2016

Movement Biomechanics and Personalized Exercise Interventions in Individuals with Hip Osteoarthritis

Leigh, Ryan

UNIVERSITY OF CALGARY

Movement Biomechanics and Personalized Exercise Interventions in Individuals with Hip Osteoarthritis

by

Ryan Leigh

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE

DEGREE OF DOCTOR OF PHILOSOPHY

GRADUATE PROGRAM IN KINESIOLOGY

CALGARY, ALBERTA

SEPTEMBER, 2016

Abstract

Hip osteoarthritis (OA) is a prevalent musculoskeletal disorder that results in increased patient morbidity and dysfunction. While exercise is a common therapeutic modality employed in the management of this disorder, effect sizes remain small. Given this finding, the overarching aim of this thesis was to better understand the 3-dimensioanl (3D) gait biomechanics of this clinical population and subsequently test novel exercise interventions to improve clinical outcomes in individuals with mild-to-moderate hip OA.

Following the Introduction, Chapter 2 explored whether tester experience influenced the reliability with which 3D gait data can be collected. This study was important since 3D gait collections would be a major part of the final two chapters. Using a coefficient of multiple correlation (CMC) statistic to estimate within-tester reliability, we found that within-tester CMC values exceeded 0.90 for both novice and experienced testers across all kinematic variables.

Chapter 3 summarized the current hip OA and exercise literature and determined whether land-based exercise is an effective intervention in hip OA subjects not awaiting surgery. Pooled data from 7 studies demonstrated exercise had no effect on pain or self-reported function immediately post intervention and the overall effect sizes remained small.

Chapter 4 characterized the 3D kinematic gait patterns of individuals with mild-to-moderate hip OA considering that to this point, the lower extremity kinematics of hip OA patients had not been fully described. We reported that hip OA subjects walked with greater peak hip abduction, reduced peak hip extension, and greater peak hip external rotation compared to age and body

mass index (BMI) matched healthy controls. Whether these subtle biomechanical abnormalities could be used as treatment targets was explored in the capstone investigation.

In Chapter 5, we targeted these 3D gait abnormalities with a novel tailored exercise intervention in mild-to-moderate hip OA subjects. This exercise protocol was compared to a tailored intervention that was based on a standard clinical assessment. No significant improvements in pain were found across either group at 8-weeks follow-up and a 3D gait derived exercise program did not result in improved clinical outcomes.

Acknowledgements

I would like to thank my wife Jeanna for her love and support over the past seven years. I often draw on her incredible inter-professional, interpersonal, and academic abilities to help navigate my own professional road. My two children, Isaac and Meredith (and the third on the way!), bring pure happiness to my day every morning and every evening. They are immeasurably more important than any professional or academic pursuit, and will always remain the most important piece in my life. Jeanna and I feel very lucky to have the family we have. I would like to thank my mother Catherine and my in-laws for their continued support during this extremely busy time in our lives. I would also like to thank my supervisor, Dr. Reed Ferber for his support during my time as a PhD student. He offered unsurpassed support from an academic standpoint as I worked through my MD responsibilities, and from a life standpoint as other important life events arose. His mantra of family first made the past six years very enjoyable. Lastly, I would like to thank my committee members Dr. Sean Dukelow and Dr. Cy Frank for their invaluable academic input.

Preface

The following three chapters are based on scientific manuscripts:

Chapter 2 Leigh RJ, Pohl MB, Ferber R. Does tester experience influence the reliability with which 3D gait kinematics are collected in healthy adults? *Physical Therapy in Sport*. 2014; 15(2): 112-6. doi: 10.1016/j.ptsp.2013.04.003.

Chapter 4 Leigh RJ, Osis ST, Ferber R. Kinematic gait patterns and their relationship to pain in mild-to-moderate hip osteoarthritis. *Clinical Biomechanics (Bristol, Avon).* 2016; 34:12-7. doi: 10.106/j.clinbiomech.2015.12.010.

Chapter 5 Leigh RJ, Osis ST, Ferber R. (In Review). A Comparison of Two Personalized Exercise Interventions in Individuals with Mild-to-Moderate Hip Osteoarthritis: A Randomized Pilot Trial. *PLoS ONE.*

This dissertation is based on a collection of stand-alone manuscripts. The author of this thesis was the main contributor to the conception, design, data acquisition, data analysis, interpretation, and writing of all chapters, and wrote under the supervision of Reed Ferber. Michael Pohl contributed to the conception, design, and interpretation of Chapter 2 and Sean Osis contributed to the conception, design, and interpretation of Chapters 4 and 5.

Table of Contents

List of Figures

List of Tables

2 CHAPTER 1: INTRODUCTION

1.1 Osteoarthritis Background:

Osteoarthritis (OA) is the most common musculoskeletal disorder in the world and is a leading cause of pain, impaired function, and reduced mobility in affected individuals (Arthritis Alliance of Canada, 2011). The most recent Canadian census estimates that OA (all causes) affects 4.4 million Canadians (13% of the population), with the incidence expected to rise to over 10.4 million individuals (25% of the population) by 2040 (Arthritis Alliance of Canada, 2011). In addition, it is estimated that approximately $10 billion in direct health care dollars are spent on the management of OA today and this number is expected to rise to $550 billion by 2040 if no changes in management take place (Arthritis Alliance of Canada, 2011). The economic and personal burden of OA is therefore significant and has been identified as a priority area of research by provincial and national health care authorities and organizations.

Early definitions of OA focused on the structural changes that take place across the cartilage-bone interface and within this chondrocentric definition, OA was thought of as an imbalance in the cartilage synthesis-degradation cycle ultimately favoring degradation (Hunter, 2011). While cartilage changes are certainly thought to be a key component in the OA process, more recent work has suggested that OA should be viewed, and therefore defined, as a failure at the organ level (synovial joint) involving many different joint tissues (Lane et al., 2011). Tissues involved may include, but are not limited to, the synovium, ligaments, peri-articular muscles, nerves, articular cartilage, and subchondral bone (Brandt et al., 2008). Inflammation within the

synovium and marked bone marrow lesions have recently been found in knee OA patients and are therefore now thought to be leading candidates for other structures in OA that do not adequately repair themselves (Wenham and Conagham, 2009).

While an understanding of the tissues involved in OA is slowly becoming more apparent with improved imaging techniques, the etiology of OA remains elusive. Traditionally, OA was thought of as non-inflammatory disease of selected synovial joints as a result of excessive "wear and tear" due to altered joint mechanics (Wilson et al., 2008). This view has since been replaced with the understanding that biomechanical, biochemical, and genetic factors/stresses all play a role in disease development and progression (Lane et al., 2011) and that OA may, in fact, fall in the inflammatory subset of rheumatologic diseases. Biochemical mediators that have been found to play an important role in the progression, and possible initiation, of OA include inter-leukin 6 (IL-6), inter-leukin 1 β (IL-1β), and tumor necrosis factor α (TNF-α) (Kapoor et al., 2011). These pro-inflammatory mediators, which are released by different joint tissues, have all been suggested to play an important role in the progression of OA by inhibiting the anabolic and promoting catabolic joint processes which ultimately leads to tissue breakdown and destruction (Kapoor et al., 2011). Whether these pro-inflammatory mediators are up-regulated in the absence of mechanical stresses remains to be determined as does the interaction and interplay between mechanical and cellular processes. More recent genetic analyses involving whole genome screening of OA affected individuals has identified a number of genes associated with the deterioration of synovial joints (Sandell, 2012). The precise influence of these genes in the ultimate phenotypic expression of OA remains unknown but a heritable component in OA is widely accepted and requires ongoing investigation.

An additional factor thought to play an important role in the progression of OA is the "illness" of OA. Given that osteoarthritis is ultimately an illness that often affects individual's personal and productive roles within society, it important to note that coping mechanisms, self-efficacy, pain perceptions, social support, and catastrophizing may all play important roles in the OA illness. How these different constructs influence OA is a relatively new area of research that should ultimately provide important information that compliments the research looking at the mechanisms underlying OA.

1.2 Hip OA Background:

To date, the majority of research studies in OA have focused on knee OA. The reasons for this are multi-factorial and include the high prevalence of knee OA and the previously well-defined biomechanics of the knee joint. The interest in using knee OA as the target joint of interest in OA studies has resulted, however, in hip OA remaining significantly understudied. Hip OA is the second most prevalent type of OA (Felson et al., 2000), and similar to knee OA, results in significant personal morbidity and economic burden to the health care system. It has been estimated that approximately 3% of the total population is diagnosed with symptomatic hip OA (Pereira et al., 2011) including both radiographic and clinical signs and symptoms, respectively. While the precise etiology of hip OA remains undetermined, it is generally accepted that hip OA results from underlying skeletal abnormalities across the hip joint that are present or manifest during adolescence and early adulthood.

A number of studies have demonstrated how congenital (e.g. hip dysplasia), developmental (e.g. slipped capital femoral epiphyses), or acquired deformities in hip morphology and

anatomy can result in degenerative joint changes due to prolonged altered joint morphology (Leunig et al., 2000). More recently, it has been suggested that subtle femoral-acetabular impingements can be precipitating factors in the development of hip OA (Ganz et al., 2008). Furthermore, it has been reported that changes in femoral head-neck angulation or acetabular coverage often result in either cam- or pincer-impingements that are sufficient to increase hip contact stress and trigger the degenerative processes associated with hip OA (Ganz et al., 2008). In a commentary on the etiogenesis of OA, Brandt et al., (2008) suggested that OA is primarily a mechanical problem that can best be defined as a failed repair of damage that has been caused by mechanical stresses. These authors further suggested that regardless of the patho-biology of hip OA, abnormal mechanical stresses are always the precipitating factor to subsequent degenerative changes. Therefore, further research into the mechanical etiology and biomechanical factors related to successful treatment and alterations in OA disease trajectory are necessary.

1.3 Hip OA Biomechanics/3D Gait Analysis Background:

As outlined above, hip OA is a musculoskeletal disorder that results primarily from changed loads and stresses across the hip joint (Brandt et al., 2008). As a result, 3-dimensional (3D) gait analysis, which quantifies joint positions and joint forces based on standard Newtonian physics (Pohl et al., 2010), has frequently been used in an effort to characterize the biomechanical impairments within this population. In 3D gait analysis, 9mm retro-reflective markers are placed individually on specific anatomical landmarks ("anatomical markers") and in clusters ("technical markers") (Figure 1-1). The anatomical and technical markers permit the calculation

of joint centers and joint coordinate systems, which are subsequently used to define the position of the limb in space during movement.

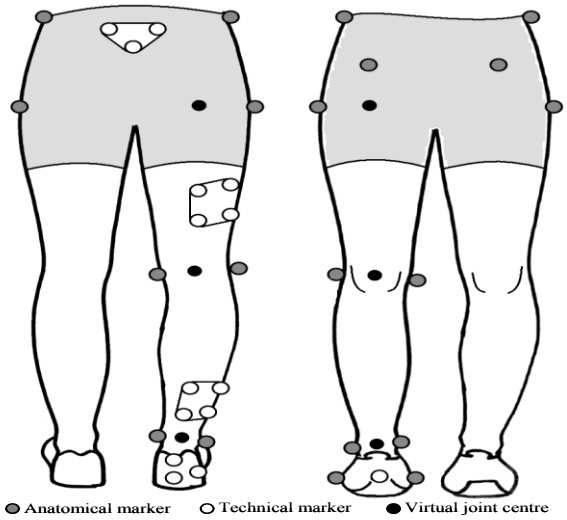


Figure 1-1. 3D gait analysis marker positions and joint centre positions.

Marker positions are captured by multiple infrared cameras that surround the patient while they walk on a motorized treadmill. Data collected during a 3D gait analysis is then processed and analyzed using gait specific software, resulting in anatomically relevant joint angles that can be interpreted by the clinician.

Altered walking gait biomechanics within a hip OA patient-population, as determined by 3D gait analysis and compared to healthy non-OA control subjects, has been investigated by a number of authors. Hurwitz et al., (1997) and Watelain et al., (2001) reported that hip OA patients demonstrate decreased hip extension range of motion (ROM), while Thurston (1985) reported that hip OA patients walk with increased anterior pelvic tilt, likely an adaptation to the aforementioned reduced hip ROM movement in the sagittal plane. More recently, Eitzen et al.,

(2012) have shown that hip OA patients walk with changes in sagittal plane kinematics across the pelvis, hip, and knee, as compared to healthy controls and individuals with hip OA have also been shown to exhibit decreased strength and flexibility and not surprisingly, decreased functional status as compared with healthy controls. There has however, to our knowledge, been no study to date that has examined the walking biomechanics of hip OA patients across all lower extremity joints (pelvis, hip, knee, ankle) in all three cardinal planes (sagittal, frontal, transverse). Elucidating a complete picture of the kinematics in this population may provide valuable information as it relates to potential compensations between joints and planes of motion as well as the impairments clinical practitioners may expect in this population. In addition, and arguably most important, an understanding of the biomechanical changes in hip OA patients may aide in the subsequent treatment and interventions within this group.

1.4 Hip OA Treatment:

While the exact pathogenesis of hip OA remains elusive, the treatment of hip OA remains an even greater challenge that has significant implications on individual morbidity and health care expenditures. At present, the most current and evidenced based approach to the management of hip OA follows the "OA treatment pyramid" outlined by Roos et al., (2012). Within this framework, first line treatment of hip OA involves education, exercise, and weight management, with the addition of pharmacological and passive treatments as second line treatment as required. At the top of the pyramid, surgical treatments are reserved for the most recalcitrant and severe OA cases.

Surgical management of hip OA through total and partial hip replacements has been found to be an effective treatment strategy in those individuals with end-stage hip disease). However, the majority of individuals with hip OA are not surgical candidates since their hip disease is not severe enough to warrant hip replacement or given that they would require too many revisions secondary to their young age. Therefore, effective non-surgical interventions are required to manage the large and ever-growing population of individuals with hip OA who are not eligible for hip replacement. At present, the armory of conservative non-surgical treatments includes joint injections, joint lubricants, pharmacological management, exercise, physiotherapeutic interventions (including manual therapy, pain relieving modalities) and education (weight loss, joint protection, disease status). However, despite the considerable number of treatment options available for managing hip OA, the effect of these interventions is mixed. For example, it has been estimated that the effect size of intra-articular corticosteroid injections for patients with hip OA is high (Effect Size (ES) = 1.5) (Dorleijn et al., 2011), with questions however as to the durability and duration of the effect. The therapeutic benefit of analgesics and non-steroidal anti-inflammatories on hip OA pain is considered to be low (ES = 0.14 and 0.29 respectively), as is the effect of only providing education for hip and knee OA individuals (ES = 0.06) (Zhang et al., 2010). Of particular interest, and the primary topic of this thesis, is the effect of exercise in hip OA given that exercise is thought to be an effective management strategy in knee OA (ES = 0.55 to 0.30; Fransen et al., 2010). Therapeutic exercise is a cost-effective treatment option in which very minor side effects are observed, and it's an accessible intervention to almost all individuals. However, to our knowledge, only five small studies have been published that examine the effect of land-based exercise on pain and function outcomes

in hip OA. A systematic review and meta-analysis of these five studies estimated that the effect of exercise on pain outcomes in hip OA is also small 0.33 (0.55 to 0.30) (Fransen et al., 2010). Following the findings in the aforementioned meta-analysis, discussion arose amongst OA researchers as to why the effect of exercise remained small in hip OA and what might be done to increase the efficacy of exercise. The first recommendation was that RCTs needed to be conducted in which only hip OA subjects were recruited since, up to 2010, all studies recruited both hip and knee OA subjects with knee OA subjects representing the majority. The subsequent sub-analysis of a small number of hip OA subjects may have resulted in underpowered findings. Second, it was suggested that further attention to individualizing (i.e. tailoring) the exercise program to the specific impairments of each hip OA subject may improve the response of the hip OA population to exercise. This individualized approach would be in alignment with a recent position stand emphasizing the importance of tailoring OA interventions to the individual. Therefore, in response to these shortcomings, and in an effort to provide a novel and significant contribution to the clinical biomechanics literature, the primary aim of the present thesis is to determine whether a novel exercise prescription methodology, specifically using 3D gait analysis, can improve clinical outcomes in individuals with mild to moderate hip OA.

1.5 Thesis Layout/Chapters:

As outlined above, the effect of exercise in hip OA has been relatively small, thereby highlighting the need for more novel approaches. However, before a comparison of two different assessment strategies is made in the final chapter of the thesis (Chapter 5), chapters

2-4 are directed at understanding other aspects of hip OA in order to establish the background and scientific foundation for the capstone pilot-RCT investigation.

Chapter 2 examined whether tester experience influences 3D gait analysis (3DGA) outcomes. Specifically, a tester with no previous 3DGA experience, but previous anatomical and clinical experience, was compared with a tester with 8 years of previous 3DGA experience (Leigh et al., 2014). Determining whether 3DGA data can be collected reliably by a novice tester was important since 3DGA was collected by a novice tester in two of our included studies. Given the increased use of 3DGA by clinicians within the clinical environment, and the suggestion that tester experience may play a role in determining 3DGA reliability, the purpose of the study in chapter 2 was to determine whether a clinician with no 3DGA experience can collect 3DGA data as reliably as a biomechanist experienced in 3DGA collections.

In Chapter 3, a comprehensive systematic review and meta-analysis was conducted examining the effect of exercise on clinical outcomes in hip OA. The review and meta-analysis examines the overall effect of therapeutic exercise on pain, function, and quality of life in individuals with hip OA and sub-analyzes the effect of tailoring the exercise intervention to the specific assessment findings of each patient. The review was conducted to better understand the effect of therapeutic exercise in hip OA patients given that a systematic review of the efficacy of therapeutic exercise in hip OA had not been published since 2010. In addition, the meta-analysis aimed to determine whether tailoring the exercise intervention to patient specific patient impairments results in improved outcomes, and whether analyzing hip OA patients only (as opposed to hip and knee OA patients together), changed the effect size of exercise.

In Chapter 4, a cross-sectional study comparing the 3D kinematic walking patterns of hip OA patients to control subjects is presented (Leigh et al., 2016). Of particular interest were the ambulation patterns in individuals with mild-to-moderate hip OA given that detection of early disease changes increases the likelihood of halting or reversing the disease trajectory (Hunter, 2011). While previous studies have assessed certain aspects of the hip OA gait pattern there has, to our knowledge, not been a study that characterized the walking kinematics of hip OA patients across all lower extremity joints (pelvis, hip, knee, ankle) in the three cardinal planes of motion (sagittal, transverse, frontal). It was expected that data from this study would help further characterize the walking patterns in the mild-moderate hip OA population as a whole, as well as potentially offer biomechanical treatment targets in a tailored exercise intervention (Chapter 5) should gait differences between hip OA and healthy individuals be found.

Chapter 5 represents the capstone project for this thesis and consists of a large pilot randomized controlled trial (RCT) that compares the outcomes of two individualized exercise programs in subjects with mild-to-moderate hip OA (Leigh et al.,2016; currently under review). Specifically, a tailored exercise program that is based on the findings of a 3D gait assessment was compared with a tailored exercise program based on the findings of a strength, flexibility, and ROM clinical assessment. It was hypothesized that the subtle biomechanical abnormalities identified in Chapter 4 might provide an effective framework for a tailored exercise intervention. Pain, function, and quality of life patient reported outcomes were then compared between groups. The overarching aim of Chapter 5 was to present a novel means of assessing hip OA patients with the goal of improving clinical outcomes following an exercise intervention.

3 CHAPTER 2:

DOES TESTER EXPERIENCE INFLUENCE THE RELIABILITY WITH WHICH 3D GAIT KINEMATICS ARE COLLECTED IN HEALTHY ADULTS?

Abstract

Objective: To determine whether tester experience influences the reliability of three-dimensional gait collections.

Design: Reliability study.

Participants: Ten healthy subjects visited a university gait laboratory on two separate days and underwent a walking gait analysis. During each visit, kinematic data were collected by a biomechanist with 8 years of 3D gait analysis experience (EXP) and a physical therapist with no previous 3D gait analysis experience (NOV).

Main Outcome Measures: Joint kinematic angles were calculated using either a functional or predictive joint identification method. Within-tester and between-tester measures of reliability were determined by calculating the root mean square error (RMS) and coefficient of multiple correlations (CMC).

Results: Within-tester RMS and CMC values were not significantly different ($P>0.05$) between the EXP and NOV testers using either a functional or predictive joint approach. Within-tester CMC values exceeded 0.90 for both testers across all kinematic variables. Between-tester CMC reliability values were greater than 0.85 for all variables measured.

Conclusions: Following basic training, a physiotherapy clinician with no previous 3D gait experience is as reliable as an experienced gait biomechanist with respect to marker placement accuracy. In addition, reliability comparisons between an experienced and novice tester appear independent of the joint identification method chosen.

2.1 INTRODUCTION

Physiotherapists, athletic therapists, and sport biomechanists often work with patients and athletes who present with common lower extremity ailments. Establishing an effective treatment plan to help manage these injuries regularly requires that the clinician identify the underlying altered movement patterns and/or aberrant movement biomechanics (McGinley, Baker, Wolfe, & Morris, 2009). Three-dimensional gait analysis (3DGA) is an effective means to measure such movement dysfunctions in a quantitative manner and thus may be an effective tool for the practicing clinician to add to their clinical repertoire.

Traditionally, 3DGA has been used in rehabilitation research settings to gather quantitative information on the mechanics of the musculoskeletal system during dynamic activities such as walking, running, and functional tasks (Cappozzo, Della Croce, Leardini, & Chiari, 2005; Pohl, Lloyd, & Ferber 2010). This information is then often used to facilitate a better understanding of several clinical conditions including osteoarthritis, running related injuries, and other neuromuscular conditions such as cerebral palsy and stroke (Barton, Levinger, Menz, & Webster 2009; Opheim, McGinley, Olsson, Stanghelle, & Jahnsen 2012). Recently, 3DGA has been adopted by physiotherapists working in musculoskeletal private practice clinics across North America (http://www.3dgaitanalysis.com). It is estimated that approximately 28 clinics across North America are now using 3DGA within their private practice to help facilitate clinical decision making.

The usefulness with which 3DGA can be used as a measurement tool, either in the research or clinical setting, depends largely in part on the reliability of the measurements obtained from the motion capture system itself (McGinley, Baker, Wolfe, & Morris, 2009). To date, several

studies have examined the topic of 3DGA reliability and whether 3D motion data can be collected reliably within and between days during walking and running (Besier, Sturnieks, Alderson, & Lloyd, 2003; Pohl, Lloyd, & Ferber 2010; Wilken et al., 2012). These studies collectively found that gait kinematic data could be acquired with good to excellent reliability across both walking and running conditions in healthy adult subjects. In the reliability studies published by Besier et al., (2003) and Pohl et al., (2010), the authors also sought to determine whether gait kinematic reliability was different when using either a predictive (MAN) or functional (FUN) approach to determine joint centers and joint axes of rotation. The predictive approach calculates joint centers and anatomical coordinate systems based solely on the placement of anatomical markers (Bell et al., 1989). The functional approach, in which the joint center/axes and anatomical coordinate systems are calculated using functional movement tasks (Schwartz and Rozumalski, 2005), is thus less dependent on the placement of anatomical markers. Given that marker placement inaccuracy is thought to be one of the leading causes of error in 3DGA (Della Croce et al., 1999), an advantage of the functional method over the predictive method, was thought to lie in its decreased reliance on the reliable placement of anatomical markers (Leardini et al., 1999). Despite the suggested advantage for the functional method, Pohl et al., (2010) found no improvement in within-tester (between-day) or between-tester reliability when comparing the FUN and MAN techniques. Similarly, Besier et al., (2003) found that only frontal plane knee kinematic reliability was improved using the FUN method compared to the MAN method. While good to excellent gait kinematic reliability was demonstrated in all of the above studies, and achieving excellent reliability does not appear to depend on the joint center technique used, both authors acknowledged that they used

experienced testers and that testers with limited 3DGA experience may not demonstrate the same reliability as those with 3DGA experience.

Given the increased use of 3DGA by clinicians within the clinical environment, and the suggestion that tester experience may play a role in determining 3DGA reliability, the purpose of the present study is to determine whether a clinician with no 3DGA experience can collect 3DGA data as reliably as a biomechanist experienced in 3DGA collections. A secondary purpose is to determine whether the chosen joint center methodology (FUN or MAN) influences this reliability comparison. It was hypothesized that: 1) the tester experienced in 3DGA would exhibit improved within-tester reliability compared to the clinician when a MAN technique was used given previous experience with gait analysis specific anatomical land-marking; 2) within-tester (between-day) reliability would be similar between the 3DGA tester and the clinician when using the FUN approach.

2.2 METHODS

A convenience sample of ten (six females, four males) healthy individuals (age = 22.5 ± 2.8 years; mass = 65.2 ± 13.7 kg; height = 1.73 ± 0.11 m; BMI = 18.9 ± 0.6) volunteered to participate in the study. The inclusion criteria required that subjects were currently free from lower extremity injury and familiar with walking on a treadmill. Subjects were excluded if they had a history of major lower extremity surgery, or if they had experienced lower extremity musculoskeletal pain in the six weeks prior to the study. All subjects provided written informed consent for the study that received approval from the Institutional Review Board.

Prior to commencement of the study data collections, a four part training session was conducted by the experienced biomechanist tester (8 years' of 3D gait analysis experience). The purpose of the training session was to train the novice tester (a physical therapist with 4 years clinical experience but no 3D gait analysis experience) on marker location placement used during motion analysis. The first two training sessions involved the experienced tester (EXP) describing and placing markers on a pilot subject while the clinician untrained in gait analysis (NOV) observed. Each of the first two training sessions lasted 45 minutes. The rationale for having the NOV tester observe the first two training sessions was to orient the NOV tester to the general protocol of motion capture marker set-up. Session three involved the NOV tester placing markers under the EXP testers' direct supervision while allowing the NOV tester to seek advice when needed. In the final training session, the NOV tester placed the markers independently of the EXP testers' feedback until after all markers had been placed, at which time the EXP tester provided feedback. The final two training sessions took 60 minutes given

that the NOV tester was entirely responsible for system set-up and subject marker placement. The gait analysis system was calibrated before each testing session by a lab technician working within the clinic. It was established a priori where cameras should best be placed and their positions remained unaltered between testing sessions.

Subjects visited the lab on two occasions separated by a minimum of two days. During each visit, subjects underwent two separate 3D gait analyses; one of these gait analyses was conducted by the EXP tester while the other test was conducted by the NOV tester. Each of these 3D gait analyses were separated by 30 minutes. The EXP and NOV testers alternated who tested first during each subjects visit to the lab on day one. For each gait analysis, 9mm spherical markers were placed on the pelvis and right lower extremity. Anatomical markers and technical marker clusters were placed in the manner described by Pohl et al. (2010). All subjects wore standard laboratory shoes (Nike Air Pegasus, Nike Inc.) for each of the testing sessions.

