ANALYSIS OF ORTHOSIS WITH BIOMECHANICAL INTERVENTIONS AND GAIT MODIFICATIONS FOR MEDIAL KNEE OSTEOARTHRITIS PATIENTS

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ANALYSIS OF ORTHOSIS WITH BIOMECHANICAL INTERVENTIONS AND GAIT MODIFICATIONS FOR MEDIAL KNEE OSTEOARTHRITIS PATIENTS

ABSTRACT

The study aimed at (1) investigating the effects of altering foot progression angles on physical balance in healthy and medial knee osteoarthritis (kOA) participants, (2) assessing the immediate effects of orthoses (valgus knee brace and wedged insoles) and gait modification techniques (toe-in and toe-out gait) in improving the physical function of kOA participants, and (3) testing the hypothesis that toe-in gait will reduce first peak of knee adduction moment (fKAM), while toe-out gait will reduce its second peak (sKAM) when combined with knee brace and laterally wedged insoles in kOA patients. Biodex Balance System was used to measure postural stability and fall risk at different foot progression angles (from -20º to 40º, with 10º increments) on 20 healthy and 20 kOA patients randomly with different static and dynamic platform settings. Five performance-based tests: (1) 30-second Chair Stand Test (30CST) (2) 40m Fast-Paced Walk test (40FPW) (3) Stair Climb Test (SCT) (4) Timed Up-and-Go test (TUG) (5) 6-Minute Walk Test (6MWT) were applied on 20 healthy and 20 kOA patients randomly to measure physical function. fKAM and sKAM were determined through 3-dimensional gait analysis with nine randomized conditions: (1) N (natural gait, without any intervention), (2) brace, (3) brace + toe-in gait, (4) wedged insole, (5) wedged insole + toe-in gait, (6) knee brace + wedged insole + toe-in gait, (7) brace + toe-out gait, (8) wedged insole + toe-out gait, (9) brace + wedged insole + toe-out gait. Fall risk was assessed by the Biodex Balance System® using three stability settings, (i) static (ii) moderate dynamic setting (FR12) and (iii) high dynamic setting (FR8). Data from the tests were analyzed using independent sample t-test, 3-way mixed methods ANOVA and repeated-measures

ANOVA. Platform settings had a significant interaction effect with participant group ($p < 0.01$) and toe angles ($p < 0.01$). Toe-out gait impaired the physical function while knee brace improved it during 40FPW, SCT and 6MWT. fKAM reduced maximally (19.7%) by brace + toe-in gait, while sKAM reduced maximally by brace + wedged insole + toe-out gait (25.5%). Fall risk increased significantly at FR8 when knee brace and wedged insoles were combined with toe-in gait (35.7%) and toe-out gait (42.9%). Changing platform settings had a more pronounced effect on balance in kOA group than healthy group. Changing toe angles produced similar effects in both the participant groups, with decreased stability and increased fall risk at extreme toe-in and toe-out angles. Physical function was improved maximally by the knee brace, while toe-out gait impaired it the most. There is a synergistic effect of toe-in gait and toe-out gait when combined with knee brace and wedged insole concurrently in the reductions in the first and the second peaks of knee adduction moment respectively but with a greater risk of fall.

Keywords: Toe-in gait, toe-out gait, valgus knee brace, laterally wedged insole, knee osteoarthritis

ANALISIS ORTOSIS DENGAN INTERVENSI BIOMEKANICAL DAN UJI MODIFIKASI UNTUK PESAKIT OSTEOARTHRITIS KAIN MEDIA

ABSTRAK

Kajian ini bertujuan untuk (1) menyelidiki kesan perubahan sudut perkembangan kaki pada keseimbangan fizikal pada pesakit osteoartritis lutut yang sihat dan medial, (2) menaksir kesan langsung ortosa (penyangga lutut valgus dan persik berlabuh) teknik pengubahsuaian (berjalan kaki dan berjalan kaki keluar) dalam meningkatkan fungsi fizikal peserta kOA, (3) menguji hipotesis yang berjalan kaki akan mengurangkan puncak momen penambahan lutut (fKAM), manakala langkah kaki keluar akan mengurangkan puncak kedua (sKAM) apabila digabungkan dengan pendakap lutut dan selekoh yang dipasangkan di pesakit kOA. Sistem Imbangan Biodex digunakan untuk mengukur kestabilan postur dan risiko jatuh pada sudut perkembangan kaki yang berbeza (dari -20º hingga 40º, dengan peningkatan 10º) pada 20 pesakit yang sihat dan 20 kOA secara rawak dengan tetapan platform statik dan dinamik yang berlainan. Lima Ujian berasaskan prestasi: (1) Ujian Stand Kursi 30 saat (30CST) (2) Ujian Walk Fast 40m (40FPW) (3) Ujian Menaiki Tangga (SCT) Ujian Pergi (TUG) (5) Ujian Jalan 6-Minute (6MWT) telah digunakan pada 20 pesakit yang sihat dan 20 kOA secara rawak untuk mengukur fungsi fizikal. Eksperimen 3: fKAM dan sKAM ditentukan melalui analisis gait tiga dimensi dengan sembilan syarat rawak: (1) N (gaya gawat semula jadi, tanpa sebarang campur tangan), (2) pendakap, (3) pendakap + (5) insole yang disandarkan + toe-in gait, (6) penyokong lutut + insole yang disandarkan + toe-in gait, (7) brace + toe-out gait, 9) brace + insole tergelincir + berjalan kaki kaki. Risiko jatuh ditaksir oleh Biodex Balance System® menggunakan tiga tetapan kestabilan, (i) statik (ii) tetapan dinamik sederhana (FR12) dan (iii) tetapan dinamik tinggi (FR8). Data daripada ujian dianalisis dengan menggunakan ujian t sampel bebas, ANOVA bercampur 3-langkah dan ANOVA berulang. Pengaturan platform mempunyai kesan interaksi yang signifikan dengan kumpulan peserta ($p < 0.01$) dan sudut kaki ($p < 0.01$). Gangguan kaki keluar merosakkan fungsi fizikal semasa pendakap lutut membaikinya semasa 40FPW, SCT dan 6MWT. FKAM dikurangkan secara maksima (19.7%) dengan cara berpegangan + kaki berjalan, sementara sKAM dikurangkan secara maksima dengan menggunakan + insole yang dicelup ke arah kaki (25.5%). Risiko kejatuhan meningkat dengan ketara pada FR8 apabila penyokong lutut dan persik berlabuh digabungkan dengan berjalan kaki (35.7%) dan berjalan kaki kaki (42.9%). Mengubah tetapan platform mempunyai kesan yang lebih jelas pada keseimbangan dalam kumpulan kOA daripada kumpulan yang sihat. Mengubah sudut jari kaki menghasilkan kesan yang sama dalam kedua-dua kumpulan peserta, dengan kestabilan menurun dan peningkatan risiko jatuh pada sudut yang luar biasa dan kaki luar. Fungsi fizikal telah dipertingkatkan secara maksima oleh penyokong lutut, sementara berjalan kaki keluar yang paling merosot. Terdapat kesan sinergistik untuk berjalan kaki dan kaki keluar apabila dikombinasikan dengan penyokong lutut dan berlubang dalam serentak dalam penurunan pada tahap pertama dan puncak kedua lutut saat lutut masing-masing tetapi dengan risiko yang lebih besar jatuh.

