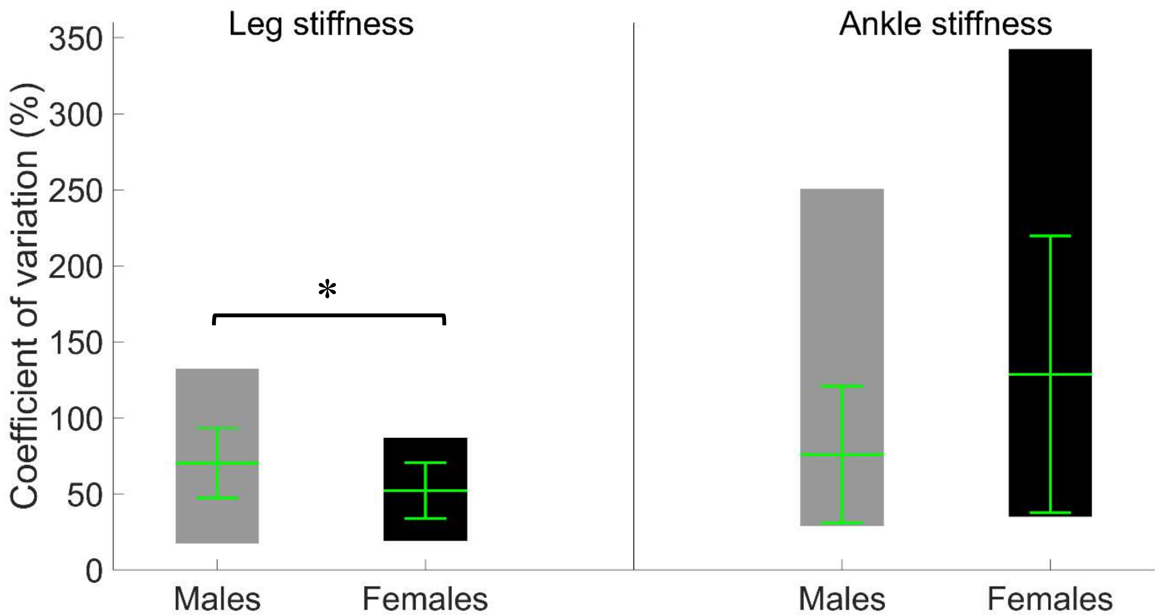

Figure 24. CV for the leg and ankle stiffnesses for males and females. The filled areas represent the range, the horizontal green lines represent the average, and the whiskers represent one standard deviation. An asterisk highlights a significant difference.

4.6.b. BMI effect

Results are shown on Figures 25 and 26. Overall, twenty-six subjects with a BMI less than 25 kg/m^2 had an average CV for the leg stiffness of 63.30 ± 20.15 and an average CV for the ankle stiffness of 83.33 ± 51.20. Fourteen subjects with a BMI of at least 25 kg/m^2 or greater had an average CV for the leg stiffness of 57.47 ± 26.44 and an average CV for the ankle stiffness of 137.39 ± 100.58. There was no significant difference in the average CV for the leg stiffness between the BMI groups.

Fifteen female subjects with a BMI less than 25 kg/m^2 had an average CV for the leg stiffness of 57.95 ± 16.41. Five female subjects with a BMI of at least 25 kg/m^2 or greater had an average CV for the leg stiffness of 35.39 ± 13.60. Females with a BMI less than 25 kg/m^2 had significantly larger average CV for the leg stiffness (p = 0.0065) than the higher BMI group.

Eleven male subjects with a BMI less than 25 kg/m^2 had an average CV for the leg stiffness of 70.60 ± 23.16. Nine male subjects with a BMI of at least 25 kg/m^2 or greater had an average CV for the leg stiffness of 69.73 ± 23.87. There was no statistically significant difference in CV for the leg stiffness between the BMI groups of males.

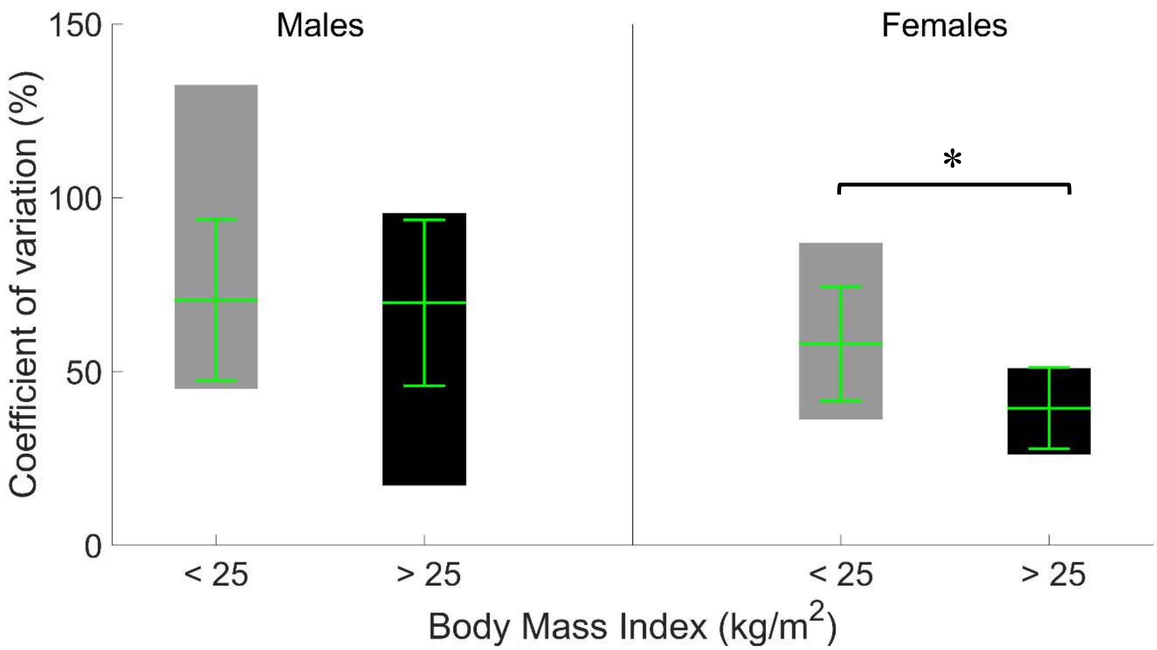

Figure 25. CV for the leg stiffness for males and females and two BMI categories. The filled areas represent the range, the horizontal green lines represent the average, and the whiskers represent one standard deviation. An asterisk highlights a significant difference.

Fifteen female subjects with a BMI less than 25 kg/m^2 had an average CV for the ankle stiffness of 99.83 ± 60.32. Five female subjects with a BMI of at least 25 kg/m^2 or greater had an average CV for the ankle stiffness of 215.04 ± 118.99. Females with a BMI of at least 25 kg/m^2 or higher had significantly larger CV for the ankle stiffness than the lower BMI group (p = 0.0479).

Eleven male subjects with a BMI less than 25 kg/m^2 had an average CV for ankle stiffness of 60.84 ± 22.25. Nine male subjects with a BMI of at least 25 kg/m^2 or greater had an average CV for ankle stiffness of 94.25 ± 59.13. Males with a BMI of at least 25 kg/m^2 or higher had significantly larger average CV for the ankle stiffness than the lower BMI group (p = 0.0402).