Eight Vicon cameras (Vicon, Oxford, UK) were used to collect marker co-ordinate data at 120 Hz. Prior to the motion trials, a standing calibration trial was performed while subjects stood in a standardized position with their feet positioned 0.3m apart and pointing straight ahead. Following the standing trial, subjects performed separate functional movements of the hip and knee which were subsequently used to determine functional joint centers of rotation (Pohl et al., 2010). Subjects then walked on the treadmill at 1.1 m/s and kinematic data for five complete gait cycles of the right limb were collected following a brief accommodation period (Fellin, Rose, Royer, & Davis, 2009). The use of a treadmill was required given the space

restrictions of the laboratory. Care was taken to ensure that any residual marker placement markings were not visible to the tester performing the second gait analysis.

Visual 3D software (C-Motion Inc., Germantown, USA) was used for filtering co-ordinate data, identifying functional joint centers and axes of rotation, and performing joint angle calculations. All data processing was performed by a separate individual who was blinded to each tester. Three-dimensional marker co-ordinate data were filtered at 10Hz using a fourth order Butterworth filter. Two custom models (MAN and FUN) were created based on manual marker placement only (MAN) and functional joint methodology (FUN) respectively. Both technical (TCS) and anatomical co-ordinate systems (ACS) were defined for the pelvis, thigh, shank, and foot for both the MAN and FUN models. For a definition of both an anatomical (ACS) and technical (TCS) frame, please refer to Cappozzo et al. (1995). In the MAN model, the hip joint centre was determined as per the techniques described by Bell et al. (1990). The FUN model used functional techniques to determine both the hip and knee joint center/axis of rotation as described by Schwartz and Rozumalski, (2005). A comprehensive description of the individual segmental ACS's for each model together with the calculation of the three-dimensional joint angles at the hip, knee, and ankle has been reported elsewhere (Pohl et al., 2010). Kinematic data were then analysed for the gait cycle and normalized to 101 data points. Time normalization was necessary to enable the coefficient of multiple correlation (CMC) analysis described below.

Two statistical measures of reliability were used to compare different aspects of the kinematic curves and thus calculate the within-tester (between-day) and between-tester reliability. The

CMC was used to compare the overall shape of the kinematic curve and was calculated as the average value subtracted from each curve (Growney et al., 1997). A second measure of reliability, root mean square (RMS) error, was used to estimate the kinematic offset between curves in the FUN and MAN conditions separately between sessions. Within-tester (between-day) reliability was calculated for each tester, using both a FUN and MAN approach, by comparing the two visits made by each subject on separate days. The experienced tester's within-tester reliability indices were then statistically compared to the indices of the novice tester in the MAN and FUN conditions separately using Wilcoxon signed rank tests (Figure 2-1).

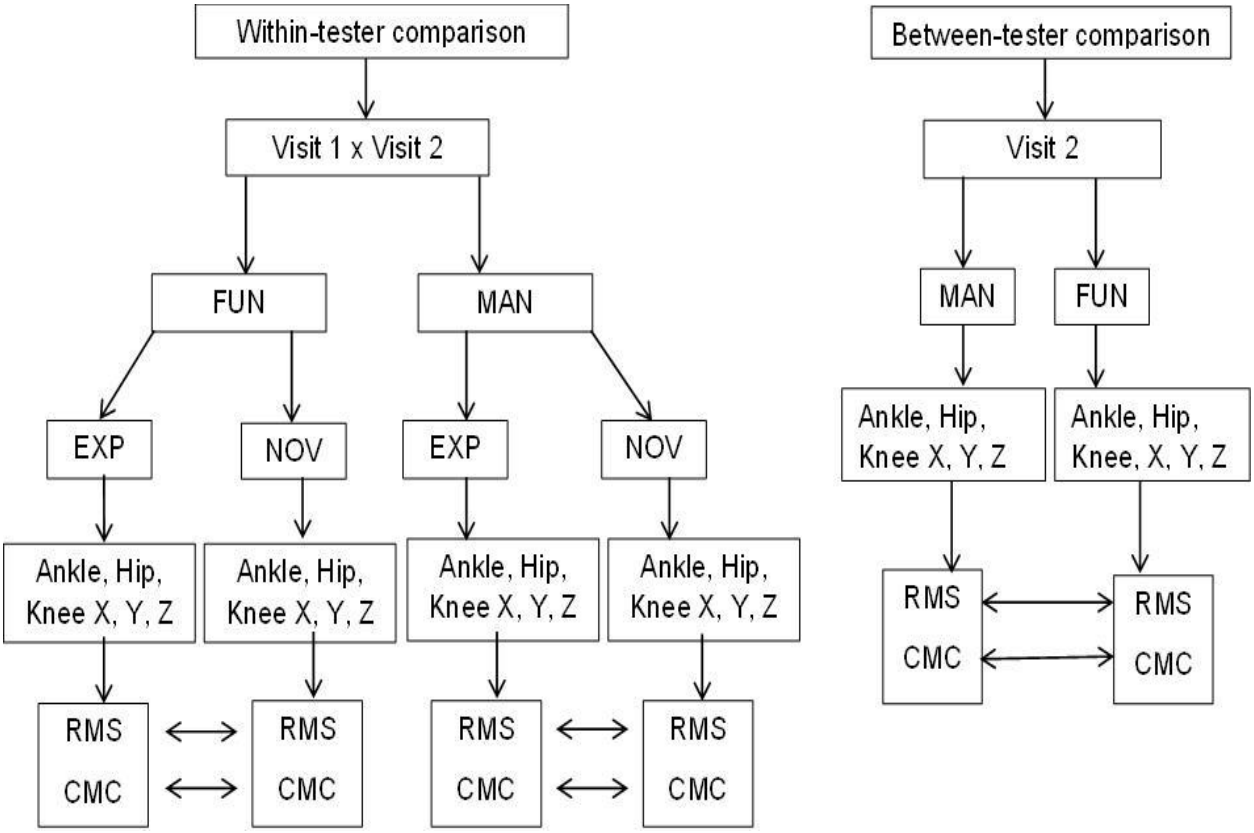


Figure 2-1. Schematic of the testing protocol for the within (left figure) and between-tester (right figure) comparisons. (↔ = comparison by Wilcoxon Signed Rank Test).

Non-parametric Wilcoxon signed rank tests were chosen given the small sample size and given that normality could not be assumed (Portney and Watkins, 2009). Between-tester reliability was calculated by using the data collected by both testers on day 2 only. Between-tester reliability using the MAN approach was then statistically compared to the FUN approach using Wilcoxon signed rank tests (Figure 1). Statistical significance was set at $P < 0.05$ and statistical analyses were performed using SPSS 19 (SPSS Inc., Chicago, USA).

2.3 RESULTS

2.3.1 Within-tester reliability:

Within-tester reliability of the NOV tester was not significantly different (P>0.05) from the within-tester reliability of the EXP tester when each tester's RMS error (Figure 2-2) and CMC reliability coefficients were compared (Table 2-1).

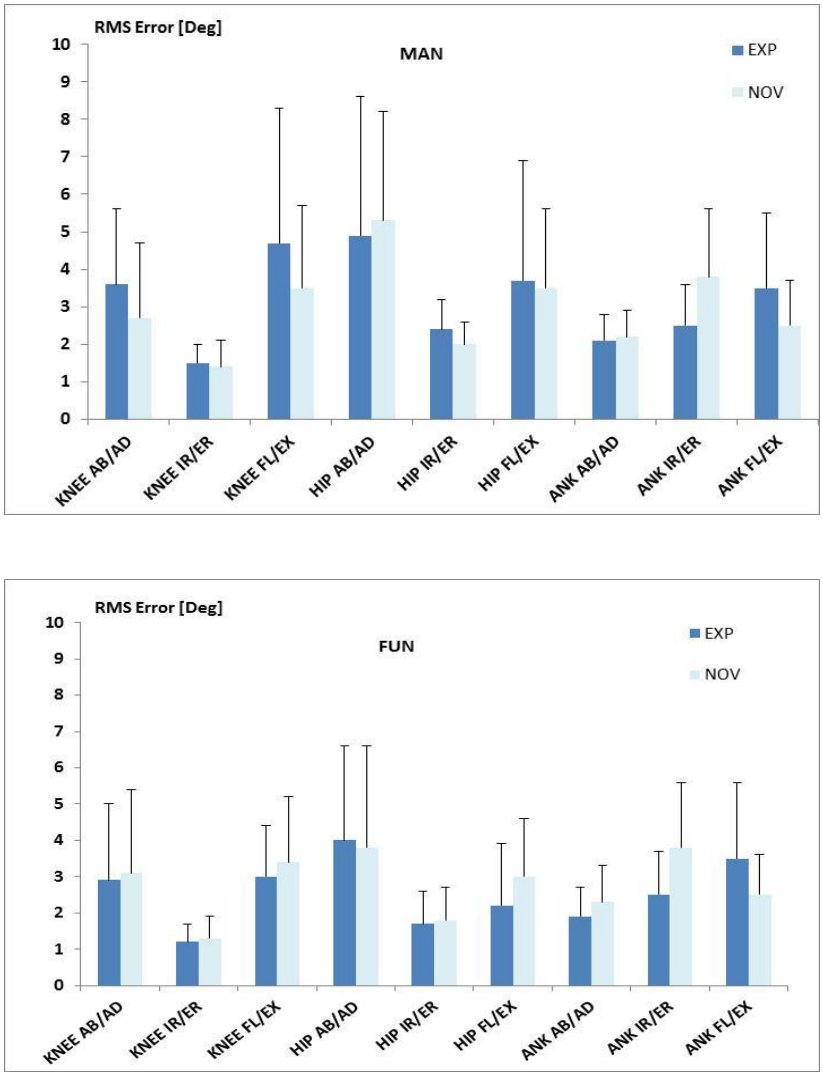


Figure 2-2. Within-tester ensemble mean (SD) RMS errors for all subjects using the MAN (top graph) and FUN (bottom graph) approach. EXP; (Experienced tester), NOV; (Novice tester).

This similarity in reliability between the NOV and EXP testers was seen in both the FUN and MAN conditions. Within-tester CMC values exceeded 0.90 for both testers in all kinematic variables measured and within-tester RMS error was less than 5 degrees for both testers. The largest difference in RMS error values between the EXP and NOV testers was 1.3˚ (ankle internal/external rotation) using the MAN technique and 1.3˚ (ankle internal/external rotation) in the FUN technique.

Table 2-1. Within-tester (between-day) mean (SD) CMC values for the experienced (EXP) and novice (NOV) testers. MAN (manual); FUN (functional).

	MAN		FUN	
	EXP	NOV	EXP	NOV
HIP AB/AD	0.999 (0.001)	0.998 (0.001)	0.999 (0.001)	0.998 (0.001)
HIP IR/ER	0.955 (0.038)	0.947 (0.078)	0.960 (0.036)	0.940 (0.079)
HIP FL/EX	0.975 (0.020)	0.941 (0.067)	0.975 (0.019)	0.940 (0.069)
KNEE AB/AD	0.995 (0.005)	0.996 (0.006)	0.995 (0.004)	0.995 (0.006)
KNEE IR/ER	0.876 (0.127)	0.928 (0.036)	0.973 (0.019)	0.966 (0.023)
KNEE FL/EX	0.980 (0.008)	0.954 (0.040)	0.981 (0.008)	0.952 (0.035)
ANKLE AB/AD	0.988 (0.010)	0.988 (0.007)	0.988 (0.010)	0.988 (0.007)
ANKLE IR/ER	0.961 (0.048)	0.931 (0.113)	0.961 (0.048)	0.932 (0.109)
ANKLE FL/EX	0.902 (0.083)	0.940 (0.054)	0.903 (0.083)	0.940 (0.054)

2.3.2 Between-tester reliability:

Between-tester RMS error was significantly lower ($P < 0.05$) in the FUN condition compared to the MAN method for knee flexion/extension (difference 2.5˚) and hip abduction/adduction (difference 0.6˚) (Figure 3). Between-tester CMC values exceeded 0.87 across all kinematic variables measured using either a FUN or MAN approach (Table 2). Between-tester CMC values were significantly different ($P<0.05$) for knee internal/external rotation (FUN; 0.93, MAN 0.88), hip flexion/extension (MAN; 0.97, FUN; 0.97) and knee flexion/extension (MAN; 0.97, FUN; 0.96) (Table 2-2).

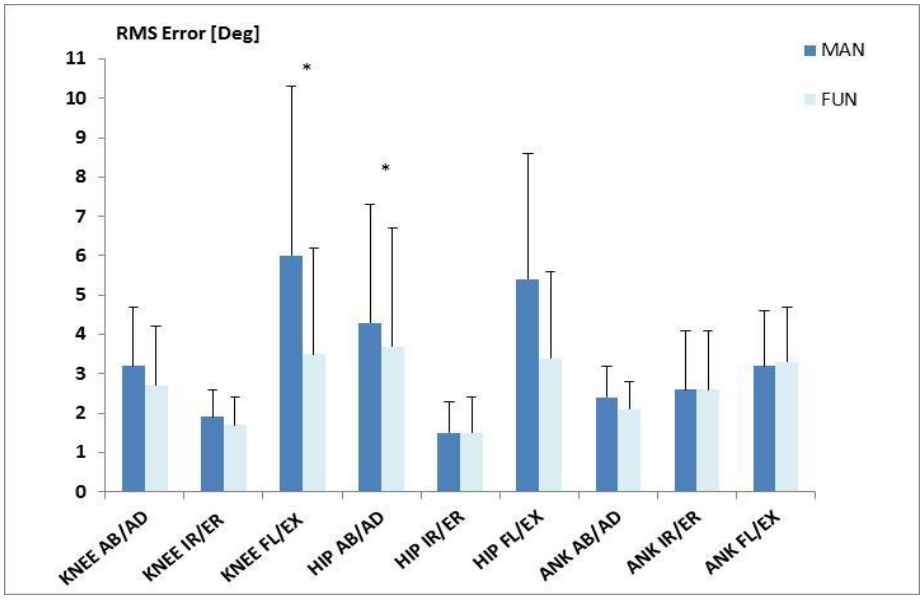


Figure2-3. Between-tester ensemble mean (SD) RMS errors for all subjects in the FUN and MAN approach. MAN (manual); FUN (functional). * $P < 0.05$.

Table 2-2. Between-tester mean (SD) CMC values in the manual (MAN) and functional (FUN) conditions.

	MAN	FUN
HIP AB/AD	0.998 (0.001)	0.998 (0.002)
HIP IR/ER	0.945 (0.083)	0.946 (0.090)
HIP FL/EX	0.971 (0.021)*	0.969 (0.022)
KNEE AB/AD	0.997 (0.003)	0.997 (0.003)
KNEE IR/ER	0.875 (0.085)*	0.929 (0.056)
KNEE FL/EX	0.965 (0.022)*	0.961 (0.023)
ANKLE AB/AD	0.992 (0.006)	0.992 (0.006)
ANKLE IR/ER	0.941 (0.071)	0.941 (0.070)
ANKLE FL/EX	0.882 (0.098)	0.882 (0.098)

*$P < 0.05$

2.4 DISCUSSION

The purpose of the present study was to determine whether a clinician, with no previous 3DGA experience, could collect gait kinematic data as reliably as a tester experienced in 3DGA collections. A further purpose was to determine if the joint centre methodology chosen influenced this reliability. It was hypothesized that the tester experienced in 3D gait analysis and the clinician untrained in 3D gait analysis would demonstrate similar within-tester reliability using a functional joint center technique (FUN) but dissimilar reliabilities when utilizing the more marker dependent predictive method (MAN).

Our results suggest that a physiotherapy clinician previously untrained in 3D gait analysis marker placement can demonstrate the same within-tester reliability as an experienced tester when marker placement accuracy is the variable of interest. This is, to our knowledge, the first study to compare the influence of tester experience on 3D gait kinematic reliability. The excellent within-tester reliability values obtained by the inexperienced and experienced 3D gait analysis testers in the present study are in accordance with those observed in previous studies in which the kinematic reliability values were good to excellent (Besier et al., 2003; Pohl et al., 2010; Wilken et al., 2012).

The finding that the experienced and inexperienced testers demonstrated similar within-tester reliability appears irrespective of whether a functional or predictive joint centre methodology is used. This finding was surprising given that joint center and axis of rotation calculations in the predictive approach (MAN) is more heavily dependent on marker placement accuracy as

compared with the functional approach (Leardini et al. 1999). With marker placement inaccuracy thought to be the largest contributor to 3D gait analysis error (Della Croce et al., 1999), we hypothesized that the experienced tester's additional experience palpating and locating 3DGA specific landmarks would confer reliability benefits when using a predictive approach (MAN). However, while the clinician did not have previous 3DGA marker placement experience, it appears that the clinician's previous clinical experience (4 years) was sufficient to ensure the same reliability as an experienced 3DGA tester. The finding that the FUN technique performed no better with respect to reliability than the MAN technique is also in accordance with Pohl et al (2010) who found no difference when using experienced testers.

Similar to the within-tester reliability findings, all between-tester CMC reliability values exceeded 0.870, suggesting excellent between-tester reliability when using either a functional or manual joint methodology approach. Our finding that between-tester reliability was excellent irrespective of the joint centre calculation technique chosen is in agreement with Pohl et al., (2010) who found that between-tester reliability values, using either a functional or manual approach, exceeded 0.90 across most joint angles. These findings suggest that reliability is not detrimentally affected when kinematic data is collected between testers with different levels of experience or when using different joint centre calculation methodologies. It should be noted that statistically significant between-tester differences in CMC values were observed across the knee transverse plane and knee and hip sagittal plane (Table 2). However, given that the CMC values exceeded 0.875 in these cases and that the difference in CMC values in the transverse and sagittal planes was between 0.002 to 0.05, the clinical significance of this difference is questionable. Similarly, while statistically significant, the clinical significance of a

0.6 and 2.5 degree difference in RMS error in hip abduction and knee flexion respectively between the functional and manual techniques is questionable (Figure 3). A recent study published by Wilken et al., (2012) found that, in a healthy lean population similar to ours, the minimal detectable change in hip frontal plane motion and knee sagittal plane motion is in excess of the 0.6 and 2.5 difference observed in our study. Given that our RMS error values may be below the minimal detectable change, the importance of such a small difference is questionable.

The results presented herein should be interpreted within the context of potential study limitations. The first pertains to the acknowledgement that the testers in the present study were not responsible for all aspects of the 3DGA collection which includes calibration of the motion analysis system, camera set-up, anatomical marker placement, and data modelling. Since these other aspects, in addition to marker placement, can introduce error into the collection of repeated gait analyses (Chiari, Della Croce, Leardini, & Cappozzo, 2005), tester experience may play a role in the reliability of gait analysis if calibration and analysis is part of the collection. However, given that anatomical marker placement accuracy is considered to be one of the largest contributor of error in gait analysis (Della Croce et al., 1999), we aimed to determine the influence of tester experience on 3DGA reliability across this variable specifically. The second limitation pertains to the use of only one 3D gait analysis experienced tester and one clinician tester. Including more than one experienced and one clinician tester in each group may have increased the generalisability of the results. Comparing the within-tester reliability of an experienced tester to a true “novice” clinician tester, who has neither 3D gait analysis nor clinical experience may have been helpful in further determining the influence of

tester experience on the reliability of kinematic gait variables. However, given that gait analysis is often performed both in the research and clinical settings by a tester with prior anatomical knowledge (e.g. kinesiologists, athletic therapists, physical therapists), it seemed more generalizable to select a clinician as opposed to someone with no anatomical knowledge. A final limitation is that the subjects recruited in the present study were all young, lean participants. It has been postulated by Besier et al. (2003) that increased percent body fat may increase the difficulty with which anatomical landmarks are identified and thus influence the accuracy of marker placement. Further study investigating the effect of adiposity on the within-tester and between-tester reliability of gait analysis is therefore needed. Lastly, it will be important to examine whether the reliability of 3DGA in an untrained clinician is similar to that of an experienced gait analysis tester when examining subjects with musculoskeletal impairments or injuries.

The results of the present study suggest that a physiotherapy clinician untrained in 3DGA data collection is as reliable as an experienced 3DGA tester with respect to marker placement accuracy. In addition, this similarity in reliability is found irrespective of whether a functional (FUN) or predictive (MAN) joint methodology is used to determine joint centers.

2.5 REFERENCES

1. Barton CJ, Levinger P, Menz HB, Webster KE. (2009). Kinematic gait characteristics associated with patella-femoral pain syndrome: a systematic review. Gait Posture. 30, 405-416.
2. Bell AL, Pedersen DR, Brand RA. (1990). A comparison of several hip center location
3. prediction methods. J Biomech. 23, 617-21.
4. Bell AL, Brand RA, Pederson DR. (1989). Prediction of hip-joint centre location from external landmarks. Hum Move Sci. 8, 3-16.
5. Besier TF, Sturnieks DL, Alderson JA, Lloyd DG. Repeatability of gait data using a functional hip joint centre and a mean helical knee axis. J Biomech. 2003. 36, 1159-68.
6. Cappozzo A, Della Croce U, Leardini A, Chiari L. (2005). Human movement analysis using stereophotogrammetry. Part 1: theoretical background. Gait Post. 21, 186-96.
7. Cappozzo A, Catani F, Croce UD, Leardini A. (1995). Position and orientation in space of bones during movement: anatomical frame definition and determination. Clin Biomech. 10(4), 171-8.
8. Chiari L, Della Croce U, Leardini A, Cappozzo A. (2005). Human movement analysis using stereophtogrammetry. Part 2: instrumental errors. Gait Post. 21,197-211.
9. Della Croce U, Cappozzo A, Kerrigan DC. (1999). Pelvis and lower limb anatomical landmark calibration precision and its propagation to bone geometry and joint angles. Med Bio Eng Comp. 37, 155-61.
10. Fellin RE, Rose WC, Royer TD, Davis IS. (2009). Comparison of methods for kinematic

11. identification of footstrike and toe-off during overground and treadmill running. J Sci Med Sport. 13, 646-50.
12. Growney E, Meglan D, Johnson M, Cahalan T, An KN. (1997). Repeated measures of adult normal walking using a video tracking system. Gait Post. 6, 147–62.
13. [http://www.3dgaitanalysis.com]
14. Leardini A, Cappozzo A, Catani F. Toksvig-Larsen S, Petitto A, Sforza V, Cassanelli G, Giannini S. (1999). Validation of a functional method for the estimation of hip joint centre location. J Biomech. 32, 99-103.
15. McGinley JL, Baker R, Wolfe R, Morris ME. (2009). The reliability of three-dimensional kinematic gait measurements: a systematic review. Gait Post. 29, 360-9.
16. Opheim A, McGinley JL, Olsson E, Stanghelle JK, Jahnsen R. (2012). Walking deterioration and gait analysis in adults with spastic bilateral cerebral palsy. Gait Post.
17. Pohl MB, Lloyd C, Ferber R. (2010). Can the reliability of three-dimensional running kinematics be improved using functional joint methodology? Gait Post. 32, 559-63.
18. Portney LG, Watkins MP. (2009). Nonparametric tests for group comparisons, In: Portney LG, Watkins MP, (Eds.), *Foundations of clinical research: Applications to practice* (pp. 503-522) 3rd ed. New Jersey: Pearson Prentice Hall.
19. Schwartz MH, Rozumalski A. (2005). A new method for estimating joint parameters from motion data. J Biomech. 38, 107-16.
20. Wilken JM, Rodriguez KM, Brawner M, Darter BJ. (2012). Reliability and Minimal Detectable Change Values for Gait Kinematic and Kinetics in Healthy Adults. Gait Posture. 35(2), 301-7

2.6 BRIDGE TO UPCOMING THESIS CHAPTERS:

Given that the final two studies of this thesis will involve a novice tester (RJL) collecting 3D gait data, it was important that this tester be able to collect this data in a reliable manner. The results of this study suggest that the novice tester is as reliable as the experienced tester in healthy young controls. It is acknowledged that the 3D gait data will be collected in individuals with hip OA in the final two studies and that this population may be more difficult to collect this data. However, in collecting 3D gait data with this population, we employed a novel marker accuracy tool that has since been shown to improve marker placement accuracy in our population of interest.

4 CHAPTER 3:

THE EFFECT OF LAND-BASED EXERCISE ON PAIN AND FUNCTION IN HIP OSTEOARTHRITIS PATIENTS NOT AWAITING SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS

Abstract

Objective: To determine whether land-based exercise is an effective intervention for improving pain and function in individuals with hip osteoarthritis (OA) not awaiting surgery and to determine whether individualized exercise regimens tailored to patient physical impairments changes the effect estimate.

Methods: Systematic review with meta-analysis of randomized controlled trials (RCTs) comparing land-based exercise to a control intervention in hip OA subjects. Standardized mean differences (SMD) and 95% confidence intervals (95% CI) were calculated for pain and physical function (self-reported and performance-based) using a random-effects model. Heterogeneity between studies was measured using an I^2 statistic. The PEDro quality index scale was used to determine the quality of evidence.

Results: Eight RCTs involving 570 participants with hip OA were identified and included in the review. Pooled data from 7 studies demonstrated exercise had no effect on pain (-0.15 (-0.60 to 0.29)) or self-reported function (-0.10 (-0.41 to 0.22)) immediately post intervention. Exercise had no effect on performance-based function outcomes (Timed Up and Go: -0.15 (-0.63, 0.34)); 40m Walk: -0.05(-0.27, 0.17)) post-intervention. Pooled data from 3 studies that prescribed a tailored exercise program resulted in a small treatment effect on pain (-0.58 (-1.04, -0.11)) post-intervention. Heterogeneity was moderate to high in all analyses performed.

Conclusions: No evidence of an effect of land-based exercise on pain and function (self-reported or performance-based) was found immediately post-intervention in individuals with hip OA.

Tailored exercise may impart a small beneficial effect on pain post-intervention but small sample sizes and significant heterogeneity precludes definitive conclusions at this time.

3.1 INTRODUCTION

Hip osteoarthritis (OA) is the second most common type of OA in the lower extremity [1]. It often results in pain and stiffness in the hip and groin region as a result of cartilage breakdown and bony changes [2]. Common sequelae include impaired mobility, decreased health-related quality of life, and psychological distress [3]. At present, conservative therapies, typically consisting of various combinations of exercise, education, and pharmaceuticals are the first line management of choice for individuals with hip OA when they are not candidates for total joint arthroplasty [4]. The use of exercise in the management of hip OA is of interest given that exercise has been shown to be efficacious in the management of knee OA [5], and given that decreased strength, flexibility, and proprioception have been noted previously in hip OA populations[6]. Of particular interest is the role of tailored exercise in the management of hip OA given the importance placed by several recent OA position papers on individualizing the patient exercise program to each patient's identified impairments [7].