Kata kunci: Jalan kaki kejalan, berjalan kaki keluar, pendakap lutut valgus, lapik dalam baji sisi, osteoarthritis lutut

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LIST OF SYMBOLS AND ABBREVIATIONS

ACL Brace	:	Anterior Cruciate Ligament Brace
ADL	:	Activities of Daily Living
BBS	:	Biodex Balance System
CG	:	Control Group
CoP	:	Centre of Pressure
CPM-ES	:	Continuous Passive Motion with Electrical Stimulation
fKAM	:	First peak of Knee Adduction Moment
FPA	:	Foot Progression Angle
GRF	:	Ground Reaction Force
IAHA	:	Intra-Articular Hyaluronic Acid
IFC	:	Interferential Current
JKOM	:	Japanese Knee Osteoarthritis Measure score
KAAI	:	Knee Adduction Angular Impulse
KAM	:	Knee Adduction Moment
KB	:	Knee Brace
KFM	:	Knee Flexion Moment
kOA	:	Knee Osteoarthritis
KO	:	Knee Orthosis
KOOS	:	Knee injury and Osteoarthritis Outcome Score
KSS	:	Knee Society Score
LEAS	:	Lower Extremity Activity Scale
LEFS	:	Lower Extremity Functional Scale
LWAS	:	Laterally Wedged Insoles with Arch Support
LWI	:	Laterally Wedged Insoles
NHP	:	Nottingham Health Profile
NMES	:	Neuromuscular Electric Stimulation

NRS	:	Numeric Rating Scale
OA	:	Osteoarthritis
OAG	:	Osteoarthritis Group
OSI	:	Overall Stability Index
PEMF	:	Pulsed Electromagnetic Field
PES	:	Pulsed Electrical Stimulation
SF-36	:	Short Form health survey
sKAM	:	Second peak of Knee Adduction Moment
SWD	:	Shortwave Diathermy
TENS	:	Transcutaneous Electric Nerve Stimulation
TI	:	Toe-in gait
TO	:	Toe-out gait
TSP	:	Temporal Spatial Parameter
TUG	:	Timed Up and Go
VAS	:	Visual Analogue Scale
V3P Brace	:	V3P Valgus Brace
VER Brace	:	Valgus External Rotation Brace
WOMAC	:	Western Ontario and McMaster University Osteoarthritis Index

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CHAPTER 1: GENERAL INTRODUCTION

1.1 Background

The research for the treatment and prevention of osteoarthritis encompasses several fields that involve the relationship between force, motion and energy. Joint degeneration can be understood more comprehensively by taking into account the mechanical factors involved. Joint loadings, angles and moments all need to be in delicate balance in order to maintain a healthy knee and can hence prevent gradual degradation (Moyer, Ratneswaran, Beier *et al.*, 2014a). One of the major consequences of knee joint degradation is knee osteoarthritis.

Knee osteoarthritis is the most commonly occurring type of osteoarthritis in the world (Badley, 2005; Lawrence, Felson, & Helmick, 2008) largely because of its wearisome mobility and load-bearing characteristics during gait. In Malaysia, the prevalence of knee osteoarthritis is found to be 10% to 20% of the population (Maly & Robbins, 2014).. Such a large prevalence requires the need of extensive research in the prevention and therapy of knee osteoarthritis and finding more economical alternatives to the existing techniques.

Out of the current existing treatment techniques for knee osteoarthritis, joint replacement is the most effective (Maly & Robbins, 2014). The technique however is invasive, complex and expensive, hence not very popular among the developing countries. Pharmacological treatments, that involve intra-articular hyaluronic acid injections and steroids, can cause pain relief but can cause increase in knee adduction moment and can alter knee biomechanics (that can last up to 6 months) (Griffin, Piper, R. *et al.*, 1991; Griffin, Ray, & Schaffner, 1988; Smalley & Griffin, 1996; Tang, Tang, Hong *et al.*, 2015). Therefore, there is a need for alternative non-surgical and non-pharmacological techniques that are cost-effective and can reduce pain & knee joint loads and improve physical & mental function.