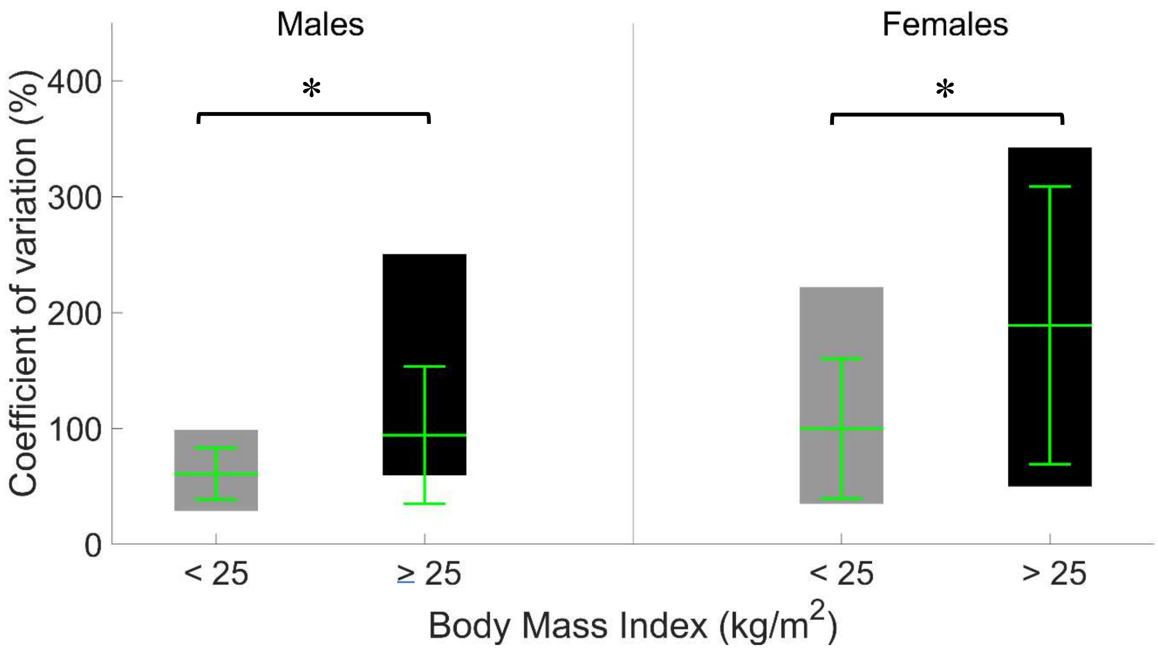

Figure 26. CV for the ankle stiffness for males and females and two BMI categories. The filled areas represent the range, the horizontal green lines represent the average, and the whiskers represent one standard deviation. An asterisk highlights a significant difference.

4.6.c. Combined BMI and gender effect

There was no significant difference in the CV for the leg stiffness between males and females with BMI of at least 25 kg/m^2 or greater, but male subjects with a BMI of at least 25 kg/m^2 or greater had a larger CV for the leg stiffness (p = 0.0063) in comparison to females in this BMI group.

There was no significant difference of the average CV for ankle stiffness between males and females with BMI at least a BMI of 25 kg/m^2 or greater. In subjects with a BMI less than 25 kg/m^2, females had a significantly higher average CV for the ankle stiffness than males (p = 0.0166).

CHAPTER V

DISCUSSION

5.1. Innovation and main findings

The purpose of this study was to investigate a simple mechanical model's capability to assess potential gait imbalances, regularity, and variability and for healthy subjects.

For the first time, to our knowledge, vertical ground reaction force curves for consecutive individual steps were optimized individually, leading to the determination of step-to-step variations in leg and ankle stiffnesses. In addition, step-specific temporal characteristics were preserved, by constraining the simulation time to the experimental stance time measured for each step, ensuring realistic leg and ankle stiffnesses.

The approach implemented, combining the ARSLIP model with an optimization scheme, provided accurate simulated vertical ground reaction forces, thus leading to a reliable assessment of leg and ankle stiffnesses. Stiffness in mechanics defines a relationship between the deformation of a body and a given force. Therefore, stiffnesses in biomechanics are useful to interpret the body's accommodations to tangible stimuli during locomotion by considering the mechanical contributions of joints, muscles, tendons, ligaments, bones, and the limb's general range of motion (Butler, 2003) (Lorimer, 2018). Active stiffness is necessary for performance and can increase the risk of bone or tissue damage when deficient or excessive (Butler, 2003) (Stergiou, 2006) (Brauner, 2014). Evaluating healthy populations' leg and ankle stiffnesses during walking will improve the determination of clinical thresholds of acceptable performance criteria.

Current pre-OA screenings for early detections involve imaging with extensive medical equipment costs. However, Chu et al. (2012) emphasizes the necessity of prompt diagnoses for pre-OA conditions for mitigation of disease onset. One of our primary objectives was to contribute to current noninvasive clinical tools to assess the risk of OA onset through evaluations of walking symmetry, regularity, and variability. Our results highlighted than even healthy subjects exhibited some degree of side-to-side asymmetry regarding both the leg and ankle stiffnesses, as well as irregularities and variability. Furthermore, the simple spring mass model with the optimization scheme can detect the idiosyncratic walking patterns in healthy young people. We expected inter-subject variability, and Figures 27 and 28 show that the approach implemented can capture the unique combinations reflective of the level of symmetry and chaos for the leg and ankle stiffnesses in each subject, which can offer insights on individualistic gait strategies.

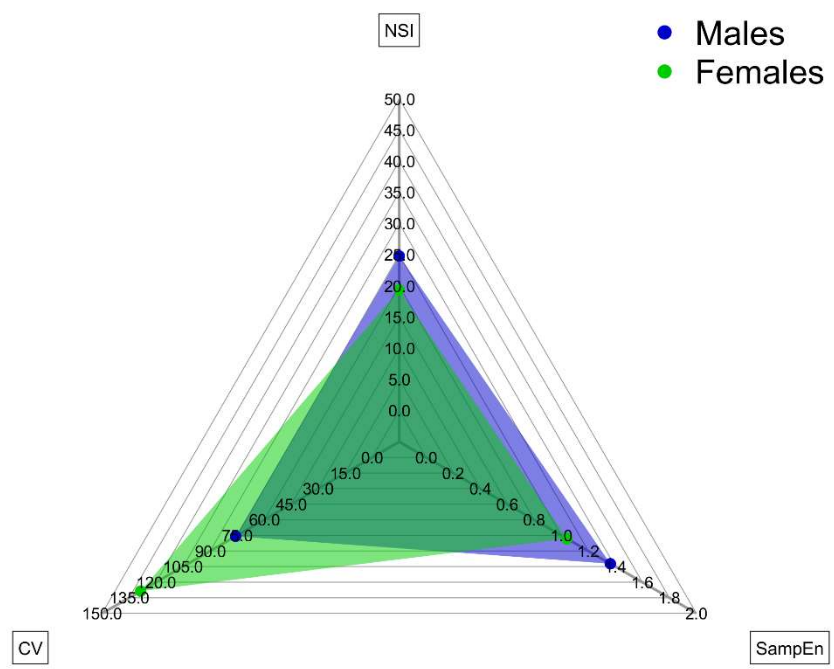

Figure 27. Spider plot of the ankle stiffness's characteristics averaged by gender.