To date, three systematic reviews have examined whether exercise is effective in the clinical treatment of hip OA [8-10]. The results of these reviews have been mixed, with some authors suggesting that exercise confers favorable benefits in a hip OA population while others suggest there is inconclusive or insufficient evidence [8-10]. Despite these differences, these reviews presented uniform recommendations advocating for the design and implementation of large-scale hip OA specific studies (i.e. restricting recruitment to hip OA subjects only) that employ a tailored or semi-tailored approach in the prescription of therapeutic exercise. Since the last review published in 2010 [8], several large randomized controlled trials (RCTs) have been

published that have attended to these recommendations. While these recent RCT's have contributed individually to the hip OA body of literature, it remains unknown how these results fit in with previous literature and whether addressing previously identified methodological limitations has resulted in a change in the effect of exercise in hip OA.

Thus, the purpose of the present systematic review and meta-analysis was to 1) determine how the inclusion of several recently published RCTs examining exercise in hip OA populations may contribute to the evidence pertaining to the clinical efficacy of exercise and 2) to determine if the point estimate of effect of exercise changes when exercise is tailored and/or when recruitment is limited to hip OA patients only. Specifically, and in keeping with the recommended set of Osteoarthritis Research Society International (OARSI) recommended OA outcome measures [11], we examined the effect of land-based exercise on pain, self-reported function, and performance-based physical function measures in hip OA patients not eligible for a total hip arthroplasty.

3.2 METHODS

3.2.1 Search Strategy

Electronic databases were searched, from beginning to March 2013, for studies published in English with no publication date or status restrictions. Pubmed , Medline Ovid , Embase , Proquest Abstracts, CINAHL , Sport Discus , PEDro and Web of Science were searched by a single author (RL). The same search strategy was used for all databases: 1) Hip Osteoarthr* 2) Osteoarthritis, Hip 3) Coxarthr* 4) 1 OR 2 OR 3 5) Exercise 6) Exercise Therapy 7) Resistance

Therapy 8) Physical Exercise 9) Rehabilitation 10) Physical Therapy 11) Physiotherapy 12) 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 13) Randomized Controlled Trial 14) 4 AND 12 AND 13.

3.2.2 Eligibility Criteria

Randomized controlled trials that investigated the effect of land-based exercise (e.g. strengthening, stretching, aerobic, balance training) on pain or self-reported or performance-based physical function outcome measures in individuals with hip osteoarthritis not awaiting a total hip replacement were included. Land-based exercise studies only were chosen given the recent publication of several large RCTs that examined the effect of land-based exercise only on hip OA patient outcomes. Studies that included subjects with a radiographic or clinical diagnosis of unilateral or bilateral hip OA were eligible for inclusion in the present review. Radiographic diagnoses of hip OA were made using either the American College of Rheumatology's (ACR) criteria for radiographic hip OA [12] or joint space narrowing scores [13]. Clinical diagnoses were made using ACR's clinical hip OA definitions [12]. No limitation was placed on radiographic severity given the discordance between x-ray changes and patient reported symptoms in OA populations[14]. Studies were excluded if they included subjects who had a previous total hip or total knee replacement in either the contralateral or study limb or were scheduled for a total hip replacement. Control groups included those groups receiving either standard-of-care treatment, education, or employing a wait and see strategy. Studies that provided either educational or pharmacological components, in addition to the exercise intervention, were only included when these programs were conducted in both the intervention and control group.

Final eligibility was determined by two independent reviewers (RL, KM), the second of whom was blinded to author, title and source.

3.2.3 Risk of Bias

Two blinded and independent reviewers (RL, KM) assessed the risk of bias within each study using the PEDro quality index measurement tool[15]. Items evaluated included adequacy of the randomization procedure, concealment of randomization, blinding of the subjects, therapists, and assessors, adequacy of follow-up, intention-to-treat analysis, and appropriate statistical analysis. The initial agreement between the authors was assessed using the kappa index (κ) where 0= no agreement, 0 to 0.4 = poor agreement, 0.41 to 0.60 = fair agreement, 0.61 to 0.80 = good agreement, 0.81 to 1.00 = excellent agreement [16]. To assess for the risk of bias across studies (publication bias), funnel plots were constructed for both pain and function outcomes. Plots were visually inspected to determine whether those studies reporting higher effect sizes were also those with higher standard errors (or decreased sample sizes).

3.2.4 Data Synthesis

Participant characteristics (including sex, age, BMI), outcome measures and point estimates of effect were extracted directly from the included publications. Intervention characteristics, specifically whether the exercise intervention was group-based versus individual, supervised versus unsupervised and the volume (frequency, intensity, duration) were also extracted by one author (RL) and checked for errors by a second (KM). In four RCTs, hip OA data were combined

with knee OA data. In these cases, study authors were contacted and asked to provide hip OA data only. Group means, standard deviations, and sample sizes were extracted from each study or provided by study authors. Mean change in pain from baseline to post-intervention (or follow-up) was calculated for the exercise and control groups irrespective of the analysis conducted by the authors of the individual studies. Mean differences between these change scores were then calculated and used to determine mean differences, standardized mean difference (SMD = mean difference divided by the pooled standard deviation) and 95% confidence intervals. The post-intervention period was defined as that period within 4 weeks of intervention completion, whereas the follow-up period was considered to be those time points greater than 5 months post-intervention. It should be noted that in one of the included studies [17], study authors adjusted their baseline WOMAC pain scores to be equal between groups (following unexpected baseline differences). However, since change scores were sought in the present review, the unadjusted baseline WOMAC pain scores were used to calculate mean differences.

Where possible, meta-analyses of SMD's were performed in Cochrane Review Manager (V5.2) using an inverse variance random effects model. To be eligible for meta-analysis and pooling, a minimum of two studies were required to measure the same outcome (e.g. pain, self-report function, or performance-based function) within similar time periods (i.e. within a maximum of 6 weeks from each other). Thresholds of trivial <0.2, small (0.2 to 0.6) moderate (0.61 to 1.2) and large (>1.2) were used to interpret the clinical effect of the exercise programs. Confidence intervals that included zero were interpreted as no-effect. Heterogeneity between studies was

measured using an I^2 statistic where an I^2 value of 25%, 50%, and 75% was considered to be low, moderate, and high respectively [18].

3.2.5 Secondary Analyses

An *a priori* sub-group analysis of treatment effect was performed in studies that recruited hip OA patients only [13, 17, 19,20]. This analysis was performed since the majority of older studies examining exercise in hip OA recruited both hip and knee OA subjects into their study (of which hip OA patients were the minority and therefore potentially underpowered). A second post-hoc sub-group analysis examined whether tailored exercise programs (as seen in the more recent RCTs) resulted in different treatment effects as compared with the evidence base as a whole which included non-tailored studies. Exercise programs were considered to be tailored if study authors explicitly stated that prescribed exercises were tailored to each individual's initial assessment findings or if therapists used a predetermined list of exercises to create individualized patient exercise programs. Progressing the volume of exercise was not considered sufficient to be considered tailored.

3.3 RESULTS

3.3.1 Study Selection and Characteristics

The search strategy returned 1158 titles from which 94 abstracts were retrieved for further review. Thirteen full-text publications were subsequently retrieved to determine their eligibility. Five publications were deemed to be ineligible due to subjects being on a surgical

waitlist [21], lack of an exercise intervention [22], study design not an RCT [23][24], and duplicate data [25] leaving eight publications for inclusion in the review (Figure 1).

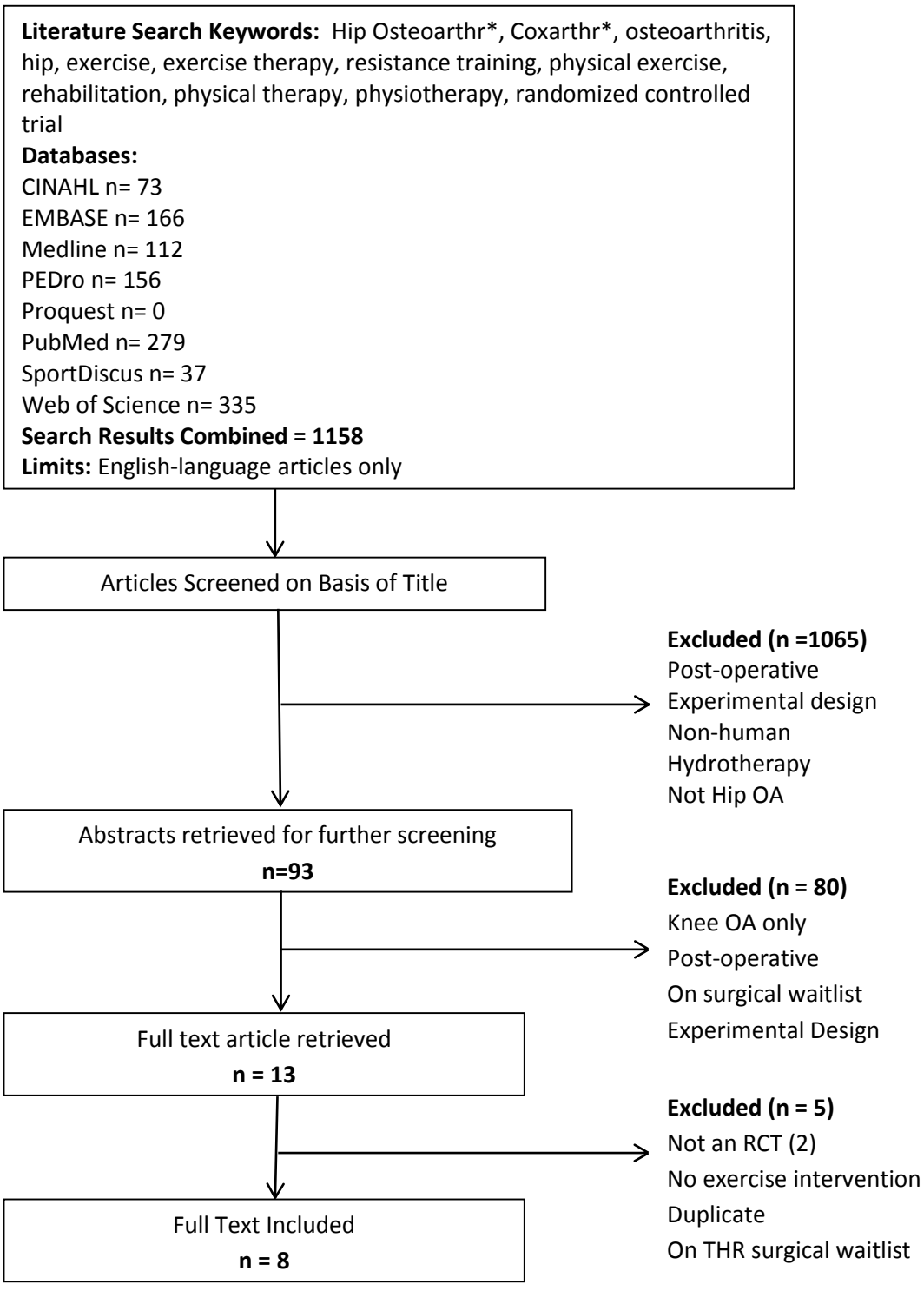


Figure 3-1. Trial Selection Process

The eight RCTs involved a total of 570 participants and the average size of each trial was 71 participants or approximately 36 subjects in the intervention and control groups (Table 3-1; found at end of chapter). Four studies recruited both hip and knee OA subjects [26-29] and study authors provided hip OA-only data when contacted. The four remaining studies limited inclusion to hip OA subjects [13, 17, 19,20]. It should be noted that in one study, nine month follow-up data was published at a later date[25]. The author of this study provided us with this data at the same time as the requested hip OA subject data was provided. Changes in pain were quantified using the Numeric Pain Rating Scale (NPRS), Visual Analogue Scale (VAS), and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscales. Self-reported function was measured using the WOMAC function sub-scale while performance-based function was measured using the timed-up-and-go and "short walk" (10 to 20m).

The volume of exercise (frequency, intensity, and duration of exercise programs) was highly variable amongst studies with program durations ranging from 8 to 12 weeks. The delivery of the exercise intervention took place either in a group setting[17, 20, 27, 28] or one-on-one with a physiotherapist[13, 19, 26, 29] with subjects asked to participate in the exercise programs 1-3 times per week in clinic (Table 1 Appendix). In six studies, subjects performed a home exercise program in addition to exercises that were performed during clinic visits [17, 19, 20, 26, 27, 28]. In four studies, subjects randomized into the exercise group received both the exercise intervention and the control group therapy [13, 17, 26, 29]. The most common intervention was an exercise program consisting of strengthening and flexibility training [13, 17, 19, 26, 29]. Strengthening without flexibility training[20, 28] and Tai Chi[27] were also employed as

interventions. Four studies met the previously outlined criteria for consideration as a tailored exercise program [13, 19, 26, 29].

In five studies, it was reported that the control group received standard-of-care treatment (e.g. General Practitioner care, medication usage as needed, with or without other health care interventions [17, 19, 20, 26, 29] while in two others studies a wait-and-see strategy was utilized[27, 28]. In one study, the control group received patient education in the form of a "hip school" [13]. For ethical reasons, it is likely that subjects in the wait-and-see and education control groups may also have accessed GP care, medications, and other health care interventions.

3.3.2 Risk of Bias

The initial agreement between reviewers in the present study was near perfect (κ=0.93) and reliability for individual items ranged from substantial (κ =0.75 Items 4 and 8; κ = 0.875 Items 2 and 9) to perfect (Items 1, 3, 5, 6 7, 10 and 11). Consensus was reached for all items following discussion between the two reviewers. The maximum quality index score was 8 points with all studies scoring either seven or eight out of ten (7.6/10 average), on the PEDro quality assessment scale (Table 3-2), thus no study was excluded due to risk of bias.

Table 3-2. Methodological Quality of Trials (Pedro Scale)

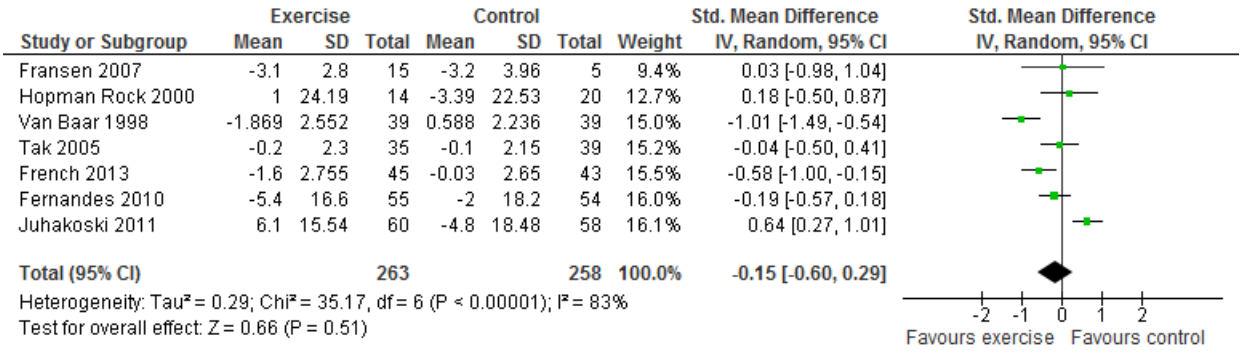
Trial	1	2	3	4	5	6	7	8	9	10	11	**Total (/10)**
Abbott, 2013	√	√	√	√	χ	χ	√	√	√	√	√	**8**
French, 2012	√	√	√	√	χ	χ	√	√	√	√	√	**8**
Juhakoski, 2011	√	√	√	χ	χ	χ	√	√	√	√	√	**7**
Fernandes, 2010	√	√	√	√	χ	χ	√	√	√	√	√	**8**
Fransen, 2007	√	√	√	√	χ	χ	√	√	√	√	√	**8**
Tak, 2005	√	√	χ	√	χ	χ	√	√	√	√	√	**7**
Hopman-Rock, 2000	√	√	χ	√	χ	χ	√	√	√	√	√	**7**
Van Baar, 1998	√	√	√	√	χ	χ	√	√	√	√	√	**8**

1) eligibility criteria were specified; 2) subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received; 3) allocation was concealed 4) the groups were similar at baseline regarding the most important prognostic indicators; 5) there was blinding of all subjects; 6) there was blinding of all therapists who administered the therapy; 7) there was blinding of all assessors who measured at least one key outcome ; 8) measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups; 9) all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"; 10) the results of between-group statistical comparisons are reported for at least one key outcome; 11) the study provides both point measures and measures of variability for at least one key outcome

Items that scored poorly were patient blinding and therapist blinding. Funnel plots indicated no evidence of publication bias for any of the reported pain outcomes. Publication bias was possible in one study for self-reported function given that a high standard error accompanied the large change in self-reported function [29].

3.3.3 Change in pain

Pooled data of seven studies [13, 17, 19, 20, 27, 28,29] revealed that exercise interventions had no effect on pain (SMD = -0.15 (-0.60 to 0.29), I^2=83%) post-intervention when compared with controls (Figure 2).



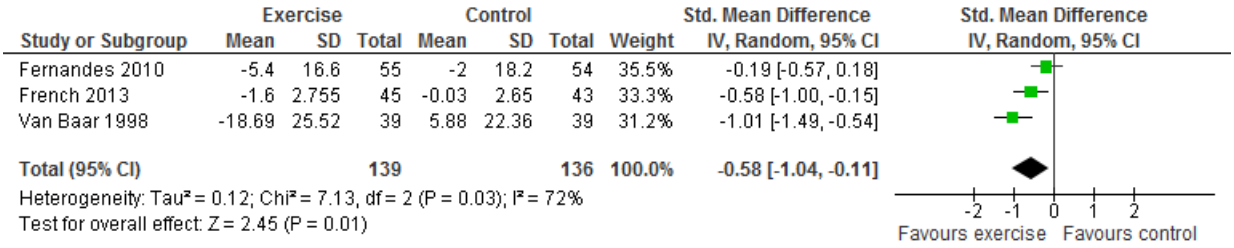


Fig. 3-2. SMD (95% CI) of effect of exercise vs. control on pain post-intervention when all studies are included (top panel) or inclusion of tailored studies only (bottom panel).

Pooled follow-up data from 4 studies [17, 20, 28, 29] revealed that this lack of effect remained at the 5 to 6 month follow-up (SMD = -0.15 (-0.55 to 0.25), I^2=64%). In contrast, two studies that followed participants for 9-10 months indicated a small pain reduction compared with baseline (SMD = -0.47 (-0.84 to -0.10), I^2=30%)[13, 29], although this was not supported by a longer term follow-up from non-pooled data [26] .

3.3.4 Self-Reported Function Outcomes

Pooled data from seven studies [13, 17, 19, 20, 27, 28, 29] revealed that exercise had no effect on self-reported function (SMD = -0.10 (-0.41 to 0.22), I^2=62%) post-intervention compared with controls (Figure 3). This was supported by pooled 6-month follow-up data from 2 studies (SMD = -0.13 (-0.43 to 0.18), I^2=0%) [17,20] and pooled 10-12 month follow-up data (SMD = -0.13 (-0.55 to 0.28),I^2=56%) [13, 17].

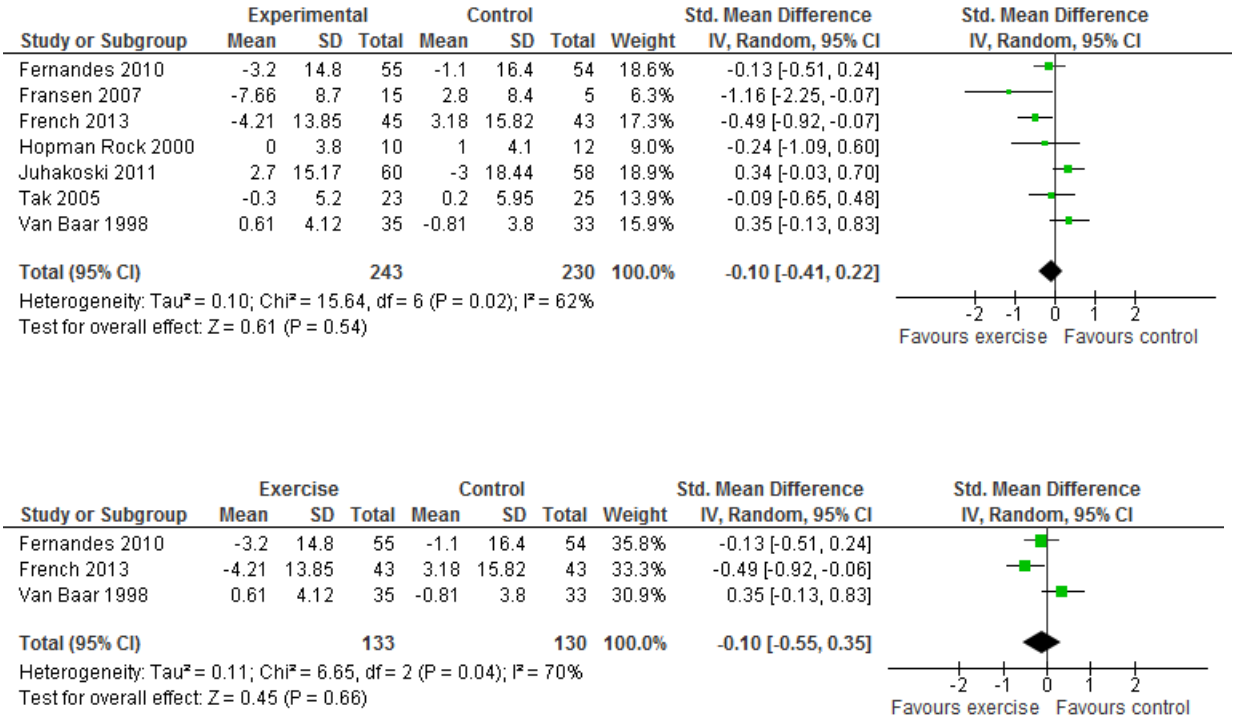


Fig. 3-3. SMD (95% CI) of effect of exercise vs. control on self-reported function post-intervention when all studies are included (top panel) or inclusion of tailored studies only (bottom panel).

3.3.5 Performance-Based Function Outcomes

Pooled data revealed exercise had no effect on the timed-up-and-go test post-intervention (SMD = -0.15 (-0.63 to 0.34), I^2=0%)) [17, 20, 28] or at 5-6 months follow-up (SMD = -0.35 (-0.72

to 0.02), I^2=0%) [20, 28]. Longer-term follow-up data from two studies that could not be pooled supported these findings [17, 26]. Similarly, pooled data from three studies [17, 19, 20, 28] revealed no effect of exercise on the time required to complete a short walk (10-20m) post-intervention (SMD = -0.05 (-0.27 to 0.17), I^2=0%) or at 5 months (SMD = -0.16 (-0.53 to 0.21), I^2=0%) [20, 28] or 12-months follow-up (SMD = -0.21 (-0.65 to 0.23), I^2=31%) [17, 26]. Non-pooled data revealed no change in sit-to-stand scores post-intervention (SMD = 0.11 (-0.31 to 0.52))[19] or at a 52-week follow-up time point (SMD = 0.35 (-0.36 to 1.05)) [26].

3.3.6 Secondary Analyses

Tailored Exercise Programs

Of the four studies that met the criteria for tailored exercise programs, three were included in a meta-analysis [13, 19, 29]. Pooled data revealed that an individualized exercise protocol resulted in moderate improvements in pain (SMD = -0.58 (-1.04 to -0.11), I^2=72%) post-intervention [13, 19, 29](Figure 2), which persisted at 9-10 months follow-up (SMD = -0.47 (-0.84 to -0.10), I^2=29%) [13, 29] as compared to the non-tailored exercise group. However, no persistent effects of semi-tailored exercise on pain (SMD = -0.08 (-0.78 to 0.62)) was observed at 52 weeks follow-up in one non-pooled study[26]. In contrast, pooled results of these three studies indicated that tailored exercise had no effect on self-reported function (SMD = -0.10 (-0.55 to 0.35), I^2=70%) [13, 19, 29] immediately post-intervention. This was supported by non-pooled data taken at follow-up [13].

Recruitment of Hip OA Subjects Only

Data pooling from four studies that recruited hip OA subjects only [13, 17, 19,20] revealed that exercise did not improve pain post-intervention (SMD = -0.04 (-0.55 to 0.48), I^2=84%) (Figure 4) or at 5 and 6 months follow-up when two studies were pooled (SMD = -0.20 (-0.84 to 0.44), I^2=79%) [17, 20]. These findings were supported by a single study that had a 10-month follow-up [13]. Similarly, exercise had no effect on self-reported function post intervention (SMD = -0.08 (-0.45 to 0.28), I^2=66%) [13, 17, 19,20] (Figure 4) or at 5 and 6 months follow-up (SMD = -0.13 (-0.43 to 0.18), I^2=0%) [17,20]. Data pooling was not possible for performance-based physical function outcomes but single studies revealed no effect of exercise on performance-based function outcomes when recruitment was limited to hip patients only [13, 17, 19,20].

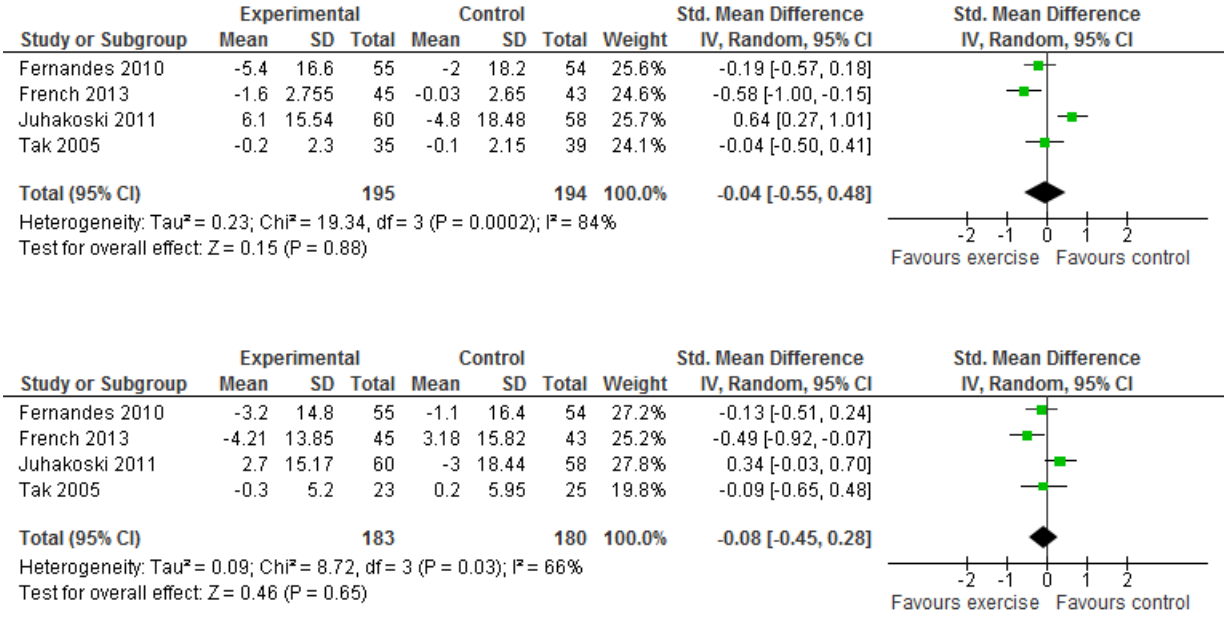


Fig. 3-4. SMD (95% CI) of effect of exercise vs. control on pain (top panel) and self-reported function (bottom panel) in studies recruiting hip OA patients only.