Non-surgical and non-pharmacological techniques that prove to be effective in reducing knee joint loading include physiotherapy (Gaudreault, Mezghani, Turcot *et al.*, 2011), resistance training (Farr, Going, McKnight *et al.*, 2010), muscle strengthening (Foroughi, Smith, Lange *et al.*, 2011), electromagnetic field therapy (Özgüçlü, Çetin, Çetin *et al.*, 2010), tai-chi (Wang, Iversen, McAlindon *et al.*, 2014), aquatic/ land-based exercises (Wang, Lee, Liang *et al.*, 2011), TENS, interferential currents, short-wave diathermy (Atamaz, Kirazli, & Akkoc, 2006) and radiation therapy (Hsieh, Lo, Liao *et al.*, 2012b). The shortcoming of these interventions is that the muscles of knee osteoarthritis patients weaken and they cannot tolerate these vigorous treatments (Cherian, Bhave, Kapadia *et al.*). The most economical and easy-to-apply interventions remain the biomechanical interventions which include laterally wedged insoles, neutral insoles, knee braces and modified walking shoes.

Among the mentioned biomechanical interventions, knee brace is the only one that targets knee adduction moment, malalignment, knee joint load reduction, pain relief and functional improvement simultaneously. A number of different types of knee braces are commercially available, but there is still a debate as to which one covers all the treatment parameters optimally. For instance, significant decrease in net knee adduction moment (KAM) was observed when using unloader (Arazpour, Bani, Maleki *et al.*, 2013), pneumatic (Della Croce, Crapanzano, & Li, 2013) and 3 point bending valgus braces (Fantini Pagani, Böhle, Potthast *et al.*, 2010) in studies that include single-visit as well as those with follow-ups. Further reduction in KAM was observed with valgus brace of 4º adjustment (as compared to neutral setting) (Fantini Pagani, Böhle, Potthast *et al.*, 2010) and valgus brace with 7 psi inflation (as compared to uninflated brace) (Della Croce, Crapanzano, & Li, 2013). Up to 26% reduction in KAM was observed by knee braces. No effects of unloader knee brace (Toriyama, Deie, Shimada *et al.*, 2011) and 3 point bending knee brace (Fantini Pagani, Potthast, & Brüggemann, 2010) were found on net

KAM in two single visit studies. Similar contradictory results were obtained from the studies that compared the efficacy of knee brace in terms of pain and functional improvement.

The studies that compared the effects of knee brace versus laterally wedged insoles reported that both have similar effects in reducing KAM (Arazpour, Bani, Maleki *et al.*, 2013; Moyer, Birmingham, Dombroski *et al.*, 2013). However, laterally wedged insoles are usually preferred over braces because of their ease of use, light weight, low cost and minimal adverse effects (van Raaij, Reijman, Brouwer *et al.*, 2010).

On the other hand, there is a growing research interest in investigating modifications in the gait pattern, as a strategy to alter the load on the knee joint, and thereby to decrease the pain and further progression of OA (Hunt & Takacs, 2014; Simic, Bennell, Hunt *et al.*, 2011; Simic, Wrigley, Hinman *et al.*, 2013; van den Noort, Schaffers, Snijders *et al.*, 2013b). Gait modification techniques present a simple and inexpensive treatment strategy that have a potential to be employed by a range of health-care professionals to reduce medial knee joint load. These modifications include a reduction in walking speed, medial knee thrust, a toe-out or toe-in foot position and medio-lateral trunk sway. Trunk sway is reported to decrease knee adduction moment the most (Gerbrands, Pisters, & Vanwanseele, 2014) but was found to be the most difficult in to employ in terms of aesthetics, maintaining balance and comfort (Shull, Silder, Shultz *et al.*, 2013). Increasing walking speed has been found to be increasing joint load, but decreasing the speed has not shown significant reduction in knee adduction moment (van den Noort, Schaffers, Snijders *et al.*, 2013a).Toe-in gait is found to be significantly reducing the early stance knee adduction moment (Shull, Huang, Schlotman *et al.*, 2015; van den Noort, Schaffers, Snijders *et al.*, 2013a), while toe-out gait reduces late stance knee adduction moment (Caldwell, Laubach, & Barrios, 2013; Hunt & Takacs, 2014).

1.2 Problem Statement

Since there is evidence from the literature that synergistic effects of a laterally wedged insoles and toe-in/out gait exist, there may be a possibility that further combinations of biomechanical interventions and gait modification methods may prove to be a better treatment regime for medial knee osteoarthritis. Similarly, there is a need of comparing the effects of orthoses against gait modification methods. These comparisons should be made in terms of the parameters that define the performance of the activities of daily living (ADLs), like physical performance measures and balance, and also in terms of the parameters that represent the progression of the disease, like knee adduction moment. Furthermore, to the best of our knowledge, there is no previous investigation of the immediate effects of foot progression angles, laterally wedged insoles and knee brace on postural stability and risk of fall.

1.3 Objectives of the Study

The main aim of this study is to explore the combination of orthoses and gait modifications in terms of knee joint load, balance and physical performance for medial knee osteoarthritis patients. The objectives of this study are:

1. To investigate the effects of varying degrees of foot progression angles and platform settings on overall postural stability and fall risk.
2. To investigate comparatively the immediate responses of orthoses and gait modification methods in improving physical performance measures.
3. To investigate the immediate combined responses of orthoses and gait modification methods on the knee adduction moment, comfort level and risk of fall.

1.4 Thesis Contribution

The thesis will contribute to the literature by exploring the biomechanical parameters as well as the physical performance parameters when the medial knee osteoarthritis patients are subjected to a combination of two types of conservative treatment techniques namely orthoses and gait modification methods. The thesis will also provide a comparison of these two types of conservative treatment techniques in terms of physical performance and biomechanical outcome measures.

1.5 Thesis Outline

The thesis is written in the article style format, where chapters 3 to 6 represent the experiments done to address objectives 1 to 3. The dissertation consists of eight chapters:

Chapter 1 presents a general introduction of the thesis, stating the objectives of the study.

Chapter 2 provides a systematic review of the literature dealing with non-surgical and non-pharmacological treatment techniques for medial knee osteoarthritis.