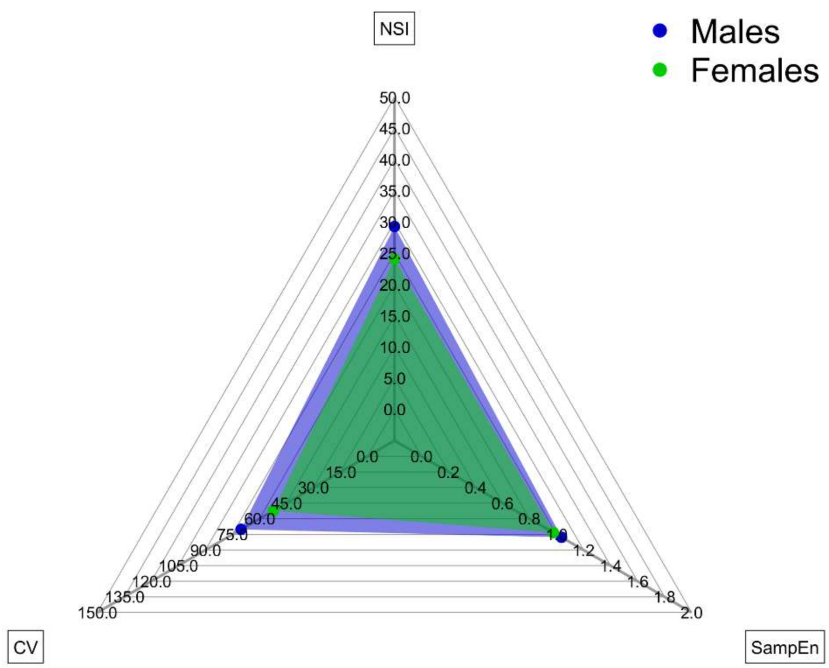

Figure 28. Spider plot of the leg stiffness's characteristics averaged by gender.

Dissimilar perspectives on gait symmetry exist in the literature. Some physiotherapy settings rely on side-to-side balances between the left and right limbs for a metric of success of rehabilitation methods (Becker, 1995) (Hesse, 1997) (Patterson, 2012) (Pirker & Katzenschlager, 2017) (Shi, 2018) due to asymmetry's clinical reputation with pathologic behaviors (Kaufman, 2001) (Stergiou, 2004) (Shakoor, 2002) (Nasirzadeh, 2017). However, this may be detrimental. For example, in unilateral prosthetic gait, increased speed is shown to improve overall symmetry in spatiotemporal and kinematic performance, but this could cause kinetic asymmetry which can cause long-term degeneration effects (Nolan, 2003) (Ramakrishnan, 2018). Furthermore, in conjunction with variability theories suggesting its fundamentality in biological systems, interpretations of gait symmetry remain controversial. However, our study investigates healthy young subjects, and our results suggest that some degree of asymmetry in leg stiffness and ankle stiffness is apparent and necessary in able-bodied bipeds to adapt to perturbations that can lead to high joint contact forces if not sufficiently attenuated biomechanically. Consistent with our results, angular changes in the sagittal plane have been found to be bilaterally asymmetric, and the ankle shows the greatest relative asymmetry (Forczek & Staszkiewicz, 2012).

5.2. Gait speed effect

Since gait was performed at self-selected speed, it is necessary to mention any speed effect. Although it is not the primary focus of this study, it can provide insights for the development of future experimental protocols. There was no correlation between subjects' self-selected speed and height or BMI, which suggests that participants may have modified their conventional locomotion behaviors to accommodate walking on a treadmill. Indeed, taller individuals usually choose a faster gait and heavier individuals usually choose a slower gait (Bohannon, 1997) (Browning & Kram, 2007).

5.2.a. Leg stiffness

The average leg stiffness values computed are comparable to values previously suggested in the literature (Geyer, 2006) (Wei, 2009) (Hong, 2013) (Jung & Park, 2014) (Ryu & Park, 2018). While investigating the relationship between gait speed and leg stiffness, Jung & Park (2014) modeled a spring mass model to emulate the center of pressure excursion during stance phase and suggested that faster walking shows a trend with increased leg stiffness up to 1.7 m/s. Similarly, Kim & Park (2011) modified stiffness and damping ratios for their model to emulate experimental ground reaction force data and found that a similar trend between leg stiffness and increased walking speeds. However, both studies only had eight subjects each for comparison of simulated ground reaction force data. The former study participates included seven males and one female, but females have been shown to exhibit lower leg stiffnesses in landing strategies (Granata, 2002) (Padua, 2005), tend to have different muscle mass qualities than men (Lephart, 2002), and are inherently different anatomically (Faber, 2001). Ryu & Park (2018) similarly found that the leg stiffness was a positively correlated function of walking speed with comparative data of 320 trials with eight healthy and young male subjects of relatively similar height and weight. Subjects from this study had relatively similar body mass and height (66.9 ± 7.9 kg, 172.0 ± 5.1 cm) while our male participants had an average weight of 80.1 ± 15.9 kg and average height of 177.7 ± 8.3 cm, so their homogenized sample results may not accommodate to our more diverse population. Additionally, our investigation only consisted of a single, subject-selected gait speed, while Ryu & Park (2018) tested four gait speeds per participant, which may better acclimate the subjects to treadmill walking. Positive correlations between walking speed and leg stiffness are suggested to contribute to more taxing propulsion demands to maintain accelerated locomotion (Kim & Park, 2011). Antoniak et al. (2019) also found consistent trends in leg stiffness and speed. In contrast, a study recent done by Akl et al. (2020) measured the dynamic leg joint stiffness of 27 young and healthy participants of 17 males and 10 females with 3D infrared motion analysis and force plates at various walking speeds and found the leg dynamic stiffness to decrease with increasing walking speeds. This negative correlation presents a similar trend to our data. However, our subject cohort exhibited higher ranges of weights and heights compared to theirs (59.6 ± 3.8 kg, 164.0 ± 3.0 cm), thus challenging direct comparisons. Overall, gait studies have been inconsistent in conclusions regarding the relation between leg stiffness and speed. For example, in running, some studies find that leg stiffness does not change with speed modifications but instead suggest that stride frequencies may require leg stiffness accommodations for altered energy absorption strategies (Farley & González, 1996) (Brughelli & Cronin, 2008).

5.2.b. Ankle stiffness

The authors who proposed the ARSLIP model used in this work found angular spring stiffness to increase with increasing speed, suggesting that the angular spring representing the ankle stability prevents large accelerations during slower locomotion (Antoniak, 2019).

Furthermore, Akl et al. (2020) found an increase in ankle stiffness with increased walking speeds. However, the later study consisted of predominantly males, which do exhibit the positive trend. Ankle stiffness was found to change with speed in athletes running (Arampatzis, 1999) and in elderly females (Collins, 2018) but neither were fully accounted for in the present study. Angular ankle stiffness has shown positive significant correlations with hip and knee stiffness, but none with leg stiffness, suggesting that leg stiffness is not associated with lower limb joint stiffness during eccentric loading (Akl, 2020). Thus, the ankle stiffness was a necessary addition to the model to simulate tangential forces.