3.4 DISCUSSION

The results of the present systematic review and meta-analysis demonstrate no evidence of an effect of exercise on pain and physical function (both self-reported and performance-based) post-intervention or at follow-up in hip OA patients not awaiting surgery when the entire evidence base is considered (seven pooled studies) or when those studies that recruited hip OA patients only were considered. However, a small beneficial effect of exercise on pain outcomes was observed post-intervention in those studies that prescribed a tailored exercise program based on individual patient findings.

The finding in the present review that pain outcomes were not different between exercise and control groups when considering the literature as a whole is in agreement with the most recent previously published systematic review and meta-analysis examining land-based exercise in hip OA[8]. Comparing results between the present review and the previous review demonstrates that the effect of exercise on pain outcomes in hip OA remains small, non-significant and relatively unchanged [8]. The relative lack of effect of exercise on pain and function outcomes in hip OA patients seen here and in previous reviews may be thought to be a consequence of small study sizes (and therefore decreased power) and/or the heterogeneous recruitment of both hip and knee OA patients (of which hip OA patients are often the minority)[7, 8]. However, the inclusion of several recently published large RCTs (> 45 subjects per treatment arm) [13, 17, 19] in the present review did change the effect of exercise compared with previous reviews. In addition, a pre-specified sub-analysis that examined pain and function outcomes in those studies that recruited hip OA patients only found no differences between control and

intervention groups. Therefore, it does not appear that previously identified methodological issues are the reason for the lack of effect of exercise on pain in hip OA patients with varying degrees of severity. Rather, other factors such as how exercises are prescribed, disease severity, and duration of symptoms may play a role in determining the response to exercise in hip OA populations. These factors may help explain the lack of consistency (as evidenced by high heterogeneity) between studies and the overall lack of systematic effect of exercise therapy in this population.

Despite the finding of unchanged pain outcomes following exercise when the literature is considered as a whole, meta-analysis of studies that tailored the exercise program to the individual physical assessment findings of each patient resulted in small improvements in hip OA pain immediately post-intervention. This finding may help partly explain the relative lack of effect of exercise on hip OA outcomes reported herein and previously and may be an important factor in whether hip OA patients respond positively to exercise. In addition, this finding supports the current stance put forth by several international OA societies and organizations that exercise should be tailored/individualized to each patient's specific problem [1,7]. It should be noted however that this finding is based on three pooled studies in which significant heterogeneity was present and as such should be considered to be preliminary and hypothesis generating at this point in time.

While pain is often the primary outcome variable in clinical exercise studies, function is also a clinically relevant outcome variable, particularly to the patient [30]. Similar to pain outcomes, there was no evidence to suggest that exercise interventions improve self-reported or

performance-based functional outcomes regardless of whether the exercise program was tailored or not. This finding is in agreement with the two most recently published systematic reviews examining hip OA and exercise [8,9]. A potential explanation as to why exercise was found not to have an effect on function in individuals with hip OA might be the well-documented morphological and skeletal abnormalities found across the hip joint in hip OA patients. It has been suggested that most, if not all, cases of hip OA can be attributed to often unrecognized deformities in the hip including subtle femoral head, head-neck, and femoral neck deformities that produce a local or global femoro-acetabular impingement (FAI) that ultimately leads to cartilage and bony breakdown [31]. Thus, if function in individuals with hip OA is primarily the result of underlying bony impingements and abnormal bone-bone contact stresses, it may attenuate the degree to which hip OA function is amendable to exercise therapy. It should be pointed out that exercise was found to improve function in hip OA patients in one previous systematic review [10]. However, higher baseline values of the dependent variable (pain) were found in the control group (as compared to the exercise group), a finding that would favor the exercise group at follow up when post-intervention scores were used to calculate mean differences between groups.

There are strengths and limitations of the present review and meta-analysis. The low risk of bias found in each of the included studies increases confidence in the truthfulness of the results and can be considered to be a strength of the review. In addition, the present review followed the PRISMA guidelines for conducting and reporting systematic reviews and meta-analyses thereby helping improve review thoroughness [32]. A limitation of the present review was the large amount of between-study variation (as evidenced by the high heterogeneity values).

Given that all studies were RCTs and paid equal attention to important methodological quality factors (e.g. randomization, allocation concealment, intention-to-treat analysis), the observed heterogeneity may be explained by differences in the clinical severities, duration of symptoms, and interventions received by study participants. This clinical heterogeneity is common in OA studies given the "heterogeneity of OA as an entity" [3] and therefore represents a source of difficulty when deciding which studies to pool. A second limitation was the element of subjectivity in deciding what constituted a tailored exercise program. While individualized care is now recommended as the standard of care in OA [7], specific criteria as to what defines a tailored exercise program has yet to be determined.

In conclusion, land-based exercise does not appear to improve pain and function in hip OA patients not awaiting surgery when the literature is considered as a whole. A secondary analysis of three pooled studies that provided a tailored exercise program did however result in small improvements in pain in hip OA patients. Heterogeneity was found to be high in both analyses however, suggesting large variability in study findings. Future research directly comparing the clinical efficacy of tailored exercise to non-tailored exercise would help to further elucidate the role of tailored exercise in the management of hip OA. Furthermore, examining the efficacy of exercise across different sub-classifications of hip OA (severity, morphology, BMI) would also provide greater insight into the effect of exercise at different stages or presentations of the disease.

Table 3-1
Summary of Included Studies: Participants, Severity/Diagnosis, Intervention, Follow-up Time Points

Authors	Sample Size (Males: Females)	Group Demographics (Mean, SD)	Severity at Baseline & OA Diagnosis Method	Exercise Group Intervention(s)	Control Group Intervention(s)	Follow-up time point(s) and outcomes
French et al. (2013)	n= 88 (31:57) (Hip OA only)	Exercise Group (n=45) Age: 61.76±9.72 BMI: not specified Control Group(n=43) Age:60.81±9.73 BMI: not specified	Heterogeneous severity (included if not on THR waitlist within next 7 months) ACR Clinical and Radiographic Diagnosis	6-8 individual physiotherapy sessions (30 min.) over 8 weeks with a daily HEP. Also included aerobic exercise 5x/week@30 min per session Strengthening and flexibility exercises delivered using pre-determined protocol but could be tailored to individual patient assessment findings.	Routine GP care and analgesics with avoidance of other interventions	9 weeks; Self-reported pain (NRS); Self-reported PF (WOMAC PF subscale); 50-foot walk test; sit-to-stand test; AROM
Abbott et al. (2013)	n=102 (45:57) (Knee and Hip OA)	Exercise Group (n=14) Age: 66.9±8.2 BMI: 29.3±6.0 Control Group (n=20) Age: 66.1±10.7 BMI: 29.5±5.8	Heterogeneous severity (included if not on THR waitlist in next 6 months; patients that went on to have THR subsequently eliminated from analysis) ACR Clinical Diagnosis	7 sessions (50') over 9 weeks and 2 boosters at week 16 (9 total sessions). Multi-modal supervised programme of aerobic, strengthening, stretching, and neuromuscular exercises. HEP 3x/wk. Also received the control group usual intervention (see adjacent). Semi-tailored based on assessment findings.	Routine GP care and other health care professionals. Allowed to seek other interventions	1 year; Pain Intensity Score (0-10); Composite WOMAC Score; TUG; sit-to-stand; 40m self- paced walk

Juhakoski et al. (2011)	n=120 (37:83) (Hip OA only)	Exercise Group (n=60) Age: 66.9±6.3 BMI: no average given Control Group (n=58) Age: 66.3±6.6 BMI: no average given	Heterogeneous severity(K-L≥1) ACR Clinical and Radiographic Diagnosis	12 supervised sessions (45 min) over 12 weeks and 4 boosters at 12 months. Programme consisted of strengthening, stretching at max effort and tension. HEP 3x/week for 2 years. Also received the control group standard of care (GP, analgesics, and physiotherapy).	Standard care (GP, analgesics, and physiotherapy as needed).	0, 3, 6,12,18,24 months; Self-reported pain (WOMAC-Pain subscale; Self-reported PF (WOMAC-PF subscale); PROM; 6-minute walk test; 10 m walk test; TUG; Sock test; Rand-36 (Finnish SF-36)
Fernandes et al. (2010)	n=109 (50:59) (Hip OA only)	Exercise Group (n=55) Age: 58.4±10.0 BMI: 24.6±3.2 Control Group (n=54) Age: 57.2±9.8 BMI: 24.9±3.8	Heterogeneous severity Minimum Joint Space <4mm for patients < 70 years old and <3mm for patients ≥70 years old and a Harris Hip Score between 60-95 points (patients that moved on to THR during study period were not included in analysis).	Exercise 2-3x/week over 12 weeks that was supervised at least once weekly. Exercise programme consisted of strengthening, functional exercises, and flexibility training. Also received the patient education provided to the control group (see adjacent).	Patient Education consisting of three group-based sessions and one individual session	4, 10, 16 months; Pain (WOMAC- Pain subscale); Self-reported physical function (WOMAC-PF subscale); Health-related QOL (SF-36 v2)

Fransen et al. (2007)	n=97 (25:72) (Knee and Hip OA)	Exercise Group (n=15) Age: 70.8±6.3 BMI: 29.6±5.9 Control Group (n=5) Age: 69.9±6.1 BMI: 30.7±5.0	Heterogeneous severity (no baseline radiographs). Diagnosis of OA as per ACR criteria and pain ≥ 1 year.	Tai Chi exercise program 2 sessions per week (60 min) for 12 weeks. The program is a modification of the Sun style of Tai Chi. Home sessions were not monitored.	No specification as to control group intervention other than "waiting list".	3 and 6 months; Pain (WOMAC-Pain subscale); Self-reported function (WOMAC Function subscale), TUG, 50-foot walk test, SF-12
Tak et al. (2005)	n=109 (34:75) (Hip OA only)	Exercise Group (n=55) Age: 67.4±7.6 BMI: 26.4±3.0 Control Group(n=54) Age: 68.9 BMI: 26.6±4.3	Heterogeneous severity (excluded if on THR waitlist) Diagnosis of OA if a diagnosis of OA had been made by GP and demonstrated clinical symptoms of OA as per the clinical criteria of the ACR.	8 supervised group sessions (60 min) over 8 weeks using fitness equipment (leg press, leg raise, rotation in sitting, leaping squat, pull down, TM, home trainer, pulleys, bowflex, and walking). Also given a home exercise program. Patients also offered ergonomic advice, and dietary recommendations. Sessions were progressed over the training period.	No specific interventions other than self-initiated contact with GP.	8 weeks and 20 weeks; Pain (VAS, HHS pain subscale); Self-reported function (HHS function subscale; TUG); QOL (Health-related QOL scale)
Hopman-Rock et al. (2000)	n=105 (18:87) (Knee and Hip OA)	Exercise Group (n=14) Age: 65.4±5.3 BMI: 28.4±4.8 Control Group (n=20) Age: 65.2±5.7 BMI: 26.8±3	Heterogeneous severity (excluded if on THR waitlist) Self-reported OA of the hip that was later confirmed by ACR radiographic and/or clinical criteria.	6 group exercise sessions over 6 weeks (120 min). First hour was education followed by second hour consisting of exercise programme (consisting of dynamic and static resisted exercises for the hip and knee). Encouraged to do the exercises at home 3x/wk.	Control group was "without intervention."	6 weeks, 6 months; Pain(VAS); TUG, 20m walk test; QOL (using 10 cm VAS); Active-assisted ROM

Van Barr et al. (1998)	n=201 (44:157) (Knee and Hip OA)	Exercise Group (n=39) Age: 68.3±8.4 BMI: not reported Control Group (n=39) Age: 67.7±9.2 BMI: not reported	Heterogeneous severity (excluded if on THR waitlist) Diagnosis of OA by ACR clinical criteria	1-3 sessions/week for 12 weeks (30 min). Individualized exercise therapy based on assessment and included strength, flexibility, mobility, and coordination exercises. In addition, the intervention group received GP mediated education and medication as needed.	Treatment by GP including education and medication as necessary	3, 6, 9 months; Pain (VAS); AAROM, strength

Abbreviations: **BMI**; Body Mass Index, **THR**; Total Hip Replacement, **ACR**; American College of Rheumatology, **K-L**; Kellgren-Lawrence; **OA**; Osteoarthritis, **GP**; General Practitioner, **HEP**; Home Exercise Program, **NRS**; Numeric Rating Scale, **WOMAC-PF**; Western Ontario and McMaster Universities Osteoarthritis Index-Physical Function, **AROM**; Active Range of Motion, **SF-36**; Medical Outcomes Study 36-Item Short-Form Health Survey, **TUG**; Timed Up and Go, **VAS**; Visual Analogue Scale, **HHS**; Harris Hip Score, **QOL**; Quality of Life, **AROM**; Active Assisted Range of Motion, **PROM**; Passive Range of Motion

3.5 REFERENCES

1. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden S, et al. OARSI recommendations for the management of hip and knee osteoarthritis, part I: critical appraisal of existing treatment guidelines and systematic review of current research evidence. Osteoarthritis Cartilage 2007; 15(9): 981-1000.
2. Hunter DJ, McDougall JJ, Keefe FJ. The symptoms of osteoarthritis and the genesis of pain. Rheum Dis Clin North Am 2008, 34(3), 623-43.
3. Lane NE, Brandt K, Hawker G, Peeva E, Schreyer E, Tsuji W, et al. OARSI-FDA initiative: defining the disease state of osteoarthritis. Osteoarthritis Cartilage 2011; 19(5): 478-82.
4. Dieppe PA, Lohmander LS. Pathogenesis and management of pain in osteoarthritis. Lancet 2005; 365: 965-73.
5. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden S, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage 2010; 18(4): 476-99.
6. Loureiro A, Mills PM, Barrett RS. Muscle weakness in hip osteoarthritis: a systematic review. Arthritis Care Res (Hoboken) 2013; 65(3): 340-52.
7. Fernandes L, Hagen KB, Bijlsma JW, Andreassen O, Christensen P, Conaghan PG, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. Ann Rheum Dis 2013; 72(7): 1125-35.

8. Fransen M, McConnell S, Hernandez-Molina G, Reichenbach S. Does land-based exercise reduce pain and disability associated with hip osteoarthritis? A meta-analysis of randomized controlled trials. Osteoarthritis Cartilage 2010; 18(5): 613-20.

9. McNairPJ, Simmonds MA, Boocock MG, Larmer PJ. Exercise therapy for the management of osteoarthritis of the hip joint: a systematic review. Arthritis Res Ther 2009; 11(3): R98.

10. Hernandez-Molina G, Reichenbach S, Zhang B, LaValley M, Felson D. Effect of therapeutic exercise for hip osteoarthritis pain: results of a meta-analysis. Arthritis Rheum 2008; 59(9): 1221-8.

11. Dobson F, Hinman RS, Roos EM, Abbott JH, Stratford P, Davis AM, et al. OARSI recommended performance-based tests to assess physical function in people diagnosed with hip or knee osteoarthritis. Osteoarthritis Cartilage 2013; 21(8): 1042-52.

12. Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, et al. The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip. Arthritis Rheum 1991; 34(5): p. 505-14.

13. Fernandes L, Storheim K, Sandvik I, Nordsletten I, Risberg MA. Efficacy of patient education and supervised exercise vs patient education alone in patients with hip osteoarthritis: a single blind randomized clinical trial. Osteoarthritis Cartilage 2010; 18(10): 1237-43.

14. Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. BMC Musculoskelet Disord 2008; 9: 116.

15. Verhagen AP, de Vet HC, de Bie RA, Kessels AG, Boers M, Bouter M, et al. The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. J Clin Epidemiol 1998; 51(12): 1235-41.

16. Landis JR, Koch GG. The Measurement of Observer Agreement for Categorical Data. Biometrics 1977; 33: 159-174.

17. Juhakoski R, Tenhonen S, Malmivaara A, Kiviniemi V, Anttonen T, Arokoski J. A pragmatic randomized controlled study of the effectiveness and cost consequences of exercise therapy in hip osteoarthritis. Clin Rehabil 2011; 25(4): 370-83.

18. Higgins JP. Commentary: Heterogeneity in meta-analysis should be expected and appropriately quantified. Int J Epidemiol 2008, 37(5): 1158-60.

19. French HP, Cusack T, Brennan A, Caffrey A, Conroy R, Cuddy V, et al. Exercise and manual physiotherapy arthritis research trial (EMPART) for osteoarthritis of the hip: a multicenter randomized controlled trial. Arch Phys Med Rehabil 2013; 94(2): 302-14.

20. Tak E, Staats P, Van Hepsen A, Hopman-Rock M. The effects of an exercise program for older adults with osteoarthritis of the hip. J Rheumatol 2005; 32(6): 1106-13.

21. Foley A, Halbert J, Hewitt T, Crotty M. Does hydrotherapy improve strength and physical function in patients with osteoarthritis--a randomised controlled trial comparing a gym based and a hydrotherapy based strengthening programme. Ann Rheum Dis 2003; 62(12): 1162-7.

22. Heuts PH, de Bie R, Drietelaar M, Aretz K, Hopman-Rock M, Bastiaenen CH, et al. Self-management in osteoarthritis of hip or knee: a randomized clinical trial in a primary healthcare setting. J Rheumatol 2005; 32(3): 543-9.

23. Ravaud P, Giraudeau B, Logeart I, Larguier JS, Rolland D, Treves R, et al. Management of osteoarthritis (OA) with an unsupervised home based program and/or patient administered assessment tools. A cluster randomized controlled trial with a 2x2 factorial design. Ann Rheum Dis 2004; 63(6): 703-708.

24. Dejong OR, Hopman-Rock M., Tak EC, Klazinga NS. An implementation study of two evidence-based exercise and health education programmes for older adults with ostoearthritis of the knee and hip. Health Edu Res 2004; 19(3): 316-325.

25. van Baar ME, Dekker J, Oostendrop RA, Bijl D, Voorn TB, Bijlsma JW. Effectiveness of exercise in patients with osteoarthritis of hip or knee: nine months' follow up. Ann Rheum Dis 2001; 60(12): 1123-30.

26. Abbott JH, Robertson MC, Chapple C, Pinto D, Wright AA, Leon de la Barra S, et al. Manual therapy, exercise therapy, or both, in addition to usual care, for osteoarthritis of the hip or knee: a randomized controlled trial. 1: clinical effectiveness. Osteoarthritis Cartilage 2013; 21(4): 525-34.

27. Fransen M, Nairn L, Winstanley J, Lam P, Edmonds J. Physical activity for osteoarthritis management: a randomized controlled clinical trial evaluating hydrotherapy or Tai Chi classes. Arthritis Rheum 2007; 57(3): 407-14.

28. Hopman-Rock M, Westhoff MH. The effects of a health educational and exercise program for older adults with osteoarthritis for the hip or knee. The Journal of Rheumatology 2000; 27(8): 1947-1954.

29. Van Baar ME, Dekker J, Oostendrop R, Bijl D, Voorn TB, Lemmen JM. The effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a randomized clinical trial. J Rheumatol 1998; 25(12): 2432-9.

30. Davis AM, Perruccio AV, Canizares M, Tennant A, Hawker GA, Conaghan PG, et al. The development of a short measure of physical function for hip OA HOOS-Physical Function Shortform (HOOS-PS): an OARSI/OMERACT initiative. Osteoarthritis Cartilage 2008; 16(5): 551-9.

31. Ganz R, Parvizi J, Beck M, Leunig M, Notzli H, Siebenrock KA. Femoroacetabular impingement: a cause for osteoarthritis of the hip. Clin Orthop Relat Res 2003(417): 112-20.

32. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009; 339: b2535.

3.6 BRIDGE TO UPCOMING THESIS CHAPTERS:

This was an important chapter in this thesis since it provided an up to date summary of the efficacy of exercise in hip OA. Given that the effect size of exercise was found to be small herein, it provided evidence and justification for more novel approaches as it relates to exercise interventions in hip OA. Subsequently, we developed a novel assessment strategy and personalized intervention with the aim to improve the effect of exercise in this population.

5 CHAPTER 4:

KINEMATIC GAIT PATTERNS AND THEIR RELATIONSHIP TO PAIN IN MILD-TO-MODERATE HIP OSTEOARTHRITIS

Abstract

Background: Mild to moderate hip osteoarthritis is often managed clinically in a non-surgical manner. Effective non-surgical management of this population requires characterizing the specific impairments within this group. To date, a complete description of all lower extremity kinematics in mild-to-moderate hip osteoarthritis patients has not been presented. The aim of the present study is to describe the lower extremity gait kinematics in mild-to-moderate hip osteoarthritis patients and explore the relationship between kinematics and pain.

Methods: 22 subjects with mild-to-moderate radiographic hip osteoarthritis (Kellgren-Lawrence grade 2-3) and 22 healthy age and BMI matched control subjects participated. Kinematic treadmill walking data were collected across all lower extremity joints. A two-way repeated measures analysis of variance estimated mean differences in gait kinematics between groups. Correlations between gait kinematics and pain were assessed using a Spearman Correlation Coefficient.

Findings: Hip osteoarthritis subjects hiked their unsupported hemi-pelvis 1.40 degrees ($P < 0.001$) more than controls and tilted their pelvis 4.65 degrees more anteriorly ($P = 0.01$). Osteoarthritis subjects walked with 4.30 degrees more peak hip abduction ($P < 0.001$), 8.57 degrees less peak hip extension ($P < 0.001$), and 10.54 degrees more peak hip external rotation ($P < 0.001$). Kinematics were related to pain in the ankle frontal plane only ($r=-0.43$, $P< 0.05$).

Interpretation: Individuals with mild-to-moderate hip osteoarthritis demonstrate altered gait biomechanics not related to pain. These altered biomechanics may represent effective

therapeutic targets by clinicians working with this population. Understanding the underlying patho-anatomic changes that lead to these biomechanical changes requires further investigation.

4.1 INTRODUCTION

Hip osteoarthritis (hip OA) can be a leading cause of pain, loss of function, and long-term disability and is managed either surgically or with conservative therapies depending on the severity of the disease and/or the level of patient disability (Badley et al., 1995; Nelson et al., 2014). While surgical interventions are effective management strategies in those with end-stage hip OA (Ewen et al., 2012), the majority of individuals with hip OA are non-surgical candidates for whom conservative management therapies are the first treatment option (Dieppe and Lohmander 2005). Given the current and expected increase in prevalence of individuals with non-surgical hip OA, an increased understanding of how milder forms of hip OA can be best managed conservatively has been identified as a priority (Fernandes et al., 2013).

Effective management of chronic conditions such as hip OA necessitates a detailed description of the impairments and functional limitations within that population in order to help guide the treating clinician (Mills et al., 2013a; Mills et al., 2013b). To date, an increasing body of literature is beginning to emerge that describes the limitations found in individuals with both mild-to-moderate and severe hip OA. It has been demonstrated that individuals with severe hip OA awaiting hip surgery report decreased functional ability and demonstrate functional impairments on objective function testing that appears related to pain and strength changes (Zeni et al., 2014). In addition, movement pattern changes, as measured by 3D gait analysis, have also been widely demonstrated in end-stage hip OA individuals, particularly in the sagittal plane of the hip, knee, and ankle (Meyer et al., 2015; Zeni et al., 2015; Schmitt et al., 2015). Of particular interest are the ambulation patterns in individuals with mild-to-moderate hip OA

given the important role that biomechanics are thought to play in the OA disease process (Brandt et al., 2008), and since detection of early disease changes increases the likelihood of halting or reversing the disease trajectory (Hunter, 2011). Studies examining the kinematic gait patterns of individuals with mild-to-moderate hip OA demonstrate that this population walks with decreased sagittal plane hip movement, compensatory changes in sagittal plane knee and ankle movements (Eitzen et al., 2012; Watelain et al., 2001), and altered frontal plane center of mass movements that may predispose them to an increased risk of falls (Lin et al., 2015). In addition, the best kinematic discriminator between healthy control subjects and individuals with early hip OA also appears to lie in the sagittal plane (Laroche et al., 2014). While the gait kinematics of individuals with mild-to-moderate hip OA is becoming more completely described (Kumar et al., 2015), there has not, to our knowledge, been a description of joint kinematics across all lower extremity segments (pelvis, hip, knee, and ankle) in all three anatomical planes (sagittal, transverse, frontal). In addition, an exploration of how gait kinematics are influenced by pain in individuals with mild-to-moderate hip OA is also needed given the potential role pain may have on gait variable outcomes. While the relationship between pain and gait kinematics has been explored in end-stage hip OA (Zeni et al., 2014) and in the sagittal plane in mild-to-moderate hip OA (Hurwitz et al., 1997), a complete description of this relationship in mild-to-moderate hip OA is still needed.

Therefore, the purpose of the present study was to provide a comprehensive description of the gait kinematics in individuals with radiographic evidence of mild-to-moderate hip OA and compare these findings with healthy age-matched controls. In addition, an understanding of how these kinematics relate to pain was sought. We hypothesized that hip OA patients would

walk with decreased range of motion (ROM) in the sagittal plane and that decreases in ROM across the transverse and frontal planes would also be observed as early-stage changes. It was further hypothesized that the increased frontal and transverse plane motions would be related to pain as hip OA patients attempted to off-load their affected hip.

4.2 METHODS

4.2.1 Recruitment and Sample

In this cross-sectional study, and based on an a priori power analyses (β=0.20; P=0.05), 22 individuals with mild-to-moderate radiographic hip OA and 22 healthy age and BMI matched subjects participated in the present study. Hip OA subjects were recruited by convenience between June 2013 and May 2014 and subject inclusion criteria were: 1) fulfillment of the American College of Rheumatology (ACR) criteria for hip OA which includes pain and radiographic changes (Altman et al., 1991); 2) standing AP radiograph of the pelvis taken within the past 2 years that demonstrates Kellgren and Lawrence (KL) Grade 2-3 changes (Kellgren and Lawrence, 1957); 3) aged 35-70 years old; 4) pain of at least 2 of 10 on a visual analogue scale (VAS) in either hip or groin. Exclusion criteria included: 1) prior ipsilateral and/or contralateral surgery or clinically diagnosed musculoskeletal, neurological, or joint pathology causing pain or affecting function of the low back, pelvis, or lower extremities; 2) current or past (within 3 months) intra-articular corticosteroid use; 3) participation in a strengthening, stretching, or rehabilitation program currently or in the past 3 months; 4) any other systemic arthritic conditions (e.g. rheumatoid arthritis, spondyloarthropathies); 5) inability to abstain from

medication for 24 hours; 6) previous medical conditions (e.g. stroke) that affect gait patterns. Use of analgesics and other prescribed medications were permitted during the study but not 24 hours before testing. In those subjects with bilateral hip OA involvement, the most painful hip was used as the joint of interest. The control group was made up of healthy individuals, matched on age and body mass index (BMI), who had previously been recruited by convenience and had completed a 3D gait analysis in our lab. The present study was approved by the University of Calgary Conjoint Health and Research Ethics Board and written informed consent was obtained from each subject prior to study commencement.