Chapter 3 evaluates the effects of different foot progression angles and balance platform settings on postural stability and fall risk in healthy and medial knee osteoarthritic adults. This chapter gives us a safe range of foot progression angles that we have used in the experiments represented in the upcoming chapters

Chapter 4 addressing objective 2 compares orthoses versus gait modification methods in terms of immediate response in improving physical performance measures in healthy and medial knee osteoarthritic adults. The chapter presents a discussion of the results and the conclusions drawn from the study. This chapter assesses the efficiency of the orthoses and gait modification techniques in terms of physical performance of the participants, while the chapters following this (Chapters 5 and 6), assesses these techniques in terms of joint kinetics and balance.

Chapter 5 presents combined effects of knee brace, laterally wedged insoles and toe-in gait on knee adduction moment, comfort level and risk of fall on moderate medial knee osteoarthritis patients. This chapter addresses the toe-in aspect of objective 3.

Likewise, **Chapter 6** presents a combined effects of knee brace, laterally wedged insoles and toe-out gait on knee adduction moment, comfort level and risk of fall on moderate medial knee osteoarthritis patients. . This chapter addresses the toe-out aspect of objective 3.

Chapter 7 presents a brief discussion of the findings of the various experiments performed for this study, as presented in Chapters 3 to 6.

Finally, **Chapter 8** summarizes the contributions of this work towards the knowledge of the effects of toe-out and toe-in gait along with knee brace and laterally wedged insoles. Limitations of the study and future directions are also stated in this chapter.

CHAPTER 2: LITERATURE REVIEW

2.1 Introduction

The chapter presents a systematic review, considering the studies evaluating the non-surgical and non-pharmacological treatment of knee osteoarthritis. The first section deals with the definition and global burden of knee osteoarthritis prevalence, different treatment techniques and the measuring variable of knee osteoarthritis severity. Subsequently, the chapter presents the methodology of the literature search and defines the tools used to assess the included studies. The results section presents a short descriptive analysis of the studies. In the conclusion, the chapter identifies the gaps in the previous works that are attempted to be addressed in the current study.

2.2 Background

Joints are the linkages between bones that make human skeleton able to move and locomote. Their deterioration can cause pain and / or partial to complete inability to walk. The major cause of synovial joint deterioration in the present world is Osteoarthritis (OA) that is found to be most common in the middle-aged and elderly population (Ganasegeran, MichaelMenke, Ramaswamy *et al.*, 2014). Among the lower limb joints the hip, knee and ankle joints are mostly affected by OA which renders them painful, inflamed and progressively immobile. OA does not only affect the structural components of the joints (cartilages, menisci, ligaments etc.) but also the neuromuscular control of the joints it attacks (Segal, Anderson, & Iyer, 2009).

As the knee joint has more mobility in regular gait cycle while performing daily activities, it is more prone to degeneration and OA than other joints (Badley, 2005; Lawrence, Felson, & Helmick, 2008). It is estimated that between the ages of 60 and 64, men acquire knee OA symptoms as 23% for right knee and 16.3% for left knee, while in women it is found to be 24.2% for right knee and 24.7% for left knee (Andrianakos, Kontelis, & Karamitsos, 2006; D'Ambrosia, 2005). The prevalence of knee OA is mostly among the females and increases rapidly over age. It is estimated that above the age of 65, 70% of the women acquire the symptoms of knee OA (Brooks, 1998). For Malaysia its prevalence is found to be 10-20% of the population (Malaysia). It is also important to note that knee OA mostly affects medial compartment of the knee joint (almost 10 times more than lateral compartment) (Ahlback, 1968). Studies have demonstrated that this is due to high peak adduction moment in the medial compartment, therefore most of the therapeutic techniques for knee OA are targeted at reducing knee adductor moment (Crenshaw, Pollo, & Calton, 2000; Schipplein & Andriacchi, 1991).

The causative factors for OA can be both endogenous and exogenous. Besides the hereditary, gender and age factors, other main causes are obesity (BMI greater than 30kg/m2), menopause, occupation involving continued kneeling or squatting posture and microtrauma (Walter, D'lima, Colwell Jr *et al.*, 2010).

The type of therapeutic technique administered for knee OA depends upon several factors, such as severity of the problem, patient's physical condition and economic condition. The surgical or invasive techniques that include high tibial osteotomy and Total Knee Arthroplasty (TKA) are effective but are very expensive (Grelsmer, 1995; Maquet, 1985). IAHA injections can provide pain relief but also cause increased knee adduction moment for 6 months after dose administration which can increase the severity of OA (Tang, Tang, Hong *et al.*, 2015). Pharmacological treatments such as NSAID's (Non-Steroidal Anti-Inflammatory Drugs) and acetaminophen while less expensive, are not efficient in relieving the symptoms and can lead to hazardous effects(Griffin, Piper, R. *et al.*, 1991; Griffin, Ray, & Schaffner, 1988; Smalley & Griffin, 1996). Physical Therapy or Physiotherapy provides effective relief but its effects are limited (Bennell, Egerton, Martin *et al.*, 2014; Deyle, Allison, Matekel *et al.*, 2005; Iversen, 2012). Two relatively uncommon non-invasive and non-pharmacological techniques are Pulse Electromagnetic Field (PEMF) and Pulsed Electrical Stimulation (PES). Pulsed electrical potentials are provided to the knee joint in order to speed up cartilage repair. Its adverse effects are undesired bone tissue changes at higher frequencies (Thawer, 1999).