5.2.c. Gait symmetry

Speed and the NSI of both the leg and ankle stiffnesses in our study had no significant correlation. An investigation of 20 males with explicit right lower limb dominance measured foot-floor reaction forces during walking found that manipulating horizontal velocity can improve symmetry at higher speeds (Goble, 2003). However, this may be contradictory with the literature that suggests a dichotomy of bilateral limb roles. For example, in gait, the dominant limb performs the propulsive function to control and maintain walking speeds while the contralateral leg is primary supporting stability (Sadeghi, 1997). In contrast, some studies suggest no correlations between velocity and gait related symmetry (Patterson, 2012) (Plotnik, 2013). Plotnik et al. (2013) tested various intentional speed-changing during overground walking to conclude that deliberate modifications in gait speed does not change the amount of present bilateral asymmetry and suggest that phase changing coordination of the legs may be altered through sensory feedback for forward locomotion. Furthermore, a review of 60 papers done by Nasirzadeh et al. (2017) did not show any relations between gait asymmetry and speed in healthy subjects nor in subjects with unilateral limb deficiencies. Our results suggest that the level of bilateral symmetry of the leg stiffness and ankle stiffness may not be primary contributors to speed maintenance strategies in gait.

5.2.d. Gait regularity and variability

Gait regularity and variability of the leg and ankle stiffnesses in our study had no significant correlation with speed. A meta-analysis found trivial correlations of leg stiffness to be highly variable at higher running speeds but has also been shown to remain constant in conditions (Brughelli, 2008). The author also suggests level of fitness to be a necessary evaluation in considering leg stiffness changes (Brughelli, 2008) (Singh, 2017).

Sanchis-Sales et al. (2016) also used self-selected walking speeds from barefoot subjects and found high dynamic ankle stiffness variability occurring when ankle joint flexion speed lowered during late and early midstance, suggesting that ankle stiffness tends to remain constant across different gait speeds. Akl et al. (2020) found positive significant increase in ankle joint stiffness with walking speed. However, they were not constrained by a treadmill for eccentric loading like the present study. Since subjects are walking on a treadmill, variability is reduced (Schmitt, 2021), so perturbations and disturbances that may recruit for more postural strategies for resilience may not need to be recruited for the experimental task. With the constrained speed of the treadmill, there are less needs for the limbs to adjust to velocity changes as in habitual settings.

5.3. Gender effect

Males and females exhibited significantly different leg stiffness and ankle stiffness strategies (Adjei, 2020) (Ryew & Hyun, 2021). Females are at an increased risk of developing OA and lower body injuries, which can be investigated through biomechanical limb representation of the spring stiffness (Butler, 2003). The model implemented in the present study highlighted gender differences in gait symmetry, regularity, and variability.

5.3.a. Gait symmetry

Our results indicate a significant gender effect on gait symmetry. Males exhibited less symmetry than females in both the leg and ankle stiffnesses. Some studies suggest that gender has an insignificant effect on gait symmetry (Auvinet, 2002) (Senden, 2009) (Patterson, 2012). A study done by Forczek & Staszkiewicz (2012) considered a 1 cm bilateral disparity of a subject to classify as asymmetrical and divides their symmetry index into different stages of the gait cycle to demonstrate that males and females exhibit differences in asymmetry in terms of spatiotemporal and angular variables and appears to vary throughout the gait cycle when comparing the performance of the same action between the left and right limbs. Our results are consistent with Kobayashi et al. (2014), who found a gender effect, with females performing more symmetrical locomotion than males. Cimolin et al. (2011) also found no significant differences in spatiotemporal, kinematic, and kinetic parameters between the left and right limbs of their 28 female subjects.

In our present study, males may have exhibited more side-to-side imbalances due to limb dominance. Preferential laterization of the lower limbs in running has been more pronounce in male than in female runners (Pappas, 2015). For example, in soccer, males were more likely to injure the anterior cruciate ligament of their dominant kicking leg, while females were more likely to injure their supporting leg (McGrath, 2015). Females injuring their nondominant leg, even in recreational activities, is a trend in a meta-analysis of functional lower limb dominance done by McGrath et al. (2015). The greater symmetry of female leg and ankle stiffnesses may indicate deficient stability, postural, and shock-absorbing strategies in the nondominant leg due to lack of bilateral diversity for sufficient coordination mechanisms in forward locomotion with inevitable perturbations. Stergiou et al. (2006) suggest that biological systems must be capable in executing a redundant task in multiple ways to promote adaptability to varying stimuli. Therefore, female ambulation may have reduced techniques in replicating repetitive, similar patterned tasks such as walking, which can be biomechanically detrimental and thus increasing joint contact forces upon perturbations. Furthermore, current literature is limited on able-bodied gait symmetry tendencies between genders regarding susceptibility for disease risk, potentially due to the literatures' controversial perspectives towards imbalance.

5.3.b. Gait regularity and variability

Some studies have found no significant gender differences in step-to-step temporal measures of variability (Auvinet, 2002) (Senden, 2009), but our present study found males to walk with more irregularity in the ankle stiffnesses and more variability in the leg stiffness than females. These results are consistent with Kobayashi et al. (2014), who found less uniformity in male walking performance, suggesting females exhibit more predictable gait executions. Less variability in the leg stiffness may reduce the compliancy of the limbs to adjust in energy absorption in highly adaptive walking surfaces and obstacles, and more consistent ankle stiffness may also challenge steadiness in similar situations for females. This may suggest that variable leg and ankle stiffnesses in men are ideal balance control strategies to prevent inconsistencies in another parameter, which may involve lumbar compensation that women may experience. A study investigating chronic low back pain effects on gait variability suggests that greater activations of the lumbar extensors that may exaggerate lumbar spine kinematics during gait can manifest muscular deconditioning or atrophy, potentially contributing to the walking fluctuations (Steele, 2014). Since females exhibit greater pelvic obliquity, which is linearly related to lower lumbar spinal movements during walking (Smith, 2002), and increased range of motion at the lower thoracic spine (Crosbie, 1997), the absence of increased variability in gait to compensate for posterior muscular weakness may contribute to higher contact forces at the joints as an offsetting mechanism. For example, lack of intuitive strategies that comprises in varied movements may increase overuse in localized areas. Thus, gender-specific interventions have been recommended for pelvic and lower limb movement improvements for treating chronic low back pain to mitigate further anatomical detriments (Rahimi, 2020).

5.4. BMI effects

BMI effects may suggest unique gait strategies based on excessive mass in maintaining locomotion. Walking with a load has been shown to increase leg stiffness (Holt, 2003) and modulate ankle stiffness (Hedrick, 2019), and having a BMI greater than 25 kg/m^2 during adulthood has been found to increase the risk of OA (Zheng & Chen, 2015). We compared results of our gait metrics between subjects who had BMI less than 25 kg/m^2 and BMI equal to or greater than 25 kg/m^2 since excessive weight has been associated with lower limb musculoskeletal disorders and fracture (Steele, 2006).