4.2.2 Pain and Self-Report Questionnaires

Pain (independent variable) was assessed for each subject using a 10 cm VAS with extremes anchored at 0 cm = "no pain" and 10 cm = "worst imaginable pain". Subjects were asked to rate their pain on average over the past 1-week with all life activities considered. Subject function was assessed using the 17 question function sub-scale of the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) questionnaire (McConnell et al., 2001), while Quality of Life was assessed using the Assessment of Quality of Life Questionnaire (V2) (AQOL-V2) (Whitfield et al., 2006).

4.2.3 Radiographs and OA Definition

Standing anterior-posterior (A-P) radiographs of the pelvis (taken within the past two years) were obtained from each participant. A-P radiographs for each subject were read and graded by different radiologists owing to the two year rolling recruitment. Only those subjects whose

radiographs demonstrated Kellgren and Lawrence (KL) grade 2-3 changes (mild-to-moderate) (Kellgren and Lawrence, 1957) were considered eligible for the present study.

4.2.4 Gait Analysis

Kinematic data were collected using an 8-camera 3D motion capture system (Vicon MX-3+, Vicon, Oxford, UK) at a frequency of 200 Hz. Prior to the collection of gait data, 9 mm spherical retro-reflective markers were placed on the pelvis and lower extremities bilaterally according to the marker set used by Osis et al. (2014a). Specifically, anatomical markers were specifically placed on the following bilateral anatomical landmarks: iliac crest; greater trochanter; anterior superior iliac spine; medial and lateral femoral condyles; fibular head; tibial tuberosity; medial and lateral malleoli; 1^{st} and 5^{th} metatarsal heads.

In order to track segment positions during gait, marker clusters comprised of rigid shells ("technical clusters") were placed over the pelvis, thighs, and shanks. A technical cluster with 3 affixed markers was placed over the pelvis, and clusters with 4 affixed markers were placed over the thighs and shanks bilaterally. A technical marker cluster was established for the foot by aligning two markers vertically along the posterior heel counter of the shoe and placing one marker laterally (Pohl et al., 2010). Following placement of anatomical and technical markers, a static standing trial was collected with each subjects' feet placed 0.3 m apart, aligned with a graphic template underfoot. This standing static trial permits a determination of the position of anatomical landmarks with respect to the technical clusters (Cappozzo, 1995) as well as the construction of joint coordinate systems (Cole et al., 1993).

Following completion of the static trial, anatomical markers were removed and subjects walked on a treadmill at a speed of 1.1 m/s for five minutes. Before the collection of dynamic walking data, subjects walked on the treadmill for 3-5 min to allow an accommodation to the speed of the treadmill and to facilitate a natural walking pattern (Pohl et al., 2010). Kinematic data from at least 10 consecutive footfalls of the target limb during stance were collected, following the accommodation period (Pohl et al., 2010). Subjects wore standardized shoes provided by the laboratory (Nike Air Pegasus, Nike Inc, USA).

Using custom MATLAB software (R2010a), technical and anatomical coordinate systems were established for each of the pelvis, thigh, shank, and foot using technical and anatomical markers respectively (Cole et al., 1993). Technical coordinate systems were defined for each segment using the technical clusters affixed to a given segment while anatomical coordinate systems were defined for each segment using anatomical markers. Hip joint centres were calculated using the greater trochanter method, whereby the hip joint centre is located 25% of the inter-trochanteric distance along the three-dimensional line connecting the ipsilateral with the contralateral trochanter marker (Weinhandl et al., 2010). Knee and ankle joint centres were calculated as the three-dimensional mid-point of the distance between the medial and lateral femoral condyles and medial and lateral malleoli, respectively. Joint angles were calculated using the singular value decomposition methods of Soderqvist et al. (1993), where distal segment orientations were calculated relative to proximal segment orientations. Peak joint angles were obtained in all three planes (sagittal, frontal, transverse) across the pelvis, hip, knee, and ankle at mid-stance (the time point corresponding to 20% of the gait cycle), terminal hip extension, and toe off. These time points correspond to events in the gait cycle that have

been reported in previous hip OA studies (Eitzen et al. 2012). Time series curves for the control and hip OA groups were constructed by normalizing the stance phase data of each subject to 101 points, followed by taking an ensemble average of these data points for each group across each joint and plane.

4.2.5 Data Analysis

Mean and standard deviations were calculated for patient demographics as well as pain and biomechanical variables. Mean differences in gait kinematics between healthy controls and individuals with hip OA were calculated using a two-way repeated measures ANOVA with group and time (i.e. mid-stance, terminal hip extension, toe-off) as the independent variables. The assumptions for the use of a two-way repeated measures ANOVA were 1) no outliers; 2) normality of the dependent variable for each level of the independent variable; and 3) equal variance between groups were tested using box-plots, Shapiro-Wilk's normality test, and Mauchly's Sphericity test, respectively. Extreme outliers (i.e. those greater than 3 box lengths away from the edge of their box) were removed while those sitting 1.5 box lengths from the edge of the box were not removed and a sensitivity analysis was used to determine whether they influenced the primary analysis. In instances when sphericity was violated, a Greenhouse Geisser correction was used. The relationship between pain and walking biomechanics was determined using the Spearman Rank-Order Correlation coefficient (rho) with pain as the independent variable and gait kinematic variables as the dependent variables. A Spearman Correlation coefficient was chosen since pain and biomechanics were not linearly related and

since outliers were present. Only those kinematic variables found to be significantly different between the control and hip OA groups (see Table 2) were used in the correlation analysis.

4.3. RESULTS

4.3.1 Demographics

No differences in demographic characteristics (i.e. age, gender, BMI) were found between groups (Table 1).

Table 4-1. Mean (SD) demographic and clinical values for Control (CON) and Hip Osteoarthritis (HIP OA) groups.

	CON (n=22)	HIP OA (n=23)	P-VALUE
Demographics			
Age (y)	53.7 (8.3)	55.9 (7.5)	0.30
Gender (Males : Females)	9M:13F	11M:12F	n/a
Height (cm)	168.8 (9.5)	170.2 (8.0)	0.55
Weight (kg)	76.5 (9.4)	76.8 (15.4)	0.79
BMI (kg/m²)	26.8 (1.5)	26.5 (4.6)	0.89
Clinical Characteristics			
Pain (/10)	n/a	3.9 (2.4)	-
Function (/68)	n/a	24.1(10.7)	-
Quality of Life	n/a	41.3 (9.2)	-
Duration of Symptoms (y)	n/a	3.7 (2.6)	-
Unilateral : Bilateral	n/a	6 Bil : 16 Uni	-

Pain measured using 10cm VAS scale where higher scores are increased pain; Function measured using Western Ontario McMaster Universities Arthritis Index where higher score is poorer function; Quality of Life measured using Assessment of Quality of Life questionnaire where higher score is worse quality of life.

4.3.2 Gait Kinematics

Significant differences in pelvis kinematics were observed between groups across all three planes (Table 4-2, Figure 1). At mid-stance, individuals with hip OA (HOA) hiked their unsupported hemi-pelvis compared with controls (CON) (CON: 0.76° (1.46) ; HOA: -0.64° (1.50) , P=0.006, where +ve = drop non-weight bearing side pelvis; -ve = hike non weight bearing side) and demonstrated increased pelvic rotation in the transverse plane of the affected stance leg (CON: 0.80° (3.73); HOA: -2.33° (4.04), P=0.01, where +ve = relative hip internal rotation; -ve = relative hip external rotation). At terminal hip extension, individuals with hip OA demonstrated an increased anterior pelvic tilt compared with controls (CON: -0.79° (3.50); HOA: -3.86° (3.64), P=0.01, where +ve = anterior tilt; -ve = posterior tilt).

Significant differences in hip kinematics were also observed between groups across all three planes (Table 4-2, Figure 1). During mid-stance, individuals with hip OA demonstrated increased peak hip abduction (CON: 2.64° (3.59) ; HOA: -1.66° (3.50) , P=0.003, where +ve = hip adduction; -ve = hip abduction) (Table 2). In terminal hip extension, individuals with hip OA exhibited decreased peak hip extension (CON: 12.53° (7.05); HOA 3.96° (5.77), P=0.005, where +ve = hip extension; -ve = hip flexion) and increased peak hip external rotation (CON: 5.57° (6.22) ; HOA: -4.97 (5.22) , P=0.0002, where +ve = hip internal rotation; -ve = hip external rotation). At toe-off, those with hip OA continued to demonstrate increased peak external rotation (CON: 7.51° (6.60); HOA: 0.17° (5.04), P=0.006).

Table 4-2. Mean Peak ROM values at Mid-Stance, Terminal Hip Extension, and Toe Off in Control (CON) and Hip Osteoarthritis (HOA) groups										
		Mid-Stance			**Terminal Hip Extension**			**Toe Off**		
		CON	HOA	*P*	CON	HOA	*P*	CON	HOA	*P*
Pelvis	Sagittal (°)	0.71(3.59)	-0.41(4.30)	0.35	-0.79(3.5)	-3.86(3.64)	0.01*	0.81(3.40)	-1.16(3.85)	0.08
	Frontal (°)	0.76(1.46)	-0.64(1.5)	0.00*	1.11(1.49)	0.73(2.18)	0.50	-1.56(1.49)	-1.73(2.31)	0.77
	Transverse (°)	0.80(3.73)	-2.33(4.04)	0.01*	0.53(3.01)	1.42(3.75)	0.39	-0.56(2.65)	1.41(3.82)	0.051
Hip	Sagittal (°)	-23.01(6.80)	-22.73(6.07)	0.88	12.53(7.05)	3.96(5.77)	0.00*	-4.32(8.20)	-7.05(5.08)	0.18
	Frontal (°)	2.64(3.59)	-1.66(3.5)	0.00*	4.07(3.21)	3.07(2.88)	0.28	-1.62(3.03)	-2.30(3.14)	0.47
	Transverse (°)	-6.09(5.98)	-9.27(6.94)	0.11	5.57(6.22)	-4.97(5.22)	0.00*	7.51(6.60)	0.17(5.04)	0.00*
Knee	Sagittal (°)	18.47(6.2)	17.61(5.3)	0.62	11.90(5.98)	21.03(6.4)	0.00*	53.78(6.8)	54.09(5.0)	0.86
	Frontal (°)	-5.35(3.8)	-3.98(3.6)	0.22	-4.50(3.5)	-4.94(3.2)	0.66	-14.81(8.0)	-13.41(7.5)	0.55
	Transverse (°)	16.44(8.8)	22.37(6.8)	0.02*	9.72(8.3)	15.68(6.3)	0.01*	5.64(6.9)	8.85(5.1)	0.08
Ankle	Sagittal (°)	3.92(3.7)	3.75(2.9)	0.86	-12.35(3.3)	-13.63(2.6)	0.15	11.70 (5.8)	10.86(4.8)	0.60
	Frontal (°)	-3.98(2.77)	-4.44(2.75)	0.58	0.67(2.72)	1.34(2.86)	0.43	3.54(3.31)	0.71(4.92)	0.03*
	Transverse (°)	0.82(5.36)	1.78(6.43)	0.59	-2.84(6.31)	-0.28(5.25)	0.15	-6.24(6.92)	-4.72(8.06)	0.50

***Denotes significant difference between CON and HOA at P< 0.05**

Pelvis: Sagittal Plane: +ve = posterior tilt, -ve = anterior tilt

Frontal Plane: +ve = drop non-weight bearing side pelvis, -ve =hike non-weight bearing side pelvis

Transverse Plane: +ve = relative hip internal rotation, -ve =relative hip external rotation

Hip: Sagittal Plane: +ve = extension, -ve = flexion

Frontal Plane: +ve = adduction, -ve = abduction

Transverse Plane: +ve = internal rotation, -ve = external rotation

Knee: Sagittal Plane: +ve = flexion, -ve = extension

Frontal Plane: +ve = adduction, -ve = abduction

Transverse Plane: +ve = external rotation, -ve = internal rotation

Ankle: Sagittal Plane: +ve = plantarflexion, -ve = dorsiflexion

Frontal Plane: +ve = inversion, -ve = eversion

Transverse Plane: +ve = external rotation of foot, -ve = internal rotation of foot

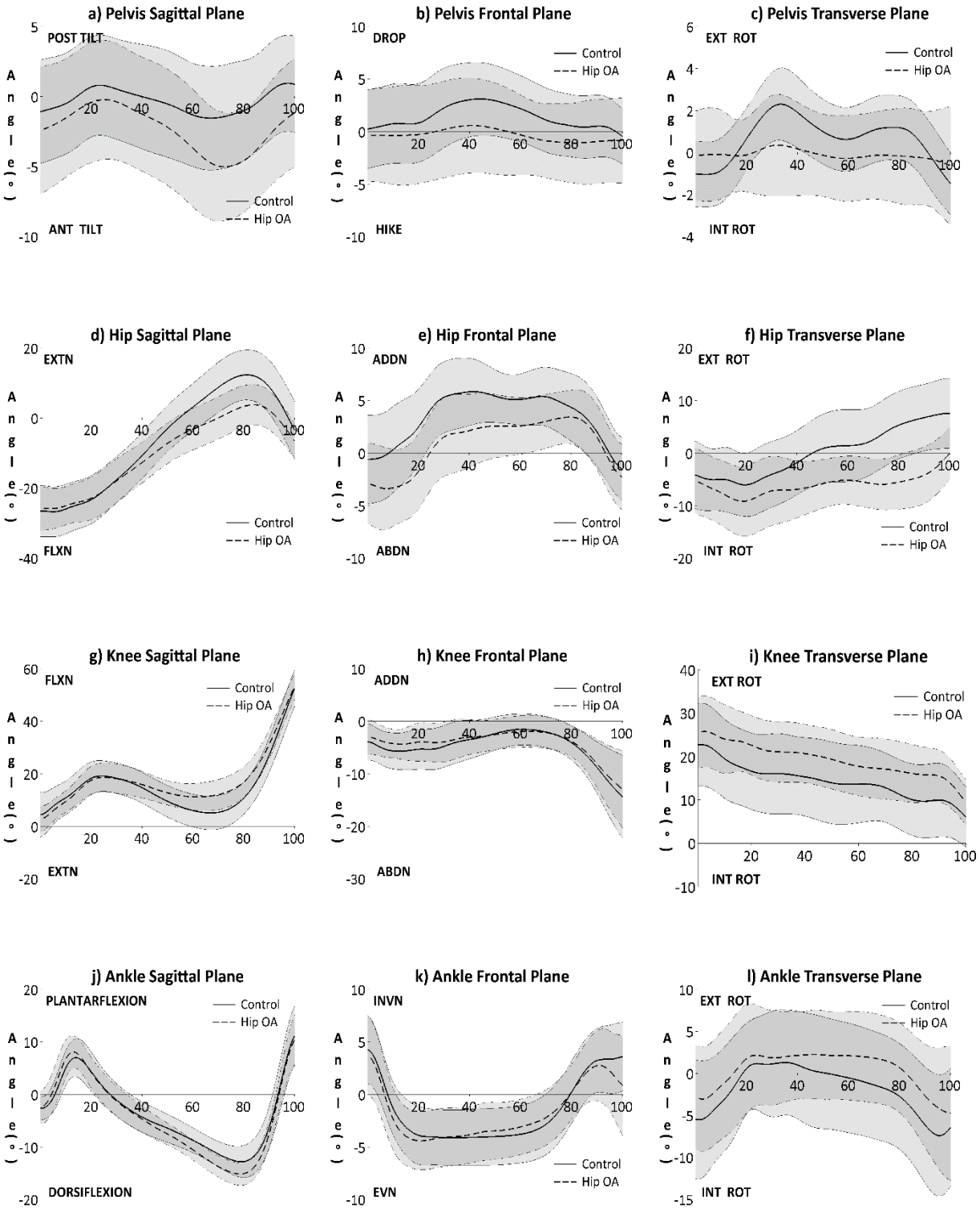


Figure 4-1. Mean ensemble joint kinematics (with grey bar standard deviations) across the pelvis, hip, knee, and ankle for Control and Hip OA groups (solid line is mean for Control group, Dashed line is mean for Hip OA group). Percent of stance phase is represented on the x-axis.

Individuals with hip OA demonstrated significantly increased knee external rotation at mid-stance as compared with controls (CON: 16.44° (8.8); HOA: 22.37° (6.8), P=0.02, where +ve = knee external rotation;), and significantly increased knee flexion (CON: 11.90 (5.98); HOA: 21.03 (6.4), P=0.0003, where +ve = knee flexion) and knee external rotation (CON: 9.72° (8.3); HOA: 15.68° (6.3), P=0.01, where +ve = knee external rotation) at terminal hip extension (Table 2).

No differences in ankle kinematics were observed between groups with the exception that hip OA patients exhibited reduced ankle inversion at toe-off (CON: 3.54°(3.31); HOA: 0.71°(4.92), P=0.03, where +ve = ankle inversion) (Figure 1, Table 2).

4.3.3 Pain-Biomechanics Relationship

No significant correlations were observed between pain and walking biomechanics in individuals with hip OA with the exception of frontal plane ankle ROM at toe off (r= -0.43, P=0.048).

4.4 DISCUSSION

The aim of the present study was to provide a comprehensive description of the gait biomechanics in a group of individuals with radiographically determined mild-to-moderate hip OA. We found that these individuals demonstrated significantly altered walking gait biomechanics as compared to a group of healthy individuals and that these alterations take place predominantly across the pelvis and hip.

Our finding that individuals with mild-to-moderate hip OA walk with decreased hip extension and increased knee flexion at terminal hip extension is in agreement with a recently published trial of hip OA patients with both severe and mild-to-moderate symptoms (Eitzen et al., 2012). It should be noted however, that the walking speeds used by Eitzen et al. (2012) were different as compared to the current study making direct comparisons difficult. However, decreased hip sagittal plane motion has also been previously reported for individuals with severe hip OA awaiting surgery (Hurwitz et al., 1997) and in those with severe bilateral hip OA (Kubota et al., 2007). Thus, results of the present study, and those of previous studies, suggest that reduced hip sagittal plane motion may be considered characteristic of hip OA regardless of severity. Previous studies have also suggested that muscle tightness, articular changes, or capsular changes in these individuals may explain the sagittal plane changes (Hurwitz et al., 1997, Holla et al., 2011). In addition, the increased anterior pelvic tilt at terminal hip extension observed in the present study likely represents a compensatory mechanism to increase forward excursion of the centre-of-mass at this time point (Thurston, 1985). To our knowledge, only one previous

study has examined hip kinematics in the transverse plane in individuals with hip OA (Watelain et al., 2001). However, in contrast to the results of the present study, Watelain et al. (2011) reported that mild-to-moderate hip OA subjects exhibited increased internal rotation at toe-off. While an explanation for these differences between studies is not readily apparent, we found that hip OA patients in our study also walked with increased pelvic rotation in the transverse plane that favoured hip external rotation. We suspect that individuals in the present study walked in a more externally rotated position as an adaptive response to the reduced active and passive hip internal rotation ROM available to hip OA patients (Holla et al., 2011).

Despite an evaluation of all planes of motion across all lower extremity joints, our results suggest that the majority of adaptations take place almost exclusively across the pelvis and hip with very few differences between groups in knee and ankle kinematics. The altered motions exhibited by hip OA patients are, however, not restricted to the sagittal plane as differences between groups were also seen across the transverse and frontal planes. Understanding whether these functional gait changes are adaptations to pain, ROM restrictions, weakness, articular changes, or whether they are primary to the hip OA disease process itself may help facilitate clinical management of this patient population. It has been suggested that the kinematic/ROM deficits observed during walking in individuals with hip OA appear to be related to passive soft tissue changes rather than a pain-avoidance mechanism (Hurwitz et al., 1997). While an association between clinical flexibility measurements and dynamic gait variables was not tested in the present study, we found a lack of correlation between pain and those kinematic variables found to be different in hip OA individuals (as compared with controls), suggesting pain may not explain the altered kinematics in this population. Regardless, a recent

randomized controlled trial in hip OA patients examining the effect of an 8-week individualized manual therapy and exercise program, as compared with sham ultrasound placebo, found no differences post-treatment across groups with respect to pain, function, strength, or flexibility (Bennell et al., 2014), suggesting change in this population may be difficult.

Limitations to the present study are acknowledged. First, gait kinetics were not presented, which may provide more information on the joint loading characteristics of this population. Second, joint angle calculations are influenced by marker placement accuracy, a well-known potential source of error in gait analysis (McGinley et al., 2009). However, since one tester was used for all gait analyses, it is expected that these errors would be minimized and be similar across groups. In addition, a recently published novel method for evaluating error in anatomical marker placement (Osis et al., 2015) was employed in the present study, thereby increasing our confidence in our marker placement accuracy. It should also be noted that it is thought that the majority of gait variables show errors that fall between 2°-5° (McGinley et al., 2009). Given that the difference between groups across the pelvis were small (~ 2 degrees), the clinical significance of these differences is of some question. Third, given the well documented discordance between radiographic severity and patient reported symptoms in OA (Bedson et al., 2008), a clear definition of what constitutes mild vs moderate vs severe disease states remains elusive (Lane et al., 2011). It is therefore acknowledged that while all the subjects included in the present study were considered mild-to-moderate from a radiographic standpoint, using patient reported symptoms (e.g. VAS) might have yielded a different definition of OA disease status in the included sample. However, the average pain score of the included individuals in the present study was 3.9 out of 10 on a 10 cm VAS scale. A second

factor influencing the determination of patient severity in the present study is the radiographic scoring technique used. In a previous study examining the reliability of three different radiographic scoring methods in hip OA, it was reported that categorical joint space width had a higher inter-rater reliability coefficient (weighted kappa = 0.71) as compared with the K-L radiographic severity score and Osteoarthritis Research Society International joint space narrowing score (weighted kappa = 0.44 and 0.47, respectively) (Gossec et al., 2009). Thus, consistency between raters when using a K-L scoring system can be considered fair at best. Since K-L scores were used in the present study, as determined by different radiologists, it can be questioned whether the diagnosis of mild-to-moderate radiographic OA was equivalent between subjects. Regardless, having one radiologist rate all hip OA patients used in the present study would have been difficult in light of the recruitment strategy.

CONCLUSIONS

Individuals with mild-to-moderate hip OA exhibit atypical gait biomechanics as compared with healthy age and BMI matched individuals. These altered gait patterns occur predominantly across the pelvis and hip joint and do not appear related to a pain-avoidance mechanism. Whether these atypical gait patterns contribute to the progression of the hip OA disease process or are a compensatory adaptation to the underlying disease warrants future research.

4.6 REFERENCES

1. Altman R, Alacron G, Appelrouth D, Bloch D, Borenstein D, Brandt K, Brown C, Cooke TD, Daniel W, Feldman D et al. Arthritis Rheum 1991 34, 505-14.
2. Badley EM. The effect of osteoarthritis on disability and health care use in Canada. *Journal of Rheumatology* 1995; (supplement 43) 22:19–22.
3. Bedson J, Croft PR. The Discordance Between Clinical and Radiographic Knee Osteoarthritis: A Systematic Search and Summary of the Literature. BMC Musculoskeletal Disorders 2008 9:116.
4. Bell AL, Pedersen DR, Brand RA. A comparison of several hip center location prediction methods. Journal of Biomechanics; 1990; 23:617-21.
5. Bennell KL, Egerton T, Martin J, Abbott JH, Metcalf B, McManus F, Sims K, Pua YH, Wrigley TV, Forbes A, Smith C, Harris A, Buchbinder R. Effect of Physical Therapy on Pain and Function in Patients with Hip Osteoarthritis: A Randomized Controlled Trial. JAMA 2014. 311(19) 1987-97.
6. Brandt KL, Dieppe P, Radin EL. Etiopathogenesis of Osteoarthritis. Rheum Dis Clin N Am. 2008 34 (531-559).
7. Cappozzo A, Catani F, Della Croce U, Leardini A. Position and Orientation in Space of Bones During Movement: Anatomical Frame Definition and Determination. Clinical Biomechanics 1995 10 (4): 171-178.
8. Cole GK, Nigg BM, Ronsky JL, Yeadon MR. Application of the Joint Coordinate System to Three Dimensional Joint Attitude and Movement Representation: A Standardization Proposal. J Biomech Eng. 1993 115 (4A): 344-9.

9. Dieppe PA, Lohmander S. Pathogenesis and Management of Pain in Osteoarthritis. Lancet 2005, 365, 965-973.
10. Eitzen I, Fernandes L, Nordsletten L, Risberg MA. Sagittal Plane Gait Characteristics in Hip Osteoarthritis Patients with Mild to Moderate Symptoms Compared with Healthy Controls: A Cross Sectional Study. BMC Musculoskeletal Disorders 2012 13: 258.
11. Ewen AM, Stewart S, St Clair Gibson A, Kashyap SN, Caplan N. Post-Operative Gait Analysis in Total Hip Replacement Patients-A Review of Current Literature and Meta-Analysis. Gait & Posture 2012. 36(1): 1-6.
12. Fernandes L, Hagen KB, Bijlsma JW, Andreassen O, Christensen P, Conaghan PG, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. Ann Rheum Dis 2013; 72(7): 1125-35.
13. Gossec et al. Comparative Evaluation of Three Semi-Quantitative Radiographic Grading Techniques for Hip Osteoarthritis in Terms of Validity and Reproducibility in 1404 Radiographs: Report of the OARSI-OMERACT Task Force. Osteoarthritis and Cartilage 2009. 17 182-187.
14. Hawker GA, Mian S, Kendzerska T, French M. Measures of Adult Pain. Arthritis Care & Research 2011 63 (S11) S240-252.
15. Holla JFM, Steultjens MPM, van der Leeden M, Roorda LD, Bierma-Zeinstra SMA, den Broeder AA, Dekker J. Determinants of Range of Joint Motion in Patients with Early Symptomatic Osteoarthritis of the Hip and/or Knee: An Exploratory Study in the Check Cohort. Osteoarthritis and Cartilage. 2011 19(4), 411-419.