The most basic of the biomechanical interventions for the therapy of knee OA is a lateral wedged insole or a lateral wedged orthosis. It is worn as a regular insole and aims to minimize knee valgus thus reducing knee adduction moment in the medial compartment. The efficacy and cost-effectiveness of lateral wedged insoles have been appreciated over the years but are not much effective in advanced degrees of OA and do not prove to be effective in pain reduction (Baker, Goggins, Xie *et al.*, 2007; Parkes, Maricar, & Lunt, 2013; Pham, Maillefert, Hudry *et al.*, 2004). Furthermore, wedged insoles have design limitations as they can be quite uncomfortable for the patient if the degree of wedging increases from 6º (Tipnis, Anloague, Laubach *et al.*, 2014). A knee brace or knee orthosis is a more advanced and focused intervention for knee OA. Several types of knee valgus braces have been designed that have the same purpose of reducing knee adduction moment and unloading medial compartment of the knee. So far many studies have authenticated their role in reducing knee adduction moment but their role in decreasing pain and unloading of the medial compartment is still debatable (Fantini Pagani, Potthast, & Brüggemann, 2010; Komistek, Dennis, Northcut *et al.*, 1999; Sorour, Ayoub, & Abd El Aziz, 2014). Another limitation is the cost-effectiveness of knee braces, as they can be quite expensive as compared to wedged insoles (Raaij, Brouwer, & Verhaar, 2010).

Recently several systematic studies and meta-analyses have been conducted to cumulate and compare different treatment options of knee OA (Maly, Culham, & Costigan, 2002; Mat, Tan, Kamaruzzaman *et al.*, 2014; Moyer, Birmingham, Dombroski *et al.*, 2013; Negm, Lorbergs, & Macintyre, 2013a; Palm, Brattinger, Stegmueller *et al.*, 2012; Segal, 2012). Segal compared brace, knee sleeve and wedged insole techniques and came to the conclusion that each has its own pros and cons and prove to be efficient in their own domain, thus none can be generally prioritized over the other (Segal, 2012). Another study by Negam *et al* reviewed the effects of low frequency (≤100Hz) pulsed subsensory threshold electric stimulations and concluded that these pulses while effective in physical function, are not that efficient in pain relief (Negm, Lorbergs, & MacIntyre, 2013b). Moyer et al addressed the variety of different mechanical methods of knee OA treatment in order to study the research advancements in the field (Moyer, Ratneswaran, Beier *et al.*, 2014b). Mali et al focused on the studies published in the year 2013 dealing with the rehabilitation of hip and knee OA and concluded that weight reduction (with diet and exercise) is the most efficient and safe way for OA treatment (Maly & Robbins, 2014). Mat et al focused on the outcomes of physical therapy techniques in increasing balance control and decreasing the risk of falling in knee OA patients. This study gathered that only Tai Chi and aerobics are significantly effective in balance control and fall risk (Sumaiyah, Tan, Kamaruzzaman *et al.*, 2015). In another study, Moyer et al reviewed studies on valgus knee braces to report their respective biomechanical effects and concluded that knee braces do make biomechanical changes but no conclusive statement can be made about this without further studies (Moyer, Birmingham, Bryant *et al.*, 2015).

Several of the previous systematic reviews do not give a clear direction for the potential decision makers and do not highlight the methodology of the selected studies that may affect the outcomes of the studies. This study aims to review the efficacy of non-surgical and non-pharmacological techniques employed for the treatment of knee OA and aims to summarize the methodology of each of these studies in order to guide the researchers who intend to modify or upgrade the existing techniques.

2.3 Methodology

2.3.1 Study Question

Based on the PICOS (Participants, Interventions, Comparisons, Outcomes, Study design) structure, the authors defined the study questions as: ‘To study the efficacy and recent advancements of non-pharmacological and non-surgical techniques for the treatment of knee OA’.

2.3.2 Literature Search

Primarily, literature search was conducted using three major databases, namely PubMed, Web of Science, and Science Direct in two months (December 2014 and January 2015). The keywords used for searches were: ‘treatment for knee OA’, ‘treatment of knee OA by knee brace’, ‘osteoarthritis and physical medicine’, ‘use of physiotherapy to treat knee OA’, ‘treatment of knee osteoarthritis by using physical medicine’, ‘knee brace’, ‘electrical nerve stimulation in knee OA’, ‘electrotherapy’ and ‘lateral wedge insoles and knee OA’.

2.3.3 Inclusion Criteria

Figure 2.1 presents the search strategy for the literature survey. The inclusion criteria for studies were:

1. Participants with knee OA (may be clinically or radiologically confirmed). No restrictions were put for Kellgren-Lawrence grade (Kellgren & Lawrence, 1957), or region of knee OA. Participants had no other major diseases (diabetes, cerebral palsy, hepatitis etc.).
2. All the studies were to be published in ISI Indexed journals (Q1 and Q2 only). By doing this, it was ensured that only high quality and high impact studies are reviewed.
3. Studies in English language only.

4. Only experimental studies.
5. Studies that involved human subjects only.
6. The review was conducted for studies for the past five years (2010 to 2014).
7. Treatment techniques were non-pharmacological and non-surgical.
8. All experimental study designs were included (randomized controlled trials, controlled trials, randomized cross-over, cross-over, case-control studies, cohort studies, experimental studies with cross-sectional analysis).
9. Studies with only well-defined methodology were included.
10. No restrictions on follow-up. Single visit studies were also included.
11. Only the studies with free full texts were considered.
12. Abstracts, editorials, letters, reviews, theses/ dissertations were excluded.
13. Participants aged 18 years and above.
14. No studies rejected on the base of geography.
15. Both funded and non-funded studies were included.