5.4.a. Gait symmetry

Our defined BMI groups did not influence bilateral asymmetry of the leg nor ankle stiffnesses. This is consistent with Ghasemi & Adibnejad (2020), with similar BMI averages to our study, who also found no significance imbalance differences between an overweight (26.78 ± 1.67 kg/m^2) group and a normal weight (21.35 ± 1.38 kg/m^2) group. Chang et al. (2021) found differences in symmetry of spatiotemporal parameters between normal (20.78 ± 1.47 kg/m^2) and overweight subjects (25.19 ± 1.62 kg/m^2). However, there was no significant disparities. Despite the significant differences in our BMI categories, a greater disparity in BMI populations may reflect symmetry differences. Cimolin et al. (2019) compared gait behavior among children classified as underweight (14.3 ± 0.7 kg/m^2), normal weight (17.6 ± 1.9 kg/m^2), and overweight (30.2 ± 5.4 kg/m^2) and found a trend between BMI and the harmonic ratio of spatiotemporal in the mediolateral axis. Their findings found that underweight subjects exhibited the least gait symmetry, potentially because of malnutrition as a deficit in gait performance that can cause unsteadiness, while subjects classified as overweight may present a sturdier locomotion (Cimolin, 2019). In obese subjects, walking with larger step widths contribute to mediolateral dynamic balance (Cimolin, 2019). This may also suggest why some studies find more bilateral symmetry in subjects with higher BMI (Ghasemi & Adibnejad, 2020), suggesting consistent rhythmic patterns demonstrated in heavier subjects (Cimolin, 2019). Despite differences in average BMI among our test samples, the range of subjects with indices as distinguished in other studies will more likely present differences in side-to-side imbalances.

5.4.b. Gait regularity and variability

No significant difference between the BMI groups was found in the regularity of leg stiffness. However, subjects with a BMI less than 25 kg/m^2 exhibited less regularity, *i.e.* more complexity, for ankle stiffness. This may be due to less muscular strength or less agency of the musculoskeletal system to utilize varied stabilization strategies. Adhikary & Ghosh (2022) showed found that lower and normal BMI subjects exhibited more vibration during the foot-to-ground impact, but timing for the beginning of those oscillations in the vertical motions was inconsistent and potentially less predictable. Lower SampEn of gait patterns has been associated with poorer levels of physical performance, and in OA, increased knee pain (Segal, 2018). The greater regularity in higher BMI subjects suggests more stability conditioned in walking with a load. However, larger ground reaction forces from increased BMI (Browning & Kram, 2007) can cause such repetitive patterns to increase localized stress at the joints due to overuse.

There were no BMI effects on the variability of the leg or ankle stiffnesses. This may be due to the limited participants in the higher BMI category for comparisons. Lehnen et al. (2017) studied alterations in the variability of spatiotemporal parameters between normal walking and walking with differently weighted backpacks unilaterally and bilaterally positioned on the body. Similar to our present study's protocol, Lehnen et al. (2007) maintained subjects' preferred speed throughout all trials and confirmed increased variability among all conditions, suggesting an increased motor repertoire when carrying excess load to adjust gait stabilization and reduce mechanical stress on the musculoskeletal system. However, a backpack load in the frontal position consisting of 10% of the subject's body weight was discouraged for the significant and considerable unsafe influences on gait spatiotemporal parameters (Lehnen, 2007). This suggests that the location of mass distributions on the body may have different effects on gait, which is not comprehensive in a BMI assessment.

5.5. Combined BMI and gender effects

BMI effects are biased towards specific genders. Due to the significant differences in averages for the BMI categories, evaluating them separately amongst each gender can further suggest a BMI threshold for increased OA risk. Furthermore, the association between being overweight or obese and having knee OA is stronger for females than males (Felson, 2008). Thus, assessing BMI categories within genders will provide better dichotomy to approaches towards mitigating OA onset by gender.

5.5.a. Gait symmetry

Females with a BMI lower than 25 kg/m^2 exhibited more asymmetry between left and right leg stiffnesses than females with higher BMI. In contrast, Chang et al. (2021) found greater gait asymmetry in spatiotemporal parameters in subjects with a large BMI, which decreases their stability and increases their risk of falling. Their BMI categories were similar to our samples' averages, but they had 26 subjects per each BMI classification, which was more than in the present study, suggesting that our sample sizes may be insufficient for assessing a definitive trend. In contrast, Cimolin et al. (2011) found no significant differences between the left and right leg in high (39.26 ± 2.39 kg/m^2) and low (22.8 ± 3.2 kg/m^2) BMI subjects. However, our present study does not rely on the same statistically significant differences between two limbs to consider asymmetry. Greater BMI disparities to segregate categories may need to be considered in identifiable differences in bilateral limb symmetry such as in Cimolin et al. (2019), who found a reverse relation with decreased BMI indicating more asymmetry, but their study focused on pediatrics while the former studies mentioned had similar age ranges as our present study. Pau et al. (2021) compared inter-limb symmetry of non-obese (21.8 ± 2.8 kg/m^2) and obese (40.4 ± 0.8 kg/m^2) subjects. They found that obese subjects exhibit more asymmetry in lower limb joint kinematics and suggest greater side-to-side imbalances to be strongly correlated with increased body weight. However, unlike interpretations of bilateral limb asymmetry in healthy male gait being functional and coordinative, in heavier subjects, asymmetry is associated with dynamic instability and poor performance. For example, the effect of bilateral asymmetry in muscle architecture was shown to negatively affect peak and mean vertical jump performance for females, but not for males (Mangine, 2014). There may be a different threshold of necessary symmetry for each gender.

Males with higher BMI exhibited even more side-to-side leg stiffness imbalances than their female counterparts with no significant differences in ankle stiffness symmetry. Males and females with a BMI of at least 25 kg/m^2 may exhibit similar ankle stabilizing strategies, but the former may be more adept to perturbations in locomotion since they have been shown to exhibit more lower body strength than females due to innate muscle morphology (Bartolomei, 2021) and lower inhabitance of fast-twitch muscle fibers in the vastus lateralis (Haizlip, 2015).

5.5.b. Gait regularity and variability

Females with a BMI lower than 25 kg/m^2 exhibited less regularity in the ankle stiffness and more variability in the leg and ankle stiffnesses in comparison to their heavier counterparts. Since weight loss has been found to reduce joint pain in the morbidly obese, defined as at least 45 kg overweight (McGoey, 1990), weighing more may aggravate the ankle more in females than in males. The disparities between females of lower and higher mass may be due to more hypermobile joints less adept tendons at the ankle, which may be a less ideal locomotion strategy among females with a higher BMI. Ko et al. (2010) found that, at higher BMI, subjects exhibited lower joint power at the ankle in the anterior-posterior direction, which could signify a less energy efficient gait. Singh et al. (2017) assessed maximal oxygen consumption of normal weight (22.6 ± 2.3 kg/m^2) and obese (36.1 ± 4.2 kg/m^2) females and found a greater correlation between maximal oxygen consumption than BMI in knee extensor moments, suggesting subjects who are less fit may be less capable of counteracting fatigue in their gait which can increase compensatory joint stress. Active ankle dorsiflexion during an isokinetic knee extension and flexion (60°/s-180°/s) was found to increase the strength of the knee extensor potentially due to its reaction to balancing the mechanical response around the knee joint by the tibialis anterior muscle that facilitates ankle dorsiflexion (Cha, 2014). The ankle extensors have been found to contribute more of the relative force during locomotion than the knee extensors and will be more reflective of gait performance (Kulmala, 2016), so assessing ankle mechanics can indicate knee joint performance and injury risks.