16. Hurwitz DE, Hulet CH, Andriachhi TP, Rosenberg AG, Galante JO. Gait Compensations in Patients with Osteoarthritis of the Hip and their Relationship to Pain and Passive Hip Motion. Journal of Orthopaedic Research 1997 15: 629-635.
17. Jaremko JL, Lambert RG, Zubler V, Weber U, Loeuille D, Roemer FW, Cibere J, Pianta M, Gracey D, Conaghan P, Ostergaard M, Maksymowych WP. Journal of Rheumatology 2014. 41(2): 359-69.
18. Kubota M, Shimada S, Koybayashi S, Sasaki S, Kitade I, Matsumura M, Kamei K, Kitano M, Takeno K, Baba H. Quantitative Gait Analysis of Patients with Bilateral Hip Osteoarthritis Excluding the Influence of Walking Speed. J Orthop Sci 2007. 12(5): 451-457.
19. Kumar D, Wyatt C, Chiba K, Lee S, Nardo L, Link TM, Majumdar S, Souza RB. Anatomic correlates of reduced hip extension during walking in individuals with mild-moderate radiographic hip osteoarthritis. J Orthop Res. 2015, 33(4):527-34.
20. Lane NE, Brandt K, Hawker G, Peeva E, Schreyer E, Tsuji W, Hochberg MC. OARSI-FDA Initiative: Defining the Disease State of Osteoarthritis. Osteoarthritis and Cartilage 2011. 19 478-482.
21. Laroche D, Tolambiya A, Morisset C, Maillefert JF, French RM, Ornetti P, Thomas E. A classification study of kinematic gait trajectories in hip osteoarthritis. Comput Biol Med. 2014 Dec;55:42-8.
22. Lin X, Meijer OG, Lin J, Wu W, Lin X, Liang B, van Dieën JH, Bruijn SM. Frontal plane kinematics in walking with moderate hip osteoarthritis: Stability and fall risk. Clin Biomech (Bristol, Avon). 2015 Oct;30(8):874-80.

23. Loureiro A, Mills PM, Barrett RS. Muscle Weakness in Hip Osteoarthritis: A Systematic Review. Arthritis Care & Research 2013 65(3): 340-352.
24. Meyer CA, Corten K, Fieuws S, Deschamps K, Monari D, Wesseling M, Simon JP,Desloovere K. Biomechanical gait features associated with hip osteoarthritis: Towards a better definition of clinical hallmarks. J Orthop Res. 2015 Oct;33(10):1498-507.
25. Mills K, Hunt MA, Leigh R, Ferber R. A systematic review and meta-analysis of lower limb neuromuscular alterations associated with knee osteoarthritis during level walking. Clin Biomech (Bristol, Avon). 2013a; 28(7):713-24.
26. Mills K, Hunt MA, Ferber R. Biomechanical deviations during level walking associated with knee osteoarthritis: a systematic review and meta-analysis. Arthritis Care Res (Hoboken). 2013b; 65(10):1643-65.
27. McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): a review of its utility and measurement properties. Arthritis Rheum 2001 45(5): 453-461.
28. McGinley JL, Baker R, Wolfe R, Morris ME. The reliability of three-dimensional kinematic gait measurements: a systematic review. Gait & Posture 2009; 29:360-9.
29. Nelson AE, Allen KD, Golightly YM, Goode AP, Jordan JM. A systematic review of recommendations and guidelines for the management of osteoarthritis: The Chronic Osteoarthritis Management Initiative of the U.S. Bone and Joint Initiative. Semin Arthritis Rheum 2014 43(6) 701-12.

30. Osis ST, Hettinga BA, Macdonald SL, Ferber R. A Novel Method to Evaluate Error in Anatomical Marker Placement Using a Modified Generalized Procrustes Analysis. Comput Methods Biomech Biomed Engin. 2015 Aug: 18(10): 1108-1116.
31. Pohl MP, Lloyd C, Ferber R. Can the Reliability of Three-Dimensional Running Mechanics be Improved using Functional Joint Methodology? Gait & Posture 2010 32 559-563.
32. Schmitt D, Vap A, Queen RM. Effect of end-stage hip, knee, and ankle osteoarthritis on walking mechanics. Gait Posture, 2015.
33. Söderkvist & Wedin. 1993. Determining the Movements of the Skeleton Using Well-configured Markers. Journal of Biomechanics., 26, 1473-1477.
34. Thurston AJ. Spinal and Pelvic Kinematics in Osteoarthrosis of the Hip Joint. Spine. 1985 10(5), 467-71.
35. Watelain E, Dujardin F, Babier F, Dubois D, Allard P. Pelvis and Lower Limb Compensatory Actions of Subjects in an Early Stage of Hip Osteoarthritis. Arch Phys Med Rehabil. 2001 82: 1705-1711.
36. Weinhandl JT, O'Connor KM. Assessment of a greater trochanter-based method of locating the hip joint center. J Biomech. 2010 Sep 17;43(13):2633-6.
37. Whitfield K, Buchbinder R, Segal L, Osborne RH. Parasimonious and efficient assessment of health-related quality of life in osteoarthritis research: validation of the Assessment of Quality of Life (AQoL) instrument. Health and Quality of Life Outcomes. 2006 23; 4:19.
38. Zeni J Jr, Abujaber S, Pozzi F, Raisis L. Relationship between strength, pain, and different measures of functional ability in patients with end-stage hip osteoarthritis. Arthritis Care Res (Hoboken). 2014 Oct; 66 (10):1506-12.

39. Zeni J Jr, Pozzi F, Abujaber S, Miller L. Relationship between physical impairments and movement patterns during gait in patients with end-stage hip osteoarthritis. J Orthop Res. 2015 Mar; 33 (3):382-9.

BRIDGE TO UPCOMING THESIS CHAPTERS:

The results of this chapter suggest that individuals with hip OA demonstrate subtle gait abnormalities as compared with healthy controls. These results are important for our capstone project in Chapter 5, since it provides justification for why we used biomechanics as a clinical target for one of our exercise interventions.

6 CHAPTER 5:

A COMPARISON OF TWO PERSONALIZED EXERCISE INTERVENTIONS IN INDIVIDUALS WITH MILD-TO-MODERATE HIP OSTEOARTHRITIS: A RANDOMIZED PILOT TRIAL

Abstract

Background: Therapeutic exercise has been proposed to be an efficacious adjunct in the management of hip OA. However, effect sizes remain small. While tailoring treatment interventions to individual patient impairments is the current recommended approach, no study to date has examined how best to assess and identify patient impairments before prescribing a tailored exercise program. Therefore, the purpose of the present study was to determine whether different pre-intervention assessment strategies affect outcomes in mild-to-moderate hip OA patients following an 8-week tailored exercise program.

Methods: Subjects with mild-to-moderate hip OA (n=40) performed an 8-week exercise intervention following randomization to two groups that differed on assessment strategy. Subjects undertook a tailored exercise program that was developed using the results of a 3D gait assessment (3DGA) (n=19) or a standard clinical assessment (CON) (n=21). Primary outcomes of interest at 8-weeks follow-up were pain (visual analogue scale) and function (WOMAC function sub-score). Within group and between group differences at follow-up were analyzed using a paired sample t-test and a one-way analysis of covariance (ANCOVA), respectively.

Results: No significant improvements in pain were found across either the CON or 3DGA groups at 8-weeks follow-up. WOMAC function improved in both groups from baseline to follow-up (CON: Δ=-5.73 (SD 8.00), *P*=0.015), but not significantly in the 3DGA group (3DGA: Δ=-0.21 (SD 7.16), *P*=0.91). Between-group differences revealed that pain was significantly less at 8-weeks in the CON group (CON: 2.88cm (2.14); 3DGA: 4.58cm (2.33), F=5.384, p=0.027).

Conclusion: An 8-week tailored exercise intervention did not result in significant changes in pain in mild-to-moderate hip OA subjects across either the 3DGA or CON groups at follow-up. Additionally, using 3D gait data to develop an exercise program did not improve outcomes over a standard clinical assessment. Multi-centre research that further characterizes patient specific impairments in hip OA patients is needed.

5.1 INTRODUCTION

Hip osteoarthritis (OA) is a prevalent musculoskeletal condition that often results in significant pain and disability in affected individuals (Cross et al., 2014). The economic burden of this particular disease on the health care system is also significant, and is expected to rise in upcoming years if no change in management takes place (Turkiewicz et al., 2014).

A number of evidence-based guidelines have been developed outlining the importance of therapeutic exercise in the management of hip OA (Fernandes et al., 2014). While several small randomized controlled trials (RCTs) have demonstrated that exercise positively influences self-reported outcomes in pain and function in individuals with hip OA, the effect sizes remain small (French et al., 2013; Juhakoski et al., 2011; Fernandes et al., 2010; . A recent high quality RCT that compared a 12-week manual therapy and exercise based intervention program to a sham ultrasound protocol found no differences between groups on pain and functional outcomes at 12 or 36 weeks post intervention (Bennell et al., 2014).

The assessment strategy used to identify patient specific impairments, which subsequently informs the prescription of exercise interventions, may play an important role in hip OA and exercise studies. Presently, the exercise programs employed in previous hip OA studies have either been generic (i.e. exercises prescribed without prior clinical assessment) (Tak et al., 2005; Van Baar et al., 2001; Hopman-Rock et al., 2000) or patient tailored exercise programs that are based on a standard clinical assessment of each patient (e.g. ROM, strength, flexibility) (French et al., 2013; Fernandes et al., 2011; Van Baar et al., 1998). While a more tailored approach to the prescription of exercise in hip OA (based on individual clinical findings) is the current

recommendation (Fernandes et al., 2013), 3D motion analysis technology, which tracks segmental limb and joint positions, has recently identified and quantified a number of subtle and atypical biomechanical gait patterns in individuals with hip OA (Leigh et al., 2016; Eitzen et al., 2012). Given the subtle gait changes identified, 3D motion analysis technology may be a useful and accurate method to identify patient impairments that can then be addressed in tailored exercise programs. To our knowledge, no studies have examined the utility of using 3D gait data to develop exercise interventions in individuals with hip OA and whether this approach is superior to a standardized treatment protocol.

A second factor that may play a role in how hip OA patients respond to exercise is disease severity. To date, previous studies examining the role of exercise in hip OA have examined either end-stage hip OA patients awaiting hip replacement surgery (Wallis et al., 2011) or have included all severity sub-types (e.g. mild, moderate, severe) in their interventions (French et al., 2013; Fernandes et al., 2010; Van Baar et al., 2013). Whether individuals with mild-to-moderate hip OA respond to exercise in a manner different from that of their severe counterparts remains unknown. The mild-to-moderate hip OA subgroup represents an important group to fully investigate given they are earlier on in the course of their disease history and may be more responsive to certain interventions (Hunter, 2011).

Therefore, the purpose of the present clinical pilot RCT trial was to investigate how 3D gait analysis can be used to develop a tailored exercise protocol for individuals with mild-to-moderate hip OA. To examine the efficacy of this approach, we investigated whether an 8-week therapeutic exercise intervention, based on 3D gait analysis data, resulted in improved

patient reported outcomes as compared to an 8-week exercise intervention developed using a standard clinical assessment.

5.2 METHODS

5.2.1 Study Design

The present study is a randomized clinical pilot trial in which mild-to-moderate hip OA subjects were randomized to receive an 8-week exercise intervention that was based either on the results of a 3D gait assessment or on the results of a standard clinical assessment. Both subjects and therapists were blind to group allocation. The trial was completed on campus at the University of Calgary. Ethics approval was received from the institutional ethics review board before commencement of the study, and all subjects signed a study consent form prior to official enrollment.

5.2.2 Participants

Study subjects were recruited both retrospectively and prospectively by convenience from a large orthopedic outpatient clinic located in Calgary, Alberta between November 2011 and May 2014. Clinic coordinators within an orthopedic outpatient clinic retrospectively searched their patient database from November 2011 to October 2013 for mild-to-moderate hip osteoarthritis patients who had been assessed by an orthopedic surgeon and deemed non-surgical candidates. These patients were then sent a study invitation letter to participate in the present study. In addition, from October 2013 (study onset) to May 2014, subjects were also recruited

in a prospective manner on a monthly basis from the same orthopedic clinic. Subjects who responded to the letter were then screened over the phone by a study coordinator and principal investigator (RJL) to determine final eligibility for enrollment in the study.

Subject inclusion criteria were similar to previous investigations (Bennell et al., 2014) and included: 1) aged 35-70 years old; 2) fulfillment of the American College of Rheumatology criteria for clinical and radiographic hip OA (Altman et al., 1991); 3) standing AP radiograph within the past two years that demonstrated Kellgren and Lawrence grade 2-3 changes (Kellgren and Lawrence, 1957); 4) pain of at least 2/10 (visual analogue scale) in either the hip or groin. Exclusion criteria included: 1) other muscular, neurological, or joint pathology causing pain or dysfunction on the affected or unaffected lower extremity (e.g. knee OA, previous stroke); 2) other clinically diagnosed hip pathology (e.g. labral tear, femoro-acetabular impingement, hip dysplasia, avascular necrosis); 3) previous hip or knee replacement on the affected or unaffected lower extremity; 4) previous traumatic injury to hip on the affected side (e.g. fracture, dislocation); 5) lower extremity trauma or surgery within the past 5 years; 6) current or recent (within past 3 months) intra-articular corticosteroid use; 7) enrollment/participation in a strengthening, stretching, or rehabilitation program currently or in the past 3 months; 8) any other systemic arthritic conditions (e.g. rheumatoid arthritis, spondyloarthropathies); 9) inability to abstain from medication for 24 hours. Study participants were informed via a study intake form that they would be randomized to one of two groups and that each group would be receiving an exercise program.

5.2.3 Randomization and Allocation Concealment

Those subjects found eligible for study inclusion were randomized to one of two groups by a clinic rehabilitation assistant not affiliated with the study. Subjects were randomized in permuted blocks of four using a published random numbers table (Portney and Watkins, 2009) in an effort to balance the number of subjects in each group at any one time. The allocation sequence was kept concealed from the clinician (RJL) assessing participants at baseline and follow-up, and from the athletic therapist administering the exercise program, by saving subject group allocations on the clinic assistant's password-secured computer until the participant presented for his/her exercise program.

5.2.4 Intervention

Following the baseline screening interview by phone and in clinic, eligible subjects underwent two separate assessments on the same day. The findings of these assessments were used to generate two different tailored exercise interventions. Subjects were aware that they would be receiving an exercise program, but were blinded as to whether the exercise program was based on the standard clinical assessment or the 3D gait assessment. Demographic data including, age, sex, BMI, duration of symptoms, and medication usage was collected at baseline.

First, a standard clinical assessment (CLIN) that included measures of strength, flexibility, and passive range of motion was performed (Appendix A). This assessment was meant to replicate a clinical assessment that would typically be performed by practitioners treating a hip OA patient and was similar to previous hip OA exercise studies (Fernandes et al., 2010). Specifically, a two-armed goniometer was used to test hip abduction PROM in supine, hip internal and external

PROM in prone with the knee bent to 90 degrees, and hamstring flexibility (straight leg raise) in supine. Hip flexor flexibility was assessed in the Thomas Test position using a digital inclinometer while quadriceps flexibility was measured as the distance of the heel to the ipsilateral gluteal muscle in prone using a standard 100 cm measuring tape. All PROM/flexibility tests were performed bilaterally. Strength of the hip abductors in side-lying, hip extensors in prone (knee flexed to 90 degrees), hip flexors in sitting, and hip external rotators in sitting were tested isometrically using a hand-held dynamometer (Nicholas MMT, Lafayette Instruments, Lafayette, USA). Each muscle group was tested twice separated by 30 seconds. The higher value of the two isometric contractions was taken as the recorded value. Stabilization straps were used to standardize subject limb position and to provide a consistent counter-resistance to subject contractions. The position of these straps in our clinic for each of the above strength measurements has been published elsewhere (Fukuchi et al., 2014). Strength measurements recorded in kilograms equivalent of force (Kg) and were standardized to limb length and patient body mass and recorded in units of N•m/Kg. All strength tests were performed bilaterally. Following this assessment, strength, flexibility and ROM impairments were identified by comparing with the unaffected opposite side limb, and tailored exercises were subsequently selected to address these impairments for those subjects randomized to the standard assessment group. Comparison to the opposite side limb was made since this is common in clinical practice where normative strength, flexibility, and ROM data is not always readily available or accessed. In instances where both limbs were affected, it was left to the clinician's discretion which impairments would be addressed by the exercise program.

Following the clinical assessment, subjects underwent a 3D gait analysis assessment (3DGA). Specifically, kinematic data were collected using an 8-camera 3D motion capture system (Vicon MX-3+, Vicon, Oxford, UK) that sampled at 200 Hz while subjects walked on a treadmill at 1.1 m/s. This speed was chosen since it has previously been reported in research involving hip OA (Leigh et al., 2016; Laroche et al., 2011).

A total of 27, 9 mm retro-reflective markers were attached to the pelvis, thighs, shanks, and feet, with an additional 18 markers also attached to anatomical landmarks for a neutral standing trial to identify joint centre locations (Osis et al., 2014). Marker trajectories were filtered with a 10 Hz low-pass 2nd order recursive Butterworth filter and lower body anatomical segments were defined using a Joint Coordinate System (Cole et al., 1993). Following placement of all the anatomical and segment markers, each participant stood on a motorized treadmill (Bertec Corporation, Columbus, OH, USA) for a 1-second static trial and standardized shoes were provided (Nike Air Pegasus, Nike Inc, USA). Standing position was controlled using a graphic template placed on the treadmill with the feet positioned 0.3 m apart and pointing straight ahead. Upon completion of the static trial, the markers on the anatomical landmarks were removed while the technical marker clusters remained. The participants were instructed to warm-up on the treadmill for 2-3 minutes, and then walk on the treadmill at the selected speed, for 20 seconds in which approximately 20-30 consecutive walking strides were collected for processing and analysis. All participants were experienced treadmill users and were permitted as much time as they required to familiarize themselves with treadmill walking before beginning the data collection. Ankle, knee and hip joint kinematic angles were

calculated in frontal, transverse, and sagittal planes of motion using 3D GAIT custom software (Running Injury Clinic Inc., Calgary, Alberta, Canada).

Discrete joint angles were obtained in all three planes (sagittal, frontal, transverse) across the pelvis, hip, knee, and ankle during mid-stance (the time point corresponding to 30% of the gait cycle), terminal hip extension, and toe off. These time points in the gait cycle were chosen since they represent common measurement time points in the hip OA literature (Eitzen et al., 2012). Subjects randomized to the 3DGA tailored exercise group received exercises that were based on their 3DGA results. Specifically, 3DGA joint angles that were found to lie 1 standard deviation outside normal for each subject were addressed with specific exercises (Appendix B provides an outline for how specific gait variables were used to prescribe specific exercises). The averaged joint angles of 22 age- and BMI-matched healthy individuals who performed a gait analysis pre-study were used to determine a normative distribution.

Less than one week following their clinical and 3DGA assessments, subjects returned to receive their group specific tailored exercise program. Each subject within either the CLIN or 3DGA exercise groups received an exercise program that consisted of 4-5 tailored exercises specific to their individual assessment findings. A certified athletic therapist (AT) described and demonstrated each exercise for each patient at this visit. Subjects were asked to perform the exercises 3-4 times per week for 8 weeks. During the 8-week program, subjects visited the AT every two weeks at which time their exercises were progressed and technique was monitored. Subjects were asked to perform their exercises to a rating of perceived exertion of 12 (somewhat difficult) for the first 4 weeks and to a rating of 15 (very difficult) for the latter 4

weeks while respecting pain in the affected hip. During the first 2 weeks of the exercise program, strengthening exercises were performed at a dose of 2 sets of 20 repetitions to emphasize endurance. During weeks 3-6, 3 sets of 15 repetitions were performed while 3 sets of 10 repetitions were performed during weeks 7-8 to emphasize strength. This progression is similar to the American College of Sports Medicine's recommendation for exercise progression (Garber et al., 2011).

5.2.5 Outcome Measures

Patients received questionnaires at baseline and at the 8-week follow-up visit. The primary outcome measures evaluated were pain and overall function as assessed using a 10 cm visual analogue scale (VAS) and the 17-point physical function sub-scale of the Western Ontario and McMaster Universities Osteoarthritis Index Scale (WOMAC)), respectively. Decreasing scores over time or negative change scores indicates improvement in each of these outcomes.

Secondary outcome measures included hip specific function (assessed using the Hip Disability Osteoarthritis Outcome Score (HOOS) ADL sub score), self-efficacy (measured using The Arthritis Self-Efficacy Scale (Lorig et al., 1989), catastrophizing (measured by the Pain-Catastrophizing Scale (Osman et al., 2000), and quality of life (measured using the Assessment of Quality of Life (V2) (AQOL-2) (Whitfield et al., 2006)). The HOOS is specific to hip OA and has been shown to demonstrate adequate measurement properties to be considered useful in hip OA populations (Thorborg et al., 2010). Increasing scores using the HOOS indicates improvement. Higher scores in the self-efficacy scale indicates increased self-efficacy while

lower scores in the pain catastrophizing scale indicates less pain catastrophizing. Higher scores in the AQOL indicates poorer quality of life.

The measure of Intermittent and Constant Osteoarthritis Pain (ICOAP), an 11-item OA specific pain scale that has previously been found to be a reliable (r=0.86) (Singh et al., 2014) and responsive measure in OA (Bond et al., 2012) was also added given its recent inception by the OARSI/OMERACT initiative.

5.2.6 Sample Size

The minimal clinically important improvement for a "good" treatment response for hip OA pain has been reported to be 15.3mm on a 100mm VAS scale (Tubach et al., 2005) and the variance of hip OA VAS pain is 26.3mm on a 100mm scale (French et al., 2013). With a power of 80% and a significance level of p=0.05, it estimated that 92 subjects total (46 per arm) would be required to detect a difference of 15.3mm between groups. This calculation is based on the equation $n = (2/d^2) \times c_{p,power}$ where n = total number of subjects per group, (d) = standardized difference (effect size/variance), and $c_{p,power}$ is a constant defined by the values chosen for the P-value and power (where $c_{p,power} = 7.9$ when power = 80% and p =0.05) (Whitley and Ball, 2002). Projecting a drop-out rate of 10%, 102 subjects total (51 per group) was the estimated a priori sample size. Given this was a pilot trial study, we aimed to recruit 40 subjects in total (20 per treatment group).

5.2.7 Data Analysis

The primary and secondary analyses were performed on a per protocol basis, defined as subjects completing the 8-week exercise program with returned questionnaires at study completion, using SPSS Statistics 20. Within group change in outcomes from baseline to post-intervention was assessed using a paired samples t-test. Between-group differences between the CLIN and 3DGA groups was assessed at the 8-week follow-up using an analysis of covariance (ANCOVA) with group as the independent variable, 8-week outcomes as the dependent variable, and baseline values as a potential unequal covariate. Statistical significance was set at $P<0.05$.

5.3 RESULTS

5.3.1 Participants

Figure 1 illustrates the flow of participants through the study trial. Overall, 1017 hip OA patients were initially screened and 739 did not meet the inclusion/exclusion criteria resulting in invitation letters being sent to 278 potential patients. Of those 278, 40 subjects were randomized (21 CLIN group, 19 3DGA group). All subjects completed the 8-week exercise intervention. However, incomplete questionnaires and/or subject non-compliance in mailing the follow-up questionnaires back to the principal investigator resulted in the observed losses to follow-up.

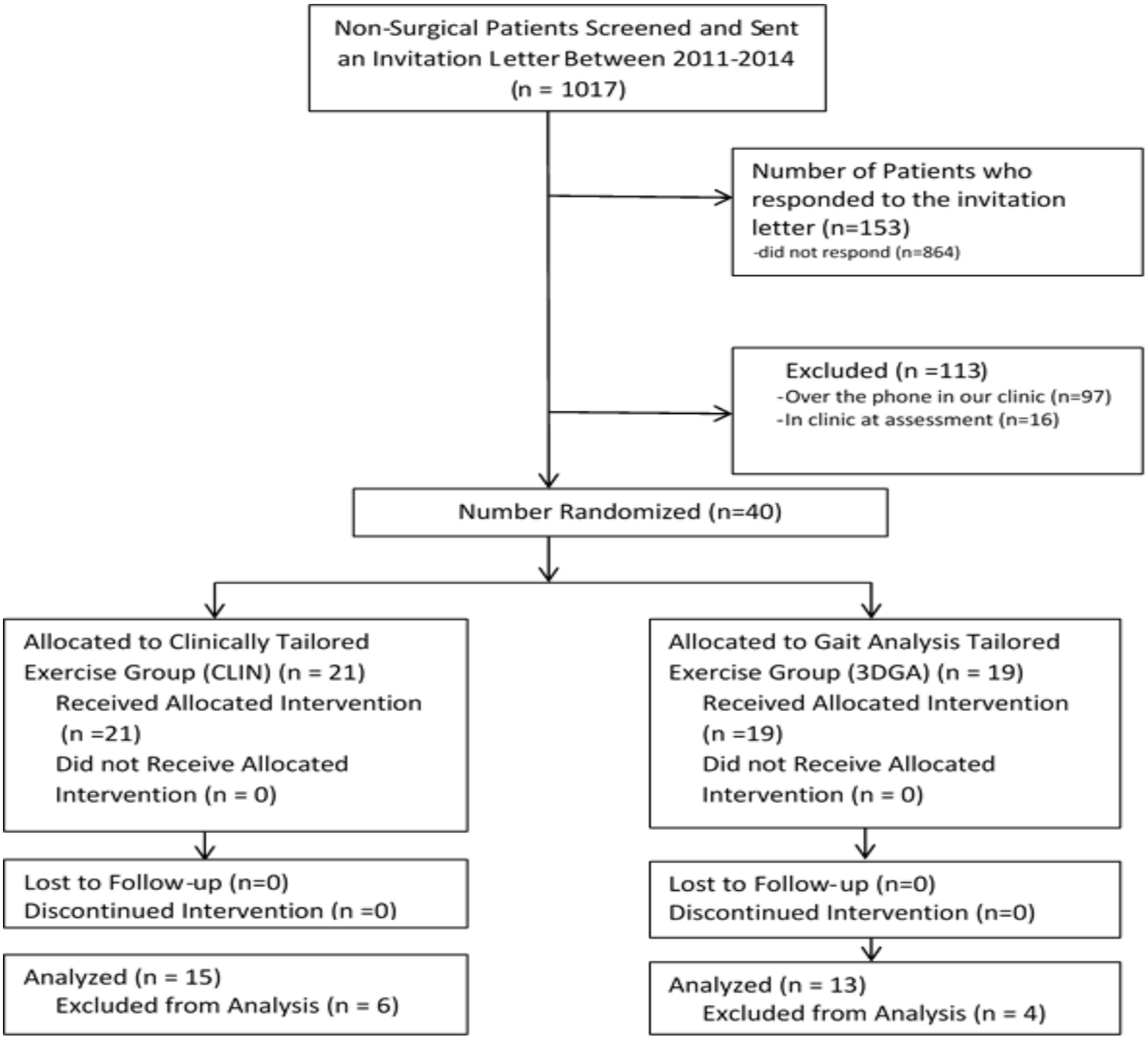


Figure 5-1. Flow of participants through study trial.

ppBaseline characteristics of the enrolled subjects are presented in Table 5-1.