2.3.4 Types of Interventions

The studies included in this review were based on a single intervention or comparison between multiple interventions. An intervention was defined as a technique which facilitates in knee OA treatment or symptomatic relief. For the ease of understanding, the studies are grouped according to the types of interventions used. The following interventions were considered for this review, as these are the most advanced and commonly used ones in the recent times:

- Knee brace: Valgus knee brace, Patellar knee brace.
- Insoles: Laterally Wedged Insoles (LWI) with and without medial arch support, Shock absorbing insoles, flat insoles
- Footwear: Modified shoes designed for OA

- Gait Modification: Toe-in gait, toe-out gait, trunk sway, mild/ medium crouch, medial thrust etc.
- Physiotherapy: Standard physiotherapy, high Resistance training, isometric exercise
- Electrical Stimulation Therapy: Pulsed Electrical Stimulation (PES), Continuous Passive Motion with Electrical Stimulation (CPM–ES), stochastic ratio electrical stimulation, TENS, IFC, SWD, NMES
- Pulsed Electromagnetic Field (PEMF) Therapy.
- Radiation Therapy
- Contralateral cane and hiking pole use

2.3.5 Methods

The review was based on Cochrane Collaboration methodology(Higgins, Green, & Collaboration, 2008). The PRISMA (Liberati, Altman, Tetzlaff *et al.*, 2009) guidelines were followed in reports, tables and meta-analysis.

2.3.6 GRADE Assessment

The quality ratings of studies were determined by GRADE (Grading of Recommendations Assessment, Development and Evaluation) (Guyatt, Oxman, Vist *et al.*, 2008). By this system, the studies are downgraded and upgraded according to certain criteria. The studies were downgraded based on the following: (1) Study limitations (e.g. lack of or improper blinding, improper sample selection); (2) Indirectness (e.g. healthy participants for research on knee OA), (3) Inconsistency of results (e.g. explanation of heterogeneity); (3) Imprecision (e.g. small sample size, too few events); (4) Publication bias (e.g. exclusion of certain outcomes). The studies were upgraded if they had shown dose-response. An overall quality rating was determined as high, moderate, low or very low by weighing these downgrading and upgrading factors. Initially, studies with randomization were given a high-quality rating and were then downgraded on the basis of downgrading qualities.

2.3.7 Risk of Bias Assessment

The risks of bias were assessed after dividing the studies into two categories, as randomized studies and non-randomized studies. The factors taken into account for randomized studies were: random sequence generation (selection bias), allocation sequence concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and wash out period (for cross-over studies). An overall risk of bias was designated to each study after weighing the individual factors.

For non-randomized studies, the factors were taken as: sample size calculation, ethical approval, blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other biases (e.g. wash-out period, vague methodology, inclination of hiding significant information, no adverse effects of the intervention). An overall risk of bias was designated to each study after weighing the individual factors.

2.3.8 Reliability of Assessment

The assessment of Risk of bias and GRADE was done independently by two reviewers. Any disagreements were resolved by mutual consensus. For determination of study designs, an Epidemiologist was consulted.

2.3.9 Summary of the Selected Studies

The authors while doing literature search felt that there was a lack of a briefly summarized account of the included studies in systematic reviews. Most of the reviews usually provide the sample sizes and major outcomes of the studies. The authors therefore, have presented in Appendix A, Table 1 the major points of distinction of the individual studies. The table can be of interest to researcher as it can facilitate in designing of their experiments.

2.3.10 Forest Plots

The Forest plots for different outcome measures from the selected studies were plotted using RevMan 5.3. The outcomes were all of continuous nature so the arguments used were mean, standard deviation/ standard error and number of subjects in each group in order to calculate Standard Mean Difference (SMD) at a fixed 95% confidence interval. Where the standard deviation was not provided, range of confidence interval was used to calculate it. SMD was calculated according to the study type, e.g. between control and experimental groups, between pre-and post-intervention data, between base-line and follow-up data. The outcomes selected for which forest plots are: Net KAM, first peak KAM, second peak KAM, Pain, walking speed and KAAI.

2.3.11 Meta-Analysis and Heterogeneity

The studies included in this review belonged to a wide range of categories on the basis of types of interventions, randomization, Kellgren-Lawrence grades of OA, follow-ups and modes of interventions (*in-vivo* or *in-vitro*) a meaningful and reliable meta-analysis could not be performed. For the same reasons heterogeneity among studies was not assessed.

2.4 Results

2.4.1 Included Studies

Initially 247 potentially relevant studies were identified through database searches, see Figure 2.1. Out of these, 133 remained after removal of duplicates. By going through their abstracts, 15 studies were excluded based on our inclusion criteria. Full texts of 118 articles were assessed, out of which 61 were selected as included studies for the review (see Figure 2.1). Out of 61 studies, 12 studies were of high quality, 27 studies were of moderate quality. 19 were of low quality and 3 were of very low-quality rating (Appendix A, Table 1). Twenty-one studies were Randomized Controlled Trial (RCT).