Our study found males with a BMI of at least 25 kg/m^2 to have more variability in ankle stiffness than their lower BMI counterparts. In males, an increase in body fat percentage with a decrease in muscular strength due to aging for example, may contribute to greater variability due to less motor control (Lee & Shin, 2022). Since BMI is not comprehensive of the presence of fat and muscle composition, just the height and weight of a subject may not be sufficient in analyzing young male locomotive strategies. Young male adults have been shown to adopt an active and bold gait strategies despite weight gain, subjectively to reduce the risk of falling by decreasing their stride length with increased body fat percentage, but their variability despite body mass metrics remain fairly consistent (Lee & Shin, 2022)

Our results also indicate that females with a lower BMI showed higher variability in ankle stiffness than their male counterparts. There may be an acceptable threshold for the variability of the ankle stiffness where transitioning between coordinative variability and detrimental variability occurs. This may suggest less stabilization strategies among lighter females potentially due to lower muscular strength. A study done by Braz & Souto Maior (2021) had healthy young adult subjects who regularly participated in resistance training lay horizontal and supine with an extended knee to emulate the heel-off during the stance phase of gait to measure ankle-dorsiflexion and plantarflexion range of motion. They measured force values of the five seconds of isometric contraction and 1-minute-long rest intervals between trials of dorsiflexion and plantarflexion for both ankles individually and assessed the largest values of three trials. Results showed that males exhibit greater absolute isometric muscle strength during ankle flexion (Braz & Souto Maior, 2021). Female ankles may not be as sufficient shock-absorbers or stabilizers for the joint due to less isometric strength.

It is suggested that anthropometric factors can explain most of the gender differences of ankle stiffness (Adjei, 2020). Young healthy females exhibit more ankle ligamentous laxity (Wilkerson & Mason, 2000) and tendons with lower Young's modulus (Kubo, 2003), and greater range of motion in the ankle than males (Cho, 2016) (Braz & Souto Maior, 2021). Furthermore, Adjei et al. (2020) found females to exhibit higher 2D ankle stiffness during quiet stance in the sagittal and frontal planes which is consistent with results from Kubo et al. (2003), who asked subjects with BMI less than 25 kg/m^2 to lay prone with the knee at full extension, ankle at zero degrees, and foot strapped to a footplate-dynamometer apparatus to estimate viscoelastic properties of tendons from ultrasonic images of lower leg muscles.

Males with higher BMI also exhibited more complexity in ankle stiffness and variability in leg stiffness than their female counterparts. These are similar patterns when comparing the two BMI categories of females. However, the only subjects classified as obese, according to the World Health Organization (> 30 kg/m^2) (WHO, 2021), in our study are male, but their female counterparts of the same BMI category in the present study do not have a significantly different BMI in comparison. This might suggest the different walking behaviors between heavier males and females. Overweight subjects tend to stiffen their lower extremity muscles (Usgu, 2021) and modify ankle behaviors (Silva, 2018) to accommodate for excess loads during gait. Silva et al. (2018) investigated overweight (27.5 ± 1.6 kg/m^2) and normal weight (22.6 ± 1.3 kg/m^2) males and suggested that overweight walkers may not be heavy enough to cause ankle movement changes in the frontal and transverse planes, so recognizing early signs of reduced ankle range of motion in the sagittal plane may suggest the need to strengthen accompanying muscles or to reduce one's BMI. Furthermore, since our higher BMI sample may not be heavy enough in comparison to their heights, chaotic changes in leg stiffness have not been observed in any of our tested categories.

5.6. Limitations and future work

The present study used ground reaction force data for the optimization schematic. However, replacing the force data with acceleration data would make the methodology's application more feasible in a clinical setting. For example, Cimolin et al. (2017) suggested the use of an inertial sensor strapped to the back of a subject to detect spatiotemporal gait parameters, facilitating time consuming analysis methods involving body markers. Kobayashi et al. (2014) found that an accelerometer attached at the back of the waist that produces the autocorrelation of trunk vertical accelerations can be used to evaluate present or longitudinal gait imbalances.

Due to the limited number of participants considered in the BMI category of individuals who had a BMI of at least 25 kg/m^2, particularly amongst female subjects, results regarding statistical significance may not be reflective of respective gait performance. Despite the current significant difference between the average BMI of each group, it may be useful to include more subject and expend the range of BMI values.

The present study only focuses on the single-legged support stance phase. Modeling the double support phase in the future can further reveal strategies that different populations utilize in the step-to-step transition and could improve our knowledge of the transition during single-support phase to the double support. Assessing symmetry would be more complex since the leg stiffness and ankle stiffnesses will need a specified tolerance to vary throughout the gait cycle in modulating for different tasks. Furthermore, since the center of pressure and the stance leg rotation contribute to the center of mass progression during gait, including the center of pressure displacement could increase the reliability of the simulations (Whittington & Thelen, 2009) (Kim & Park, 2011) (Hong, 2013). With the roller feet, adding a damper parallel to a spring in the traditional spring-mass model has been shown to improve the fit of simulated vertical ground reaction forces, which could improve the optimized fitness values in the present study (Hong, 2013) (Kim & Park, 2011). Speed was not the focus of the present study, but in addition to participants' self-selected walking speeds, including more trials at different speeds may reveal additional gait strategies. Since subjects are walking on a treadmill to maintain a constant, known speed, their selected speed may not fully reflect their overground walking behaviors.

Since walking is variable and chaotic, assessing fluctuations of symmetry during gait could reveal more insights on stabilization strategies throughout the gait cycle, based on gender or BMI. However, levels of symmetry and chaos may be controversial when assessing gait performance due to multifactorial contributions to movement functionality versus instability, so more healthy thresholds for gait behaviors must be established to prescribe more effective diagnosis when screening for pathological tendencies. Due to the disparities in muscle-type fibers composing of the lower limbs in males and females (Haizlip, 2015), different gait strategies may be encouraged in healthy young individuals to mitigate injury and disease. Furthermore, apparent limb dominance, particularly in males (Pappas, 2015), should be noted from subjects to see if preference is designated bilaterally and to categorize functions of each leg for different genders. Fatigue was not considered but may show female strategies in maintaining gait since slow twitch muscle fibers comprise more of the female lower limbs (Haizlip, 2015).