Table 5-1. Baseline characteristics of randomized subjects (mean (SD))

	CLIN Group (n=21)	3DGA Group (n=19)
Demographic		
Sex (Female : Male)	11F : 10M	10F : 9M
Age (y)	56.2 (8.3)	54.9 (7.5)
Weight (kg)	76.7 (12.6)	76.2 (16.2)
Height (m)	1.69 (7.5)	1.70 (9.8)
BMI (Kg/m²)	26.7 (4.0)	26.8 (4.8)
Hip Joint Severity		
Mild (n=)	13	12
Moderate (n=)	8	7
Duration of Symptoms (y)	4.4 (3.8)	5.4 (3.6)
Number of Affected Hips		
Unilateral	16	13
Bilateral	5	6
Medication Usage (%)	52% (11/21)	53%(10/19)
Analgesics	14% (3/21)	11%(2/19)
NSAIDs	29% (6/21)	26% (5/19)
Other	10% (2/21)	26% (5/19)
Clinical		
VAS (cm)	3.45 (2.39)	3.87 (2.39)
ICOAP		
Constant	5.45 (5.33)	5.63 (5.14)
Intermittent	10 (5.30)	10.3 (5.2)
WOMAC (/96)	29.7 (18.0)	29.9 (14.6)
Pain (/20)	7.25 (3.16)	6.76 (2.9)
Function (/68)	21.9 (12.9)	22.2 (9.8)
Stiffness (/8)	3.1 (1.29)	2.7 (1.2)
HOOS		
Pain (/100)	61.2 (15.9)	63.6 (14.1)
Function (/100)	69.8 (20.8)	65.1 (15.9)
Sports (/100)	58.2 (22.4)	48.4 (21.5)
QOL (/100)	45.5 (16.5)	42.1 (17.2)
Other Symptoms (/100)	65.3 (17.8)	57.2 (14.7)
AQOL-6D	39.4 (7.9)	41.0 (8.2)
Arthritis Self-Efficacy	160.3 (31.7)	160.1 (23.1)
Pain Catastrophizing Scale	10.7 (9.8)	11.8 (10.5)

BMI, Body Mass Index; NSAIDs, Non-steroidal Anti-Inflammatories; VAS, Visual Analogue Scale (0 = no pain); ICOAP, Intermittent and Constant Osteoarthritis Pain Score (0 = indicates no

pain); WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index Score; HOOS, Hip Disability Osteoarthritis Outcome Score (0= no problems); QOL, Quality of Life; AQOL-6D, Assessment of Quality of Life V2 for the CLIN and 3DGA exercise groups.

5.3.2 Clinical Outcomes

At baseline, differences in self-reported VAS scores (CLIN: 3.45 (SD 2.39); 3DGA: 3.87 (SD 2.39)), mean ICOAP constant pain score (CLIN: 5.45 (SD 5.33); 3DGA: 5.63 (SD 5.14)), mean HOOS pain score (CLIN: 61.2 (SD 15.9); 3DGA: 63.6 (SD 14.1)), and mean HOOS function score (CLIN: 69.8 (SD 20.8); 3DGA: 65.1 (15.9)) were noted (Table 1). Statistical testing of baseline differences was not performed as recommended by several authors previously (Roberts and Torgerson, 1999; Altman, 1985).

At 8-weeks follow-up, the mean change in VAS scores from pre to post-intervention were not significant across either group (CLIN: Δ=-0.89cm (SD 2.33), *P*=0.11; 3DGA: Δ=+0.61cm (SD 2.16), *P*=0.28) (Figure 2). Significant change in the WOMAC function sub-score was noted pre-to-post intervention in the CLIN group but not the 3DGA group (CLIN: Δ=-5.73 (SD 8.00), *P*=0.015; 3DGA: Δ=-0.21 (SD 7.16), *P*=0.91). No significant differences pre-to-post intervention were noted for the HOOS ADL sub-score (CLIN: Δ=+5.98 (SD 13.79), *P*=0.128; 3DGA: Δ=+1.03 (SD 7.57), *P*=0.63), the Arthritis Self Efficacy Scale (CLIN: Δ=+4.53 (SD 27.65), *P*=0.536; 3DGA: Δ=-6.77 (SD 19.51), *P*=0.2350), or the AQOL-2 (CLIN: Δ=+3.36 (SD 6.54), *P*=0.08; 3DGA: Δ=-0.33 (SD 4.81), *P*=0.792). A significant change in the Pain Catastrophizing Scale score was noted in the CLIN group but not the 3DGA group pre-to-post intervention (CLIN: Δ=3.69 (SD 5.96), *P*=0.026; 3DGA: Δ=1.79 (SD 5.44), *P*=0.241).

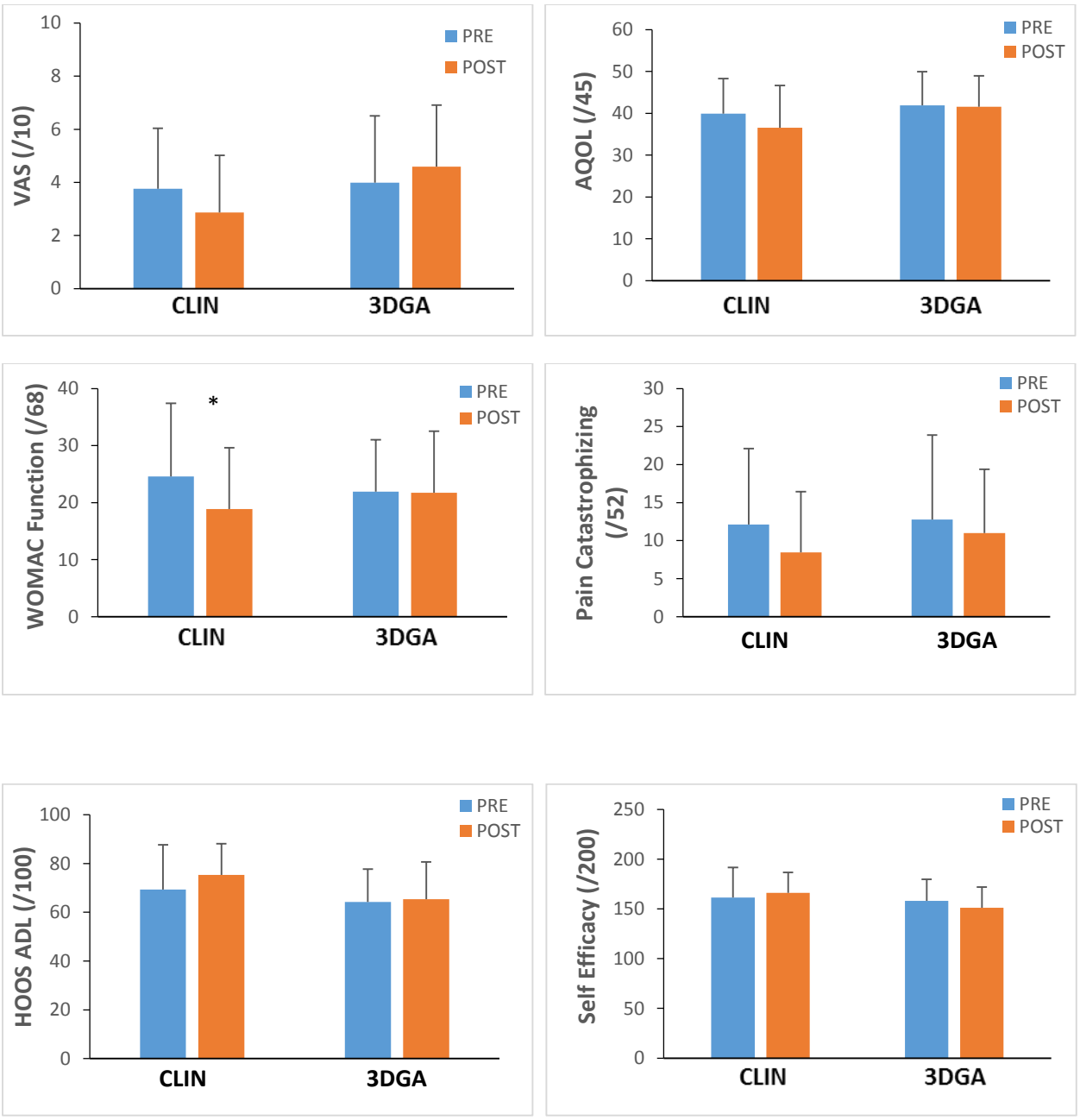


Figure 5-2. Baseline (Pre) and follow-up scores (Post) across groups following the 8-week exercise intervention (* denotes significant at P<0.05).

Between-group differences (CLIN vs 3DGA) at the 8-week follow-up time point were assessed using a one-way analysis of covariance (ANCOVA) (Table 2). At 8-weeks post-intervention, VAS scores were significantly lower in the CLIN versus the 3DGA group (CLIN: 2.88 (SD 2.14); 3DGA:

4.58 (SD 2.33), F=5.384, *P*=0.027). No significant between group differences were found at the 8-week follow up for any of WOMAC function (CLIN: 18.87 (SD 10.76); 3DGA: 21.71 (SD 10.83), F=3.235, *P*=0.084), HOOS ADL (CLIN: 75.32 (SD 12.86); 3DGA: 65.24 (SD 15.34), F=3.216, *P*=0.086), AQoL-2 (CLIN: 36.57 (SD 10.05); 3DGA: 41.60 (SD 7.33), F=2.55, *P*=0.122), Arthritis Self Efficacy Scale (CLIN: 166.0 (SD 20.65); 3DGA: 151.23 (SD 20.73), F=3.73, *P*=0.065), or the Pain Catastrophizing Scale (CLIN: 8.44 (SD 8.01); 3DGA: 11.00 (SD 8.38), F=1.67, *P*=0.207).

Table 5-2. One-way Analysis of Covariance (ANCOVA) comparing CLIN and 3DGA at the 8-week follow-up time point					
	Group	Baseline	Follow-up	F-value	Sig
Primary Outcomes					
VAS (/10)	CLIN (n=19)	3.76 (2.29)	2.88 (2.14)	F = 5.384	P = 0.027*
	3DGA (n=17)	3.99 (2.51)	4.58 (2.33)		
WOMAC Function (/68)	CLIN (n=15)	22.53 (10.53)	18.87 (10.76)	F = 3.235	P = 0.084
	3DGA (n=14)	21.93 (9.09)	21.71 (10.83)		
Secondary Outcomes					
HOOS ADL	CLIN (n=14)	69.30 (18.30)	75.32 (12.86)	F = 3.216	P = 0.086
	3DGA (n=13)	64.28 (13.45)	65.24(15.34)		
AQoL-6D	CLIN (n=14)	39.93 (8.37)	36.57 (10.05)	F = 2.55	P = 0.122
	3DGA (n=15)	41.93 (8.03)	41.60 (7.33)		
Arthritis Self Efficacy Scale	CLIN (n=15)	161.47 (30.19)	166.00 (20.65)	F = 3.73	P = 0.065
	3DGA (n=13)	158.00 (21.59)	151.23 (20.73)		
Pain Catastrophizing Scale	CLIN (n = 16)	12.13 (9.99)	8.44 (8.01)	F = 1.67	P = 0.207
	3DGA (n =14)	12.79 (11.11)	11.00 (8.38)		

*Denotes significant (P<0.05) pair-wise difference between CLIN and 3DGA groups

5.4 DISCUSSION

The aim of the present pilot study was to propose how 3D gait data may be used in the development of exercise interventions in hip OA, and to determine whether a clinical assessment using 3D gait data results in improved outcomes as compared with a standard clinical assessment. Overall, we found that an 8-week exercise intervention resulted in small to no improvements in our primary and secondary outcomes across both groups, and that using a 3D gait based assessment did not result in improved outcomes over a standard clinical assessment. To our knowledge, this is the first time that gait analysis assessment results have been used in the physical rehabilitation literature to guide exercise prescription.

One of the main objectives of the present study was to determine how 3D gait results could be used to prescribe an exercise program for individuals with mild-to-moderate hip OA. In order to use 3D gait data as a means to develop an exercise program, a number of questions needed to be answered before study onset. First, in an effort to appreciate what “abnormal” gait kinematics were, we established “normal” gait kinematics by assessing and averaging the gait kinematics of 22 healthy age and weight matched individuals before enrollment began. Abnormal gait kinematics were considered to be those gait variables that sat one standard deviation outside of the averaged kinematics for the 22 healthy individuals. It is acknowledged that there exists variability in 3D gait analysis (Schwartz et al., 2004) and that falling one standard deviation outside “normal” may not represent an abnormal gait. However, we aimed to establish a quantitative cut-point that could be used for all subjects. A second question that we had to address was which kinematic variables should be analyzed and used when

developing the 3D gait based exercise program. While any number of gait variables could have been chosen to build the exercise program, we chose a priori to focus on the peak pelvic and hip joint angles in all three planes (i.e. sagittal, transverse, frontal), knee in the sagittal plane, and ankle in the sagittal plane. These gait variables have been shown previously to be affected during walking in hip OA patients (Leigh et al., 2016, Eitzen et al., 2012) and as such were pre-selected as the gait variables from which the exercise program would be designed. Whether we selected the appropriate gait variables (peak joint angles), at the right point in time (mid-stance, terminal hip extension, and toe-off), and/or left out important variables is unknown. Future studies examining gait kinetics and the entire kinematic wave-form may offer more information to guide the clinical decision making process when using 3D gait data in OA studies. Lastly, determining what exercises should be prescribed based on 3D gait kinematic results remains a relatively subjective practice on behalf of the clinician with little guidance from the literature. While hip flexion contractures have been shown to be correlated with decreased dynamic peak hip extension and anterior pelvic tilt during walking in hip OA (Lee et al., 1997) (and as such, a hip flexor lengthening stretch would presumably be an appropriate prescribed exercise for decreased peak hip extension), it is unknown how other 3D gait derived peak joint angles correlate with clinical impairments of altered flexibility and strength. Future studies that examine the relationship between gait variables and clinical variables would be useful in establishing possible relationships between each.

A second aim of the present study was to determine whether a tailored exercise program, developed using 3D gait data, results in improved clinical outcomes as compared with an exercise program developed using standard clinical assessment findings. Previous findings of

significant differences in gait kinematics between those with mild-to-moderate hip OA and those without (Leigh et al., 2016; Eitzen et al., 2012) suggested that 3D gait data results may be useful in the development of tailored exercise programs in hip OA individuals. However, using 3D gait data did not result in improved pain and function outcomes as compared with a standard clinical assessment group. Several reasons may explain this finding. First, the exercises we prescribed in the 3DGA group for a given identified abnormal kinematic variable may not have been the correct exercise for that variable. For example, most patients in the 3DGA group were identified as having decreased peak hip internal ROM. In an effort to improve hip IR ROM, exercises were prescribed that would lengthen the external rotator musculature and increase hip IR range (see Appendix). Prescribing an exercise that aims to increase hip internal rotation by moving into hip internal rotation may have in fact aggravated symptoms for the subjects in this group, helping explain why the VAS scores in the CLIN group were significantly improved post treatment as compared with the 3DGA group. There is however, to our knowledge, no precedent that exists in the literature to drive the decision making process between 3D kinematic findings and exercise prescription and, as such, this process warrants further research. A second possible explanation why the 3DGA group demonstrated poorer outcomes as compared with the CLIN group is that the gait kinematics that hip OA patients adopt may in fact be an adaptive gait pattern that helps these patients decrease joint contact stresses. Attempts at changing the gait patterns of hip OA patients may ultimately aggravate their symptoms and result in poor outcomes post intervention.

Overall, the 8-week exercise intervention program did not result in clinically important improvements in either the 3D gait group or the standard clinical assessment group. While

WOMAC function significantly improved in the standard assessment group from a statistical standpoint, a change of 5 points on the WOMAC function sub-scale is not considered a clinically meaningful change (Tubach et al., 2005). The effect of exercise across groups in the present study should be considered in the context of other hip OA exercise based studies conducted. To date three studies have examined the effect of tailored exercise in hip OA (French et al., 2013; Fernandes et al., 2010; Van Baar et al., 1998). All three of these trials found no effect of exercise on pain outcomes in individuals with hip OA when compared with education or a standard of care group. In a recent large, well designed RCT recruiting hip OA subjects only, changes in pain and function were measured following a 12-week intensive exercise and manual therapy intervention and compared with a sham delivered ultrasound intervention (Bennell et al., 2014). No changes in pain or function were noted between groups, leading the study authors to suggest that previous exercise trials suggesting an exercise effect for hip OA may have overestimated treatment effects due to the lack of adequate subject blinding.

There are a number of possible explanations why exercise did not improve pain or function in a clinically important manner in the present study. Given that this trial was a pilot study, a lack of adequate power may have resulted in a Type II error. The observed lack of power was however not only a consequence of the small sample size in each group but also the smaller than expected effect size in both groups. An effect size of approximately 0.25 was observed in the present trial, suggesting a smaller than expected effect of exercise. A second explanation for the relative lack of change in pain and function outcomes within each group may be a result of the exercise dose itself. Subjects in the present trial were prescribed 4-5 different strengthening or stretching exercises that were tailored to their assessment findings and progressed bi-

weekly. This number of exercises was chosen in an effort to promote adherence to the program. The particular volume and dose of exercise that is most efficacious in hip OA remains to be determined. A third explanation for the relative lack of change in pain scores in our study may be that a minimum VAS score was not established at study intake. Given the large variance in self-reported pain scores and the finding that 1.5 cm represents the minimal clinically important change in pain in OA populations (Tubach et al., 2005), a set minimum score of 3/10 may be desired to circumvent encountering a floor effect. However, the finding that changes in pain and function scores were also small using other outcome measures suggests a floor effect may not have influenced the VAS pain scores. Lastly, exercise may impart only small effects on outcomes in hip OA, regardless of assessment technique or other factors. It seems reasonable to question whether exercise mediated changes in soft tissue length and strength would have a significant effect on hip OA pain given the predominantly osseous/structural bony changes that characterize hip OA (Kumar et al. 2013).

There are strengths and limitations to the present pilot study. One strength of this study was the double-blind design. Blinding of both the subject and the treating therapist to group allocation was possible since two exercise programs were delivered. This is unique since subjects in most exercise-based studies are aware they are receiving the “active” exercise intervention. In addition, this allocation was concealed from therapist and patient using a secure centralized storage mechanism. Completion of the 8-week program was high in the present study (> 90%) as was adherence with 90% of subjects reporting in their log-books that they performed their exercises 3-4x/week as recommended. A second strength of the study is the biomechanics methodology employed. While it is known that deviations in the placement

of anatomical markers to conduct 3DGA can result in large variances in the data, the current study employed a novel feedback tool to improve reliability of biomechanical data (Osis et al., 2016). Results from a sub-analysis within the current trial have demonstrated a marked improvement in the reliability of discrete biomechanical variables (Ferber et al., 2015).

There are, however, also limitations in the present study. First, as mentioned above, a number of technical factors need to be investigated before a conclusive evaluation of the use of 3D gait data in the development of exercise programs in hip OA can be made. A second limitation is that the pelvic radiographs of included subjects were interpreted and scored by more than one radiologist. Given that our recruitment took place primarily retrospectively, it was difficult to circumvent this limitation. Future studies may aim to employ only one radiologist in an effort to define a more homogenous radiographic population. A third limitation in the present study is that there was not a true control group with which the CLIN and GATE groups were compared. While subjects were unaware whether they were receiving a clinical or gait analysis derived exercise program, all were aware that they were in fact receiving an exercise program. A true sham exercise control group would have controlled for treatment biases associated with subjects realizing they were receiving an intervention. Lastly, one therapist (RJL) was responsible for interpreting the 3D gait and clinical assessment results and for developing the subsequent exercise program based on these results. Interpretation of the assessment results and subsequent selection of exercises can be strengthened by involving a second therapist and reaching a paired consensus. This approach would however not be overly generalizable to the clinical setting where one therapist often makes clinical decisions for their patient's.

In summary, this pilot study aimed to outline how 3D gait data may be used to prescribe an exercise program in mild-to-moderate hip OA patients and to determine whether using 3D gait data resulted in improved outcomes following an 8 week tailored exercise intervention in subjects with mild-to-moderate hip OA. Whether the use of 3D gait data helps improve outcomes in mild-to-moderate hip OA patients following a tailored exercise program requires larger, multi-center studies that can recruit large numbers of subjects. In addition, studies defining what constitutes “normal” gait and how 3D gait identified biomechanical impairments relate to clinical findings such as strength, flexibility, and ROM also requires further research. Lastly, realizing improved outcomes in patients with hip OA will require ongoing novel approaches to assessment and treatment that include and are in addition to accepted current approaches.

REFERENCES

1. Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, Bridgett L, Williams S, Guillemin F, Hill CL, Laslett LL, Jones G, Cicuttini F, Osborne R, Vos T, Buchbinder R, Woolf A, March L. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis. 2014; 73(7):1323-30.
2. Turkiewicz A, Petersson IF, Björk J, Hawker G, Dahlberg LE, Lohmander LS, Englund M. Current and future impact of osteoarthritis on health care: a population-based study with projections to year 2032. Osteoarthritis & Cartilage. 2014; 22(11):1826-32.
3. Fernandes L, Hagen KB, Bijlsma JW, Andreassen O, Christensen P, Conaghan PG, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. Ann Rheum Dis. 2013; 72(7): 1125-35.
4. French, H.P., et al., Exercise and manual physiotherapy arthritis research trial (EMPART) for osteoarthritis of the hip: a multicenter randomized controlled trial. Arch Phys Med Rehabil. 2013; 94(2): 302-14.
5. Fernandes, L., et al., Efficacy of patient education and supervised exercise vs patient education alone in patients with hip osteoarthritis: a single blind randomized clinical trial. Osteoarthritis Cartilage. 2010; 18(10): 1237-43.
6. Juhakoski, R., et al., A pragmatic randomized controlled study of the effectiveness and cost consequences of exercise therapy in hip osteoarthritis. Clin Rehabil. 2011; 25(4): 370-83.
7. Bennell KL, Egerton T, Martin J, Abbott JH, Metcalf B, McManus F, Sims K, Pua YH, Wrigley TV, Forbes A, Smith C, Harris A, Buchbinder R. Effect of Physical Therapy on Pain

and Function in Patients with Hip Osteoarthritis: A Randomized Controlled Trial. JAMA. 2014; 311(19): 1987-97.

8. Tak, E., et al., The effects of an exercise program for older adults with osteoarthritis of the hip. J Rheumatol. 2005; 32(6): 1106-13.
9. Van Baar, M.E., et al., Effectiveness of exercise in patients with osteoarthritis of hip or knee: nine months' follow up. Ann Rheum Dis. 2001; 60(12): 1123-30.
10. Hopman-Rock, M. and M.H. Westhoff. The effects of a health educational and exercise program for older adults with osteoarthritis for the hip or knee. The Journal of Rheumatology. 2000; 27(8): 1947-1954.
11. Van Baar ME, Dekker J, Oostendrop R, Bijl D, Voorn TB, Lemmen JM. The effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a randomized clinical trial. J Rheumatol. 1998; 25(12): 2432-9.
12. Leigh RJ, Osis ST, Ferber R. Kinematic gait patterns and their relationship to pain in mild-to-moderate hip osteoarthritis. Clin Biomech. 2016; 34:12-7.
13. Eitzen I, Fernandes L, Nordsletten L, Risberg MA. Sagittal Plane Gait Characteristics in Hip Osteoarthritis Patients with Mild to Moderate Symptoms Compared with Healthy Controls: A Cross Sectional Study. BMC Musculoskeletal Disorders. 2012; 13: 258.
14. Wallis, J.A. and N.F. Taylor, Pre-operative interventions (non-surgical and non pharmacological) for patients with hip or knee osteoarthritis awaiting joint replacement surgery--a systematic review and meta-analysis. Osteoarthritis Cartilage. 2011; 19(12):1381-95.
15. Hunter DJ. Osteoarthritis. Best Pract Res Clin Rheumatol. 2011;25(6):801-14.

16. Altman R, Alacron G, Appelrouth D, Bloch D, Borenstein D, Brandt K, Brown C, Cooke TD, Daniel W, Feldman D et al. Arthritis Rheum. 1991; 34: 505-14.

17. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957; 16(4):494-502.

18. Portney and Watkins. Foundations of Clinical Research: Applications to Practice. 3rd Edition. Upper Saddle River: Prentice Hall; 2009.

19. Fukuchi RK, Stefanyshyn DJ, Stirling L, Duarte M, Ferber R. Flexibility, muscle strength and running biomechanical adaptations in older runners. Clin Biomech. 2014; (3):304-10.

20. Laroche D, Duval A, Morisset C, Beis J-N, d'Athis P, Maillefert J-F, Ornetti P. Test-retest reliability of 3D kinematic gait variables in hip osteoarthritis patients Osteoarthritis and Cartilage. 2011; 19: 194-199.

21. Osis ST, Hettinga BA, Macdonald SL, Ferber R. A novel method to evaluate error in anatomical marker placement using a modified generalized Procrustes analysis. Comput Methods Biomech Biomed Engin. 2014;18(10):1108-1116.

22. Cole GK, Nigg BM, Ronsky JL, Yeadon MR. Application of the joint coordinate system to three-dimensional joint attitude and movement representation: A standardization proposal. Journal of Biomechanical Engineering. 1993; 115(4A): 344-349.

23. Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, Nieman DC, Swain DP. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and

neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med Sci Sports Exerc. 2011; 43(7):1334-59.

24. Lorig K, Chastain RL, Ung E, Shoor S, Holman HR. Evaluation of a scale to measure perceived self-efficacy in people with arthritis. Arthritis Rheum. 1989;32(1):37-44.
25. Osman A, Barrios FX, Gutierrez PM, Kopper BA, Merrifield T, Grittmann L. The Pain Catastrophizing Scale: further psychometric evaluation with adult samples. J Behav Med. 2000; 23(4):351-65.
26. Whitfield K, Buchbinder R, Segal L, Osborne RH. Parsimonious and efficient assessment of health-related quality of life in osteoarthritis research: validation of the Assessment of Quality of Life (AQoL) instrument. Health Qual Life Outcomes. 2006; 23:4:19.
27. Thorborg K, Roos EM, Bartels EM, Petersen J, Hölmich P. Validity, reliability and responsiveness of patient-reported outcome questionnaires when assessing hip and groin disability: a systematic review.Br J Sports Med. 2010;44(16):1186-96.
28. Singh JA, Luo R, Landon GC, Suarez-Almazor M. Reliability and clinically important improvement thresholds for osteoarthritis pain and function scales: a multicenter study. J Rheumatol. 2014; 41(3):509-15.
29. Bond M, Davis A, Lohmander S, Hawker G. Responsiveness of the OARSI-OMERACT osteoarthritis pain and function measures. Osteoarthritis Cartilage. 2012;20(6):541-7.
30. Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, Bombardier C, Felson D, Hochberg M, van der Heijde D, Dougados M. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: the minimal clinically important improvement.Ann Rheum Dis. 2005;64(1):29-33.