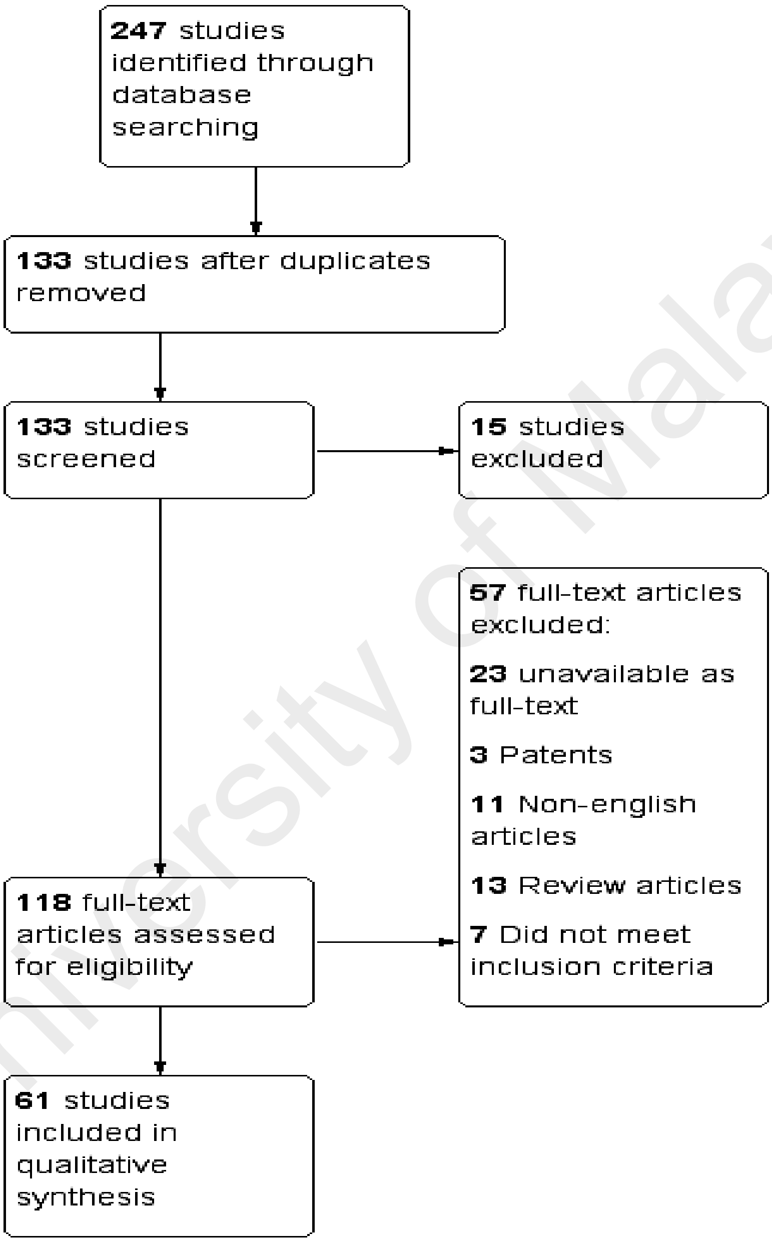


Figure 2.1 Search strategy for literature survey.

2.4.2 Follow-Up

Twenty four studies were single visit (Abdallah & Radwan, 2011; Boyer, Federolf, Lin *et al.*, 2012; Della Croce, Crapanzano, & Li, 2013; Esrafilian, Karimi, & Eshraghi, 2012; Fantini Pagani, Potthast, & Brüggemann, 2010; Fantini Pagani, Willwacher, Kleis *et al.*, 2013; Hinman, Bardin, Simic *et al.*, 2013; Hunt, Birmingham, Giffin *et al.*, 2006; Jones, Zhang, Laxton *et al.*, 2013; Kean, Bennell, Wrigley *et al.*, 2013; Kinney, Besier, Silder *et al.*, 2013; Kutzner, Küther, Heinlein *et al.*, 2011; Leitch, Birmingham, Jones *et al.*, 2011; Riskowski, 2010; Shull, Shultz, Silder *et al.*, 2013; van den Noort, Schaffers, Snijders *et al.*, 2013b; Yeh, Chen, Hsu *et al.*, 2014), while the rest had follow-ups ranging from 2 weeks (Fantini Pagani, Böhle, Potthast *et al.*, 2010; Jones, Nester, Richards *et al.*, 2013; McWalter, Hunter, Harvey *et al.*, 2011; Özgüçlü, Çetin, Çetin *et al.*, 2010) to 18 months (Messier, Ettinger, Doyle *et al.*, 1996) (see Appendix A, Table 2).

2.4.3 Funding

Out of 61 studies, 41 studies reported funding source, 7 were unfunded, while 13 did not mention any funding source or grant for their study (Appendix A, Table 2).

2.4.4 Participants

A total of 3149 participants were recruited for 61 studies in which 2767 retained, with a retention rate of 87.8% (Appendix A, Table 2). Female participants took part in the studies mostly; with an approximate percentage of 70% (this value is approximate because not all studies provided gender-wise participants information). Five studies (Abdallah & Radwan, 2011; Hiyama, Yamada, Kitagawa *et al.*, 2012; Khademi-Kalantari, Mahmoodi Aghdam, Akbarzadeh Baghban *et al.*, 2014; Riskowski, 2010; Yeh, Chen, Hsu *et al.*, 2014) reported to have worked with taking female participants only, while one study (Fantini Pagani, Potthast, & Brüggemann, 2010) employed only male participants.

2.4.5 Risk of Bias in Randomized Studies

The risk of bias summary and graph are presented in Figures 2.2, and 2.3 respectively. The selection bias (random sequence generation) was found to be high in 9 studies. High risk was allocated to studies that did not clearly mention randomization process, only the word 'randomization' was used or any such randomization process was used that had inherent high risk (e.g. randomization according to date of birth, alternate numbers shuffling etc.). If no evidence in favour of either high or low risk was found, the risk of bias was said to be 'unclear'. No study had high risk of bias for allocation concealment, because most of the studies were unlikely to be affected by this risk.