Aging is one of the most well-known declines in gait performance (Hausdorff, 2001) (Brach, 2010) and prevalence for OA (Felson, 1987) (Das & Farooqi, 2008) (Loeser, 2017). Kobsar et al. (2014) found gait asymmetry to increase with age, suggesting an increased risk of falling, lower limb injury, and higher joint contact forces. Kobayashi et al. (2014) found gait symmetry and regularity in the vertical and anteroposterior direction to decline with elderly age and that aging had a greater effect than gender, but older females were more imbalanced than older males. Aging and obesity can further increase the risk of OA (Das & Farooqi, 2008) (Zheng & Chen, 2015) potentially due to gait modifications (Ko, 2010). Evaluating differences in symmetry, regularity, and variability for older populations with different BMI can suggest detrimental walking behaviors to alleviate upon aging and weight gain.

5.7. Conclusions

Patterns presented in gait have ambiguous interpretations among various literature, and large inter-subject variability when evaluating healthy characteristics of walking can challenge early detections for disease. This study is a first step towards the development of efficient clinical tools to predict joint degeneration. We implemented a simple walking model that, combined with an optimization scheme, can reproduce vertical ground reaction forces and predict step by step leg and ankle stiffnesses. Moreover, this approach relies on sparse experimental data.

We also sought to highlight the roles of gender and BMI on locomotion characteristics that may lead to OA. For example, male tendency to use an asymmetrical, irregular, and variable gait may be beneficial since each limb is capable of navigating and executing diverse performance in activities. However, characterizing healthy gait will require more complex assessments that are indicative of gender and BMI to discover detrimental influences on habitual walking. The next step is to establish a clinical index related to the risk of OA by combining several gait-related parameters obtained using acceleration data.

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APPENDICES

Sensitivity analysis

After optimization of the parameters, simulations were run for the first step while individually varying each parameter by ± 5% in 0.1% increment. The fitness was computed for each trial ($F_i,\ i = 1, \ldots, 606$) and compared to the optimized fitness (F_{opt}) to compute the relative fitness error:

$$Relative\ fitness\ error = \frac{F_i - F_{opt}}{Fopt} * 100 \qquad i = 1, \ldots, 606$$

Results for one subject are shown on Figure 27. These results are similar for all the subjects. They highlight the higher dependency of the model to the initial leg length, initial leg angle and angle velocity, and leg stiffness.

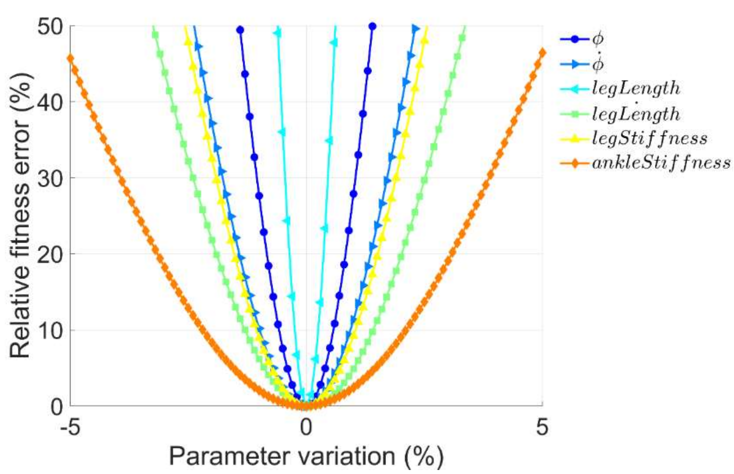

Figure 29. Sensitivity analysis for the initial parameters of the study. Each variable was individually modified by ± 5% to compute the relative fitness error.

Table 10. Subject's anthropometric data and gait speed (Ekanayake, 2019).

Subject #	Gender	Height (m)	BMI (kg/m^2)	Speed (m/s)
3	F	1.52	24.2	0.58
4	F	1.60	27.1	0.94
7	F	1.68	18.6	1.21
10	F	1.56	21.7	0.8
18	F	1.60	18.6	1.12
20	F	1.57	26.5	0.94
29	F	1.52	19.7	1.07
30	F	1.60	19.5	1.21
35	F	1.65	27.1	1.43
38	F	1.63	24	1.12
40	F	1.68	22.6	1.07
41	F	1.65	25	1.16
42	F	1.63	20.9	0.94
44	F	1.70	19.6	1.21
45	F	1.55	24.6	0.98
48	F	1.63	21.3	1.07
51	F	1.60	24.8	0.89
52	F	1.75	23.6	0.67
57	F	1.63	22.3	1.03
58	F	1.70	27.4	1.12
2	M	1.70	21.1	0.58
5	M	1.83	22.8	0.94
8	M	1.80	23	0.94
9	M	1.83	25.4	1.03
12	M	1.93	23.7	0.85
16	M	1.73	22.3	1.12
19	M	1.75	30.4	1.03
21	M	1.68	23.4	1.34
23	M	1.83	25.8	0.94
34	M	1.78	34.9	1.12
36	M	1.73	29.6	1.12
37	M	1.78	25.3	1.3
39	M	1.88	32.7	0.76
43	M	1.80	21.6	0.67
46	M	1.75	19.2	0.98

47	M	1.63	24.4	1.12
49	M	1.73	29.5	0.89
54	M	1.96	24.9	1.07
55	M	1.73	20.5	0.85
56	M	1.70	25.1	0.85

Table 11. Subjects' average leg stiffness and ankle stiffness normalized by the theoretical leg stiffness k_0 (k_0 = …).

Subject #	Average Normalized Leg Stiffness	Average Normalized Ankle Stiffness
3	53.4	2.2
4	137.7	0.9
7	75	0.4
10	80.3	0.5
18	74.9	1.4
20	23.3	6.7
29	126.2	4.7
30	16.8	6.8
35	69.8	2.5
38	24.1	7.5
40	29.9	4.9
41	31.6	7.2
42	20	5.1
44	23.9	6.8
45	96.7	4.5
48	67.4	1.1
51	29.2	7.6
52	46.4	1.7
57	16.9	4.6
58	31.2	4.1
2	139.8	5.2
5	67.6	1.8
8	99.9	3.8
9	51.9	2.8
12	63.1	4.9
16	41.3	4.7
19	89.5	2.8
21	58.5	3.9
23	44.2	5.6
34	154.2	6.1
36	96.2	1.9
37	30.1	5
39	101.5	4.6
43	100.6	7.3

46	141.7	4.2
47	72.9	6.2
49	42.1	4.6
54	110	5.3
55	223	8.8
56	165.1	10.7

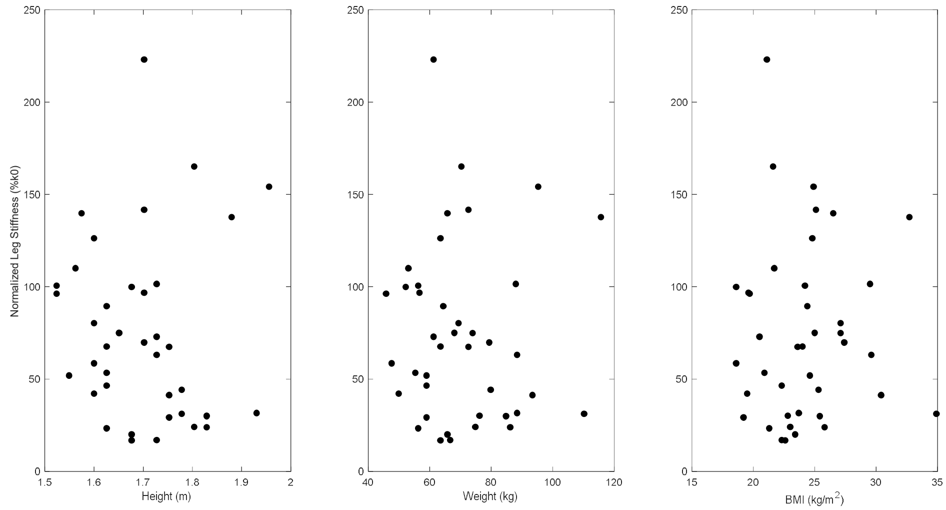

Figure 30. Subjects' average normalized leg stiffness versus height (left), weight (middle), and body mass index (right)