31. Whitley E, Ball J. Statistics review 4: sample size calculations. Crit Care. 2002;6(4):335-41.
32. Roberts C and Torgerson DJ. Baseline imbalance in randomized controlled trials. British Medical Journal. 1999; 319:185.
33. Altman DG. Comparability of randomised groups. Statistician. 1985; 34: 125–136.
34. Lee LW, Kerrigan DC, Della Croce U. Dynamic implications of hip flexion contractures. Am J Phys Med Rehabil. 1997; 76(6): 502-8.
35. Kumar D, Wyatt CR, Lee S, Nardo L, Link TM, Majumdar S, Souza RB. Association of cartilage defects, and other MRI findings with pain and function in individuals with mild-moderate radiographic hip osteoarthritis and controls. Osteoarthritis Cartilage. 201;21(11):1685-92.
36. Osis ST, Hettinga BA, Macdonald S, & Ferber R. Effects of Simulated Marker Placement Deviations on Running Kinematics and Evaluation of a Morphometric-Based Placement Feedback Method. PLoS One. 2016; Jan 14:11(1).
37. Ferber R, Osis ST, Hettinga BA, Watari R & Leigh R. (2015, July). The use of feedback to reduce the errors associated with placement of anatomical markers for gait analysis. Paper presented at the XXVth Congress of the International Society of Biomechanics, Glasgow, Scotland.

7 CHAPTER 6:

SUMMARY & FUTURE DIRECTIONS

In an effort to provide a novel and significant contribution to the clinical biomechanics literature, the primary aim of the present thesis was to determine whether a novel exercise prescription methodology, specifically using 3D gait analysis, can improve clinical outcomes in individuals with mild to moderate hip OA. In order to fulfill this aim, several studies were conducted to establish the background and scientific foundation for the capstone pilot-RCT investigation.

Chapter 2 examined whether tester experience influences 3D gait analysis (3DGA) outcomes. Specifically, a tester with no previous 3DGA experience, but previous anatomical and clinical experience, was compared with a tester with 8 years of previous 3DGA experience (Leigh et al., 2014). We calculated joint kinematic angles using either a functional or predictive joint identification method and determined within-tester and between-tester measures of reliability by calculating the root mean square error (RMS) and coefficient of multiple correlations (CMC). Overall, within-tester RMS and CMC values were not significantly different between the experienced and novice testers using either approach and within-tester CMC values exceeded 0.90 for both testers across all kinematic variables. Between-tester CMC reliability values were greater than 0.85 for all variables measured. We concluded that following basic training, a physiotherapy clinician with no previous 3D gait experience is as reliable as an experienced gait biomechanist with respect to marker placement accuracy. In addition, reliability comparisons between an experienced and novice tester appear independent of the joint identification method chosen. However, there are several limitations to this research which warrants further attention in future studies.

Future Direction 1: The first limitation pertains to the acknowledgement that the testers in this study were not responsible for all aspects of the 3DGA collection which includes calibration of the motion analysis system, camera set-up, anatomical marker placement, and data modelling. Since these other aspects, in addition to marker placement, can introduce error into the collection of repeated gait analyses (Leardini et al., 2005), tester experience may play a role in the reliability of gait analysis if calibration and analysis is part of the collection

The second limitation pertains to the use of only one 3D gait analysis experienced tester and one clinician tester. Including more than one experienced and one clinician tester in each group may have increased the generalisability of the results. Comparing the within-tester reliability of an experienced tester to a true "novice" clinician tester, who has neither 3D gait analysis nor clinical experience may have been helpful in further determining the influence of tester experience on the reliability of kinematic gait variables. However, given that gait analysis is often performed both in the research and clinical settings by a tester with prior anatomical knowledge (e.g. kinesiologists, athletic therapists, physical therapists), it seemed more generalizable to select a clinician as opposed to someone with no anatomical knowledge.

A final limitation is that the subjects recruited in the present study were all young, lean participants. It has been postulated by Besier et al. (2003) that increased percent body fat may increase the difficulty with which anatomical landmarks are identified and thus influence the accuracy of marker placement. Further study investigating the effect of adiposity on the within-tester and between-tester reliability of gait analysis is therefore needed. Lastly, it will be important to examine whether the reliability of 3DGA in an untrained clinician is similar to that

of an experienced gait analysis tester when examining subjects with musculoskeletal impairments or injuries.

In our Chapter 3 systematic review and meta-analysis, we estimated the effect size of therapeutic exercise in hip OA to be small, while previous systematic reviews and papers have suggested small to moderate effect sizes (French et al., 2012, Fernandes et al., 2010). Several factors likely influence the precise role of therapeutic exercise in hip OA, including the type, duration, intensity, and frequency of exercise itself, as well as factors specific to OA including disease severity, type, and duration of symptoms. Therefore, identifying the specific exercise parameters that could result in maximal outcomes in exercise based hip OA studies is needed as suggested in previous hip OA reviews (Fernandes et al., 2013).

Future Direction 2: An understudied factor that is beginning to receive more attention in the OA literature, and that may influence exercise based outcomes in hip OA, is the concept of different OA phenotypes (Blagojevic et al., 2010). It has been proposed that given the heterogeneous nature of OA (Hunter, 2011), different phenotypes, or "sub-groups" of OA, may exist and that OA should not be viewed as a single common disease. In this way, it stands to possibility that hip OA patients with particular characteristics, or sub-groups, may respond differentially to exercise depending on various factors including, but not limited to, the structural form of their hip, walking gait biomechanics, severity of OA disease, genetic make-up, and clinical presentation of strength and flexibility. While sub-groups may encompass other characteristics besides the aforementioned factors, the focus of our future research is specific to joint structure. For example, an initial study that may help answer this question, would be a

retrospective examination of the anatomical features of those hip OA individuals who have shown a good response to an exercise intervention. Given the variable response of hip OA patients to exercise interventions, this would likely require multi-centre collaboration between study sites to ensure that the number of OA patients reviewed was adequate. The anatomical features identified in responders would likely be gleaned from pelvic radiographs given that this is the most common modality used in hip OA studies. While MRI can offer finer boney detail along with the appreciation of soft tissue structures, the features available on plain radiograph may be sufficient to identify specific anatomical features that may correlate to responder sub-groups. Given that one of the major drawbacks of retrospective analyses is the inability to control for known and unknown confounding factors, a proposed follow-up study to this would be a prospective study comparing hip OA patients with a known responder phenotype to hip OA patients with heterogeneous phenotypes while assessing clinical outcomes.

Chapter 4 was a cross-sectional study comparing the 3D kinematic walking patterns of hip OA patients to control subjects (Leigh et al., 2016). Of particular interest were the ambulation patterns in individuals with mild-to-moderate hip OA given the important role that biomechanics are thought to play in the OA disease process (Brandt et al., 2008), and since detection of early disease changes increases the likelihood of halting or reversing the disease trajectory (Hunter, 2011). While previous studies have assessed certain aspects of the hip OA gait pattern there has, to our knowledge, this was the first study that characterized the walking kinematics of hip OA patients across all lower extremity joints (pelvis, hip, knee, ankle) in the three cardinal planes of motion (sagittal, transverse, frontal). The primary finding of this investigation was that patients with mild-to-moderate hip OA demonstrate altered walking

kinematics as compared with their healthy counterparts. However, limitations to the present study were acknowledged.

Future Direction 3: First, gait kinetics were not presented, which may provide more information on the joint loading characteristics of this population. Second, as discussed in Chapter 3, joint angle calculations are influenced by marker placement accuracy and are a well-known potential source of error in gait analysis (McGinley et al., 2009). However, since one tester was used for all gait analyses, it is expected that these errors would be minimized and be similar across groups. Moreover, a published novel method for evaluating error in anatomical marker placement from our laboratory (Osis et al., 2015) was employed in this study, thereby increasing our confidence in our marker placement accuracy. Future studies should investigate the utility and impact of this marker placement tool in clinical populations and to address whether the influence of the aforementioned postulation by Besier et al. (2003) that increased percent body fat may increase the difficulty with which anatomical landmarks are identified and thus influence the accuracy of marker placement.

Third, given the well documented discordance between radiographic severity and patient reported symptoms in OA (Bedson et al., 2008), a clear definition of what constitutes mild vs moderate vs severe disease states remains elusive (Lane et al., 2011). It is therefore acknowledged that while all the subjects included in this study were considered mild-to-moderate from a radiographic standpoint, using patient reported symptoms (e.g. VAS) might have yielded a different definition of OA disease status in the included sample. A second factor influencing the determination of patient severity in the present study is the radiographic

scoring technique used. Future hip OA clinical research studies should involve a single radiologist and have that individual rate the disease severity for future hip OA investigations.

While understanding why hip OA patients walk with atypical biomechanics is an important research topic, one can argue that if this adaptation is pathologic but positively adaptive (i.e. adopting a gait mechanical pattern in order to off-load the affected hip and thereby reduce pain), it may be best to investigate whether interventions to change the altered gait are, in fact, in the patient's best interest. Alternatively, if it can be demonstrated that these altered gait patterns are pathologic and negatively adaptive by increasing joint contact stresses, studies that aim to positively affect these stresses may be warranted. While we examined the relationship between pain and walking mechanics in an effort to help explain why hip OA patients move the way they do, recent work has begun to examine the correlation between walking kinematics and radiographic joint features (Kumar et al., 2015). These authors found that reduced hip extension was correlated with K-L severity grade and cartilage lesions on the posterior and inferior aspects of the femur. Further findings similar to these will help inform how altered gait mechanics should be managed in the hip OA population.

A potentially informative cross-sectional study would be to measure and compare joint contact forces when hip OA patients walk with their preferred gait pattern versus when constrained to walk with a more "normal" gait. If, for example, joint contact stresses are lower when patients walk with their "abnormal" pattern as compared with the constrained "normal" pattern, this may suggest that their walking pattern is positively adaptive and that interventions aimed at changing their walking pattern are unnecessary. While implanted hip joint force transducers

would be considered the gold standard in measuring contact forces, the practicality of this is extremely low. More realistic would be dynamic optimization solutions to estimate hip joint contact forces (Correa et al., 2010). In addition, it would be interesting to further investigate why some hip OA patients walk with altered gait mechanics, while others walk with gait patterns similar to their non-affected healthy counterparts. While disease severity likely plays an important role, other anatomic factors that are pain generating including capsules, labrums, synovia, and ligaments may influence walking patterns.

In Chapter 5, we randomized mild-to-moderate hip OA patients to two different tailored exercise interventions and assessed clinical outcomes in each group. To our knowledge, this is the first study that has utilised tailored assessment strategies in the hip OA literature. Several strengths of this study were noted including the double-blind design, completion of the 8-week program was high (> 90%) as was adherence with 90% of subjects reporting in their log-books that they performed their exercises 3-4x/week as recommended. Another significant strength was the objective biomechanics methodology and utilization of a novel feedback tool to improve reliability of biomechanical data (Osis et al., 2016).

Future Direction 4: There are, however, also limitations identified within this study. First, there was not a true control group with which the two randomized groups were compared. While subjects were unaware whether they were receiving a clinical or gait analysis derived exercise program, all were aware that they were in fact receiving an exercise program. A true sham exercise control group would have controlled for treatment biases associated with subjects realizing they were receiving an intervention. Moreover, one therapist was responsible for

interpreting the 3D gait and clinical assessment results and for developing the subsequent exercise program based on these results. Interpretation of the assessment results and subsequent selection of exercises can be strengthened by involving a second therapist and reaching a paired consensus. This approach would however not be overly generalizable to the clinical setting where one therapist often makes clinical decisions for their patient's.

While determining the most effective way to personalize exercise interventions in hip OA remains a priority, we believe that there may be further opportunity for personalization that extends beyond just exercise interventions only. It has been suggested recently that hip OA, traditionally thought of as a non-inflammatory joint disease, has a large inflammatory component, specifically in those individuals who fit a metabolic phenotype (Courties et al., 2015). Specifically, individuals with a metabolic syndrome profile (central obesity, dyslipidemia, altered blood glucose, and hypertension), have larger numbers of adipocytes which in turn themselves produce increased levels of circulating adipokines (e.g. leptin, adiponectin, resistin) and pro-inflammatory mediators (including TNF-α, IL-1, IL-6). Adipokines and pro-inflammatory mediators have been implicated in joint/cartilage destruction and upregulating existing inflammatory processes (Wang et al., 2015). Given this finding, a potentially informative future study would involve tailoring interventions to the specific phenotype (sub-group) of a given individual with hip OA. Moreover, comparing outcomes in these sub-groups to a hip OA control group that has not been "phenotyped", and subsequently has not received personalized interventions, may provide further insight into how best to deliver OA interventions.

Establishing effective treatment interventions for individuals with hip OA remains a challenge for researchers and clinicians alike. The heterogeneous nature of OA, the often discordant relationship between patient pain and joint structural change, the slow progressing nature of the disease, and the lack of a precise precipitant in many cases of OA, all contribute to the relative lack of effective treatment strategies in OA. However, more sensitive imaging modalities, advances in proteomics, genomics, and molecular biology, as well as the commitment towards personalizing interventions in OA will undoubtedly help facilitate improved outcomes in osteoarthritis.

CONCLUSION

The prevailing aim of this thesis was to explore, develop, and test novel interventions that would improve clinical outcomes in individuals with mild-to-moderate hip OA. This aim was grounded in the recent recommendation that OA research should be patient centered with a focus towards novel assessment and treatment strategies. In chapter 4, we fully described the lower extremity kinematics of hip OA patients for the first time. We think this makes an important contribution to the hip OA biomechanical literature since it not only describes the movement patterns of this population, but also outlines impairments that may be targets of future interventions. In chapter 5, two different exercise interventions are compared. To date, exercise interventions in hip OA have either been generic or semi-tailored. We believe this thesis represents the first time that a completely tailored intervention has been tested in hip OA, and certainly the first time a novel assessment strategy has been employed in hip OA. Despite the limitations that accompany the pilot nature of the work, we think this makes a new contribution to the clinical OA research literature since different assessment strategies have

been compared for the first time in individuals with hip OA. The movement towards tailored and personalized interventions in OA, as were employed in our study, will depend in large part on effective, novel, and sensitive assessment strategies that can identify patient specific impairments. We hope this study acts as a catalyst for others to examine new methodologies to assess hip OA and subsequently provide personalized interventions.

REFERENCES (FOR INTRODUCTION AND FUTURE DIRECTIONS):

1. The Impact of Arthritis in Canada: Today and Over the Next 30 Years. www.arthritisalliance.ca. 2011. Hunter DJ. Osteoarthritis. Best Pract Res Clin Rheumatol. 2011; 25(6):801-14.
2. Lane NE, Brandt K, Hawker G, Peeva E, Schreyer E, Tsuji W, Hochberg MC. OARSI-FDA Initiative: Defining the Disease State of Osteoarthritis. Osteoarthritis and Cartilage 2011; 19: 478-482.
3. Brandt KL, Dieppe P, Radin EL. Etiopathogenesis of Osteoarthritis. Rheum Dis Clin N Am. 2008; 34: 531-559.
4. Wenham CY, Conaghan PG. Imaging the Painful Osteoarthritic Knee Joint: What Have we Learned? Nat. Clin Rheumatol. 2009; 5(3): 149-58.
5. Wilson DR, McWalter EJ, Johnston JD. The measurement of joint mechanics and their role in osteoarthritis genesis and progression. Rheum Dis Clin North Am. 2008; 34(3):605-22.
6. Kapoor M, Martel-Pelletier J, Lajeunesse D, Pelletier JP, Fahmi H. Role of proinflammatory cytokines in the pathophysiology of osteoarthritis. Nat Rev Rheumatol. 2011;7(1):33-42
7. Sandell LJ. Etiology of osteoarthritis: genetics and synovial joint development. Nat Rev Rheumatol. 2012 Jan 10;8(2):77-89
8. Felson DT, Lawrence RC, Dieppe PA, Hirsch R, Helmick CG, Jordan JM, Kington RS, Lane NE, Nevitt MC, Zhang Y, Sowers M, McAlindon T, Spector TD, Poole AR, Yanovski SZ,

Ateshian G, Sharma L, Buckwalter JA, Brandt KD, Fries JF. Osteoarthritis: new insights. Part 1: the disease and its risk factors. Ann Intern Med. 2000. 17;133(8):635-46.

9. Pereira D, Peleteiro B, Araújo J, Branco J, Santos RA, Ramos E. The effect of osteoarthritis definition on prevalence and incidence estimates: a systematic review. Osteoarthritis Cartilage. 2011;19(11):1270-85.
10. Leunig M, Casillas MM, Hamlet M, Hersche O, Nötzli H, Slongo T, Ganz R. Slipped capital femoral epiphysis: early mechanical damage to the acetabular cartilage by a prominent femoral metaphysis. Acta Orthop Scand. 2000;71(4):370-5.
11. Ganz R, Leunig M, Leunig-Ganz K, Harris WH. The etiology of osteoarthritis of the hip: an integrated mechanical concept. Clin Orthop Relat Res. 2008;466(2):264-72.
12. Pohl MB, Lloyd C, Ferber R. Can the reliability of three-dimensional running kinematics be improved using functional joint methodology? Gait Post. 2010: 32; 559-63.
13. Eitzen I, Fernandes L, Nordsletten L, Risberg MA. Sagittal Plane Gait Characteristics in Hip Osteoarthritis Patients with Mild to Moderate Symptoms Compared with Healthy Controls: A Cross Sectional Study. BMC Musculoskeletal Disorders 2012 13: 258.
14. Hurwitz DE, Hulet CH, Andriachhi TP, Rosenberg AG, Galante JO. Gait Compensations in Patients with Osteoarthritis of the Hip and their Relationship to Pain and Passive Hip Motion. Journal of Orthopaedic Research 1997 15: 629-635.
15. Thurston AJ. Spinal and Pelvic Kinematics in Osteoarthrosis of the Hip Joint. Spine. 1985 10(5), 467-71.

16. Watelain E, Dujardin F, Babier F, Dubois D, Allard P. Pelvis and Lower Limb Compensatory Actions of Subjects in an Early Stage of Hip Osteoarthritis. Arch Phys Med Rehabil. 2001 82: 1705-1711.

17. Roos EM, Juhl CB. Osteoarthritis 2012 year in review: rehabilitation and outcomes. Osteoarthritis Cartilage. 2012;20(12):1477-83

18. Dorleijn DM, Luijsterburg PA, Reijman M, Kloppenburg M, Verhaar JA, Bindels PJ, Bos PK, Bierma-Zeinstra SM. Effectiveness of intramuscular corticosteroid injection versus placebo injection in patients with hip osteoarthritis: design of a randomized double-blinded controlled trial. BMC Musculoskelet Disord. 2011;12;12:280.

19. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, Dougados M, Hochberg M, Hunter DJ, Kwoh K, Lohmander LS, Tugwell P. OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage. 2010;18(4):476-99.

20. Fransen M, McConnell S, Hernandez-Molina G, Reichenbach S. Does land-based exercise reduce pain and disability associated with hip osteoarthritis? A meta-analysis of randomized controlled trials. Osteoarthritis Cartilage 2010; 18(5): 613-20.

21. Leigh RJ, Pohl MB, Ferber R. Does tester experience influence the reliability with which 3D gait kinematics are collected in healthy adults? Physical Therapy in Sport. 2014; 15(2): 112-6.

22. Leardini A, Chiari L, Della Croce U, Cappozzo A. Human movement analysis using stereophotogrammetry. Part 3. Soft tissue artifact assessment and compensation. Gait Posture. 2005;21(2):212-25.

23. Besier TF, Sturnieks DL, Alderson JA, Lloyd DG. (2003). Repeatability of gait data using a functional hip joint centre and a mean helical knee axis. J Biomech. 36, 1159-68.

24. Fernandes L, Hagen KB, Bijlsma JW, Andreassen O, Christensen P, Conaghan PG, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. Ann Rheum Dis 2013; 72(7): 1125-35.

25. French HP, Cusack T, Brennan A, Caffrey A, Conroy R, Cuddy V, et al. Exercise and manual physiotherapy arthritis research trial (EMPART) for osteoarthritis of the hip: a multicenter randomized controlled trial. Arch Phys Med Rehabil 2013; 94(2): 302-14.

26. Fernandes L, Storheim K, Sandvik I, Nordsletten I, Risberg MA. Efficacy of patient education and supervised exercise vs patient education alone in patients with hip osteoarthritis: a single blind randomized clinical trial. Osteoarthritis Cartilage 2010; 18(10): 1237-43.

27. McGinley JL, Baker R, Wolfe R, Morris ME. (2009). The reliability of three-dimensional kinematic gait measurements: a systematic review. Gait Post. 29, 360-9.

28. Osis ST, Hettinga BA, Macdonald SL, Ferber R. A novel method to evaluate error in anatomical marker placement using a modified generalized Procrustes analysis. Comput Methods Biomech Biomed Engin. 2014;18(10):1108-1116.

29. Besier TF, Sturnieks DL, Alderson JA, Lloyd DG. Repeatability of gait data using a functional hip joint centre and a mean helical knee axis. J Biomech. 2003. 36, 1159-68.

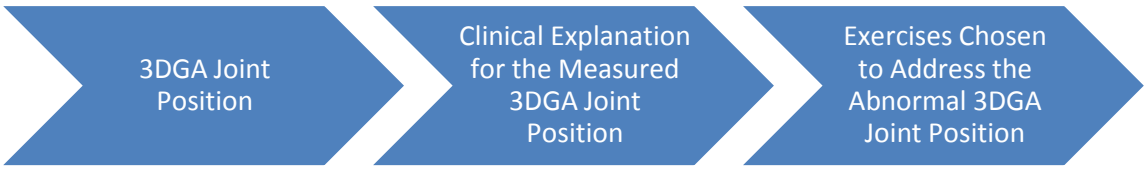
30. Bedson J, Croft PR. The discordance between clinical and radiographic knee osteoarthritis: a systematic search and summary of the literature. BMC Musculoskelet Disord. 2008; 2:9:116.
31. Kumar D, Wyatt CR, Lee S, Nardo L, Link TM, Majumdar S, Souza RB. Association of cartilage defects, and other MRI findings with pain and function in individuals with mild-moderate radiographic hip osteoarthritis and controls. Osteoarthritis Cartilage. 201;21(11):1685-92.
32. Correa TA ,Crossley KM, Kim HJ, Pandy MG. Contributions of individual muscles to hip joint contact force in normal walking. J Biomech. 2010: 28;43(8):1618-22.
33. Courties A, Gualillo O, Berenbaum F, Sellam J. Metabolic stress-induced joint inflammation and osteoarthritis. Osteoarthritis Cartilage. 2015;23(11):1955-65.
34. Wang X, Hunter D, Xu J, Ding C. Metabolic triggered inflammation in osteoarthritis. Osteoarthritis Cartilage. 2015;23(1):22-30.

APPENDIX A. Variables Measured in the Pre-Randomization Standard Clinical Assessment

Variable			Measurement Position
Muscle Strength	Hip Flexion		Seated, lower legs over the edge of plinth, dynamometer placed 4 finger widths above patellar base, subject asked to “lift the leg to the ceiling”
	Hip Extension		Prone, knee bent to 90 degrees, dynamometer placed 4 fingers above popliteal crease line, subject asked to “lift the leg to the ceiling”
	Hip Abduction		Side-ly, hip in neutral, dynamometer placed over 4 fingers over the lateral tibio-femoral joint line, subject asked to “lift the leg to the ceiling”
	Hip Internal Rotation		Seated, legs over the edge of plinth, dynamometer placed 2 fingers above medial malleolus, subject asked to “push leg outwards away from body”
	Hip External Rotation		Seated, legs over the edge of plinth, dynamometer placed 2 fingers above lateral malleolus, subject asked to “pull leg inwards towards opposite leg”
	Knee Extension		Seated, legs over the edge of plinth, dynamometer placed 2 finger widths above anterior tibio-fibular joint, subject asked to “kick leg forward”
Muscle Length	Hip Flexor		Thomas Test Position, inclinometer placed along the top of the mid-thigh
	Hamstring		Supine, knee straight, hip flexed to end-range, goniometer placed over the greater trochanter, stationary arm parallel to bed, moving arm along along femur
	Gastrocnemius		Prone, knee straight, ankle dorsiflexed to end-range, goniometer placed over the lateral malleolus, stationary arm along fibula, moving arm along lateral aspect foot
	Soleus		Prone, knee bent, ankle dorsiflexed to end-range, goniometer placed over the lateral malleolus, stationary arm along fibula, moving arm along lateral aspect foot

Joint ROM	Hip Internal ROM		Prone, knee bent to 90 degrees, goniometer placed over tibial tubercle, stationary arm perpendicular to the plinth, moving arm parallel to the tibial crest, lower leg moved away from body
	Hip External ROM		Prone, knee bent to 90 degrees, goniometer placed over tibial tubercle, stationary arm perpendicular to the plinth, moving arm parallel to the tibial crest, lower leg moved towards mid-line
	Hip Abduction ROM		Supine, knee straight, goniometer placed over the anterior superior iliac spine, stationary arm on a line between each ASIS, moving arm along the mid-line of the thigh, leg moved away from mid-line

Appendix B. Pre-Randomization Clinical Decision Making Algorithm for How Exercises Were Selected from 3DGA Joint Angle Outputs.



Anterior Pelvic Tilt	**Tight Hip Flexors/Anterior Capsule, Weak Hip Extensors**	**Hip Flexor Lengthening and/or Gluteus Maximus Strengthening**
Posterior Pelvic Tilt	**Unusual in Hip OA**	
Pelvic Hike/Drop	**Weak Contralateral Hip Abductor, Tight Quadratus Lumborum**	**Contralateral Hip Abductor Strengthening**
Pelvic Rotation	**Weak Hip External Rotators, Tight Internal Rotators**	**Hip Abductor Strengthening, Internal Rotator Lengthening**
Increased Hip Flexion/ Decreased Hip Extension	**Tight Hip Flexors/Ant Capsule and/or Weak Hip Extensors**	**Hip Flexor Lengthening, Hip Extensor Strengthening**
Increased Hip Abduction	**Pain Response, Increased Base of Support, Decreased Hip Abductor Strength**	**Hip Abductor Strengthening**
Increased Hip External Rotation	**Tight Hip External Rotators, Weak Hip Internal Rotators**	**Hip External Rotator Lengthening**
Increased Knee Flexion/ Decreased Knee Extension	**Decreased Quadriceps Control Strength**	**Strengthening**
Increased Ankle Plantar-Flexion/ Decreased Dorsi-Flexion	**Tight Ankle Plantar-Flexors**	**Plantarflexor Strengthening**