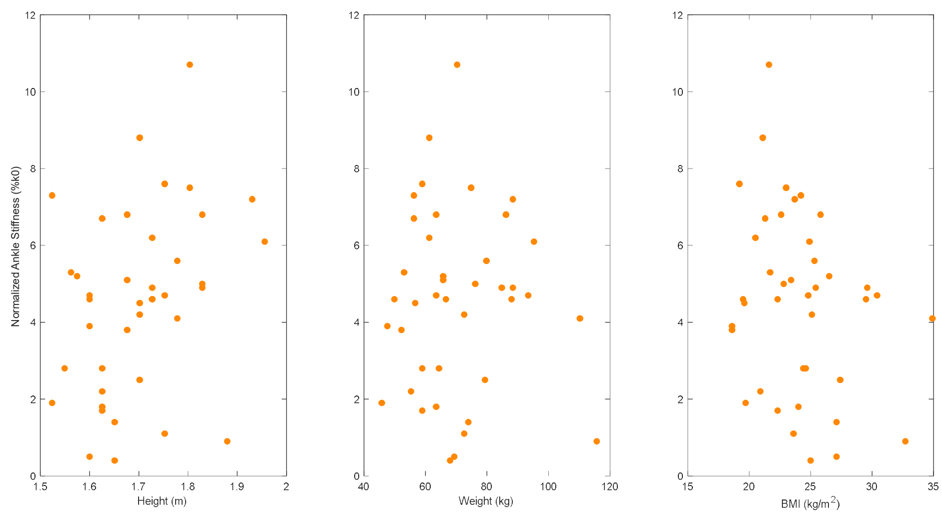

Figure 31. Subjects' average normalized ankle stiffness versus height (left), weight (middle), and body mass index (right)

Table 12. Subjects' average normal symmetry index (NSI) for the leg stiffness and ankle stiffness.

Subject #	NSI - leg (%)	NSI - ankle (%)
3	37.73	17.18
4	13.69	8.08
7	29.44	16.44
10	41.05	23.13
18	32.95	26.48
20	26.41	19.28
29	34.14	19.75
30	40.74	17.92
35	14.37	17.73
38	28.00	14.55
40	16.14	20.05
41	13.40	8.37
42	7.18	19.03
44	21.41	22.69
45	31.43	37.70
48	15.14	20.03
51	16.11	17.17
52	22.78	20.95
57	23.33	17.60
58	16.55	22.70
2	42.28	15.90
5	34.80	24.59
8	19.69	17.71
9	20.13	29.90
12	20.25	32.76
16	24.86	18.31
19	32.51	42.83
21	20.34	29.59
23	20.90	28.17
34	25.89	28.67
36	32.42	20.72
37	33.09	27.12
39	10.59	10.14
43	42.97	35.18
46	22.99	25.31

47	32.78	14.42
49	37.19	25.70
54	33.85	23.45
55	39.97	19.13
56	38.02	26.14

Table 13. Subjects' Sample Entropy (SampEn) for the leg stiffness and ankle stiffness.

Subject #	SampleEn - Leg Stiffness	SampEn - Ankle Stiffness
3	1.16	2.08
4	1.05	0.17
7	1.17	1.12
10	1.15	1.86
18	0.89	0.82
20	0.54	0.68
29	1.14	1.21
30	1.03	1.64
35	0.50	0.72
38	0.62	1.00
40	1.20	1.49
41	1.58	0.49
42	1.43	1.54
44	0.90	0.92
45	1.16	0.78
48	0.29	1.06
51	0.72	1.65
52	1.30	0.47
57	1.05	0.54
58	0.64	0.59
2	0.97	1.96
5	1.50	1.36
8	1.01	1.40
9	0.80	0.73
12	0.71	1.26
16	1.27	1.13
19	1.02	1.40
21	0.52	1.34
23	1.12	1.33
34	1.65	1.71
36	0.97	1.06
37	1.00	1.42
39	1.03	0.54
43	1.00	1.38
46	1.07	1.20

47	0.94	1.67
49	1.06	1.62
54	0.85	1.52
55	1.29	2.04
56	0.98	1.21

Oklahoma State University Institutional Review Board

Date: Thursday, April 13, 2017

IRB Application No EG176

Proposal Title: Effects of age on biomechanical imbalances in relation to osteoarthritis onset

Reviewed and Processed as: Expedited

Status Recommended by Reviewer(s): Approved **Protocol Expires: 4/12/2018**

Principal Investigator(s):

Jerome Hausselle	Eranda Ekanayake
Stillwater, OK 74078	Stillwater, OK 74078

The IRB application referenced above has been approved. It is the judgment of the reviewers that the rights and welfare of individuals who may be asked to participate in this study will be respected, and that the research will be conducted in a manner consistent with the IRB requirements as outlined in section 45 CFR 46.

☐ The final versions of any printed recruitment, consent and assent documents bearing the IRB approval stamp are attached to this letter. These are the versions that must be used during the study.

As Principal Investigator, it is your responsibility to do the following:

1.Conduct this study exactly as it has been approved. Any modifications to the research protocol must be submitted with the appropriate signatures for IRB approval. Protocol modifications requiring approval may include changes to the title, PI advisor, funding status or sponsor, subject population composition or size, recruitment, inclusion/exclusion criteria, research site, research procedures and consent/assent process or forms. 2.Submit a request for continuation if the study extends beyond the approval period. This continuation must receive IRB review and approval before the research can continue.
3.Report any adverse events to the IRB Chair promptly. Adverse events are those which are unanticipated and impact the subjects during the course of the research; and
4.Notify the IRB office in writing when your research project is complete.

Please note that approved protocols are subject to monitoring by the IRB and that the IRB office has the authority to inspect research records associated with this protocol at any time. If you have questions about the IRB procedures or need any assistance from the Board, please contact Dawnett Watkins 219 Scott Hall (phone: 405-744-5700, dawnett.watkins@okstate.edu).

Sincerely,

Hugh Crethar, Chair
Institutional Review Board

VITA

Truc Thanh Ngo

Candidate for the Degree of

Master of Science

Thesis: WATCH YOUR STEP! TOWARDS PREDICTING OSTEOARTHRITIS ONSET BASED ON SIDE-TO-SIDE IMBALANCES

Major Field: Mechanical and Aerospace Engineering

Biographical:

Education:

Completed the requirements for the Master of Science in Mechanical and Aerospace Engineering at Oklahoma State University, Stillwater, Oklahoma in May, 2022.

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