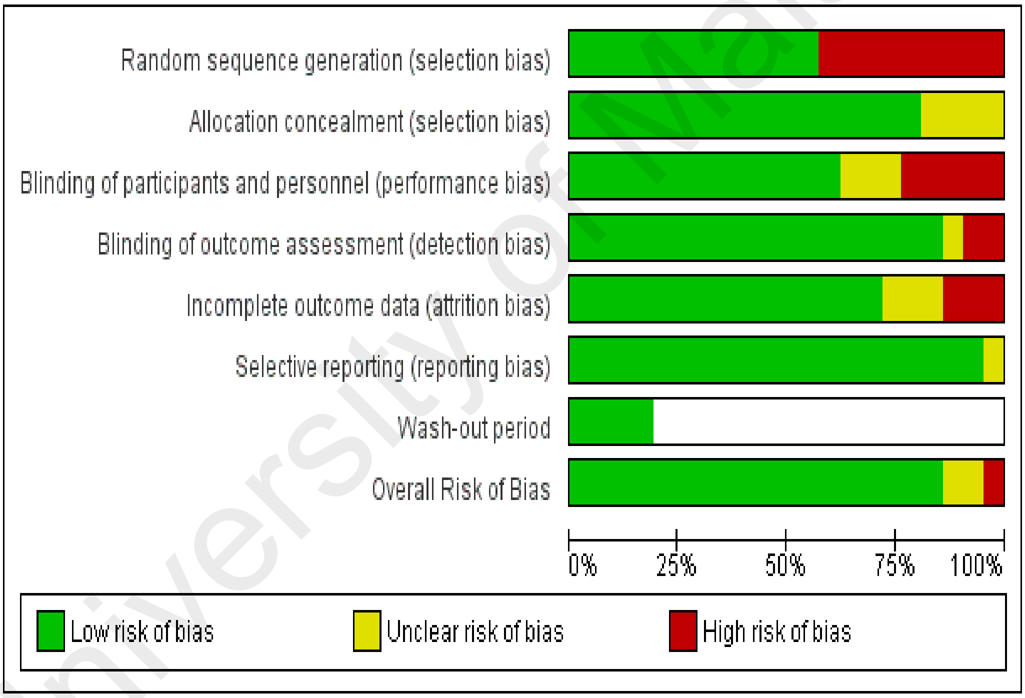


Figure 2.2: Risk of bias graph for randomized studies.

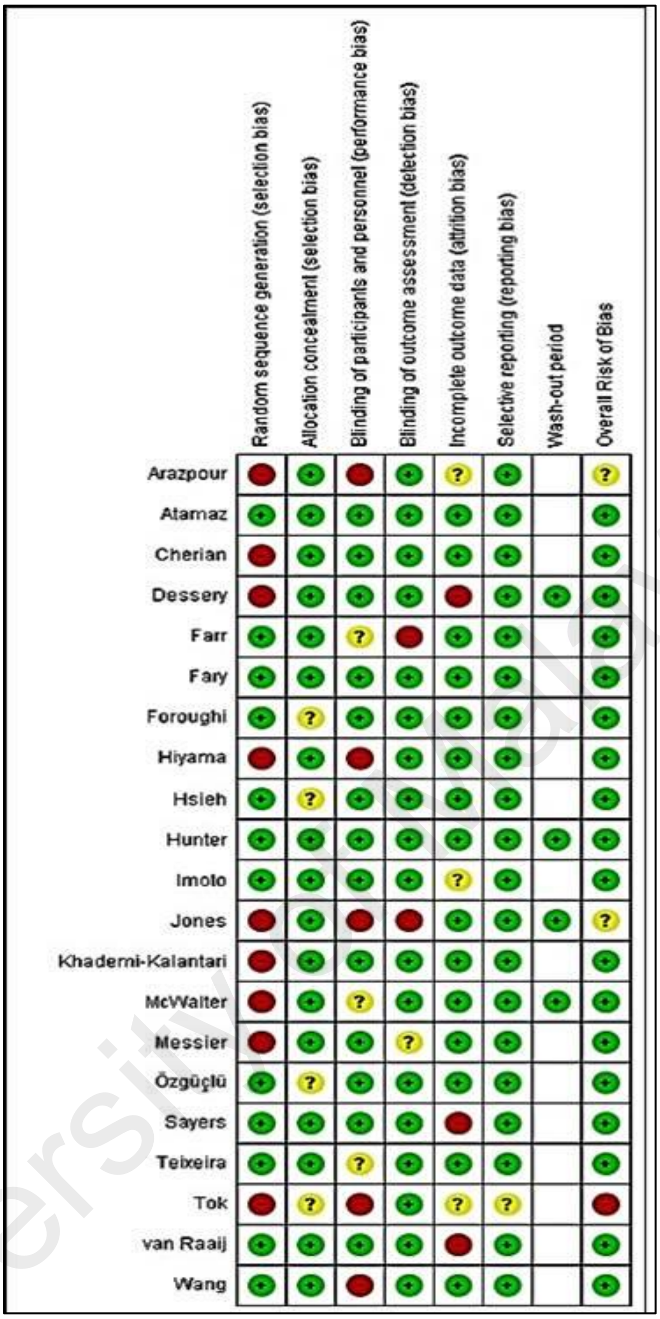


Figure 2.3: Risk of bias summary for randomized studies.

Overall performance and detection biases were also found to be low for these studies, as some of them were single/ double blinded, while in most of them blinding was not possible due to nature of interventions used. High risks of bias were given to the studies where blinding was possible and could have possibly affected the outcomes. Attrition bias and reporting bias were also found to be low among the selected studies. A high attrition bias was rated to the studies where there was a large loss to follow-up. Wash-out period was for randomized-crossover studies, as it is important that the effects of one intervention do not carry-over to another intervention. No high risk of bias for this effect was found in the selected studies.

Only one study was found to have high overall risk of bias because of its high and unclear risk of bias components (Tok, Aydemir, Peker *et al.*, 2011). Two studies were rated to have unclear overall risk of bias (Arazpour, Bani, Maleki *et al.*, 2013; Jones, Nester, Richards *et al.*, 2013), while rest of the 18 studies were rated to have low risk of bias.

2.4.6 Risk of Bias in Non-Randomized Studies

The judgement criteria for non-randomized studies were stricter, because of inherent risk in their study design. Since no randomization was done in these studies, we introduced two bias criteria for them: sample size calculation and ethical approval. The risk of bias summary and graph for non-randomized studies are presented in Figures 2.4 and 2.5. Out of 40 non-randomized studies, 11 studies did not do (or did not report) any sample size calculation, thus were rated a high risk of bias. Four studies had high risk of bias for ethical approval as they did not take (or did not report) approval from an ethical review board despite having human subjects. Studies were given high performance or detection bias if: participants and assessors or either one of them were not blinded and blinding of outcomes assessment could have affected the results. This criterion for performance bias resulted in only 4 studies having low risk of bias. Reporting bias remained low in the non-randomized studies same as in randomized studies. Other biases were rated high for 14 studies on the basis of: vague methodology, no wash-out period between interventions, and inclination of hiding significant information or no reporting of adverse effects of the intervention. Overall risks of bias were high for 6 studies on the basis of high risk components present in them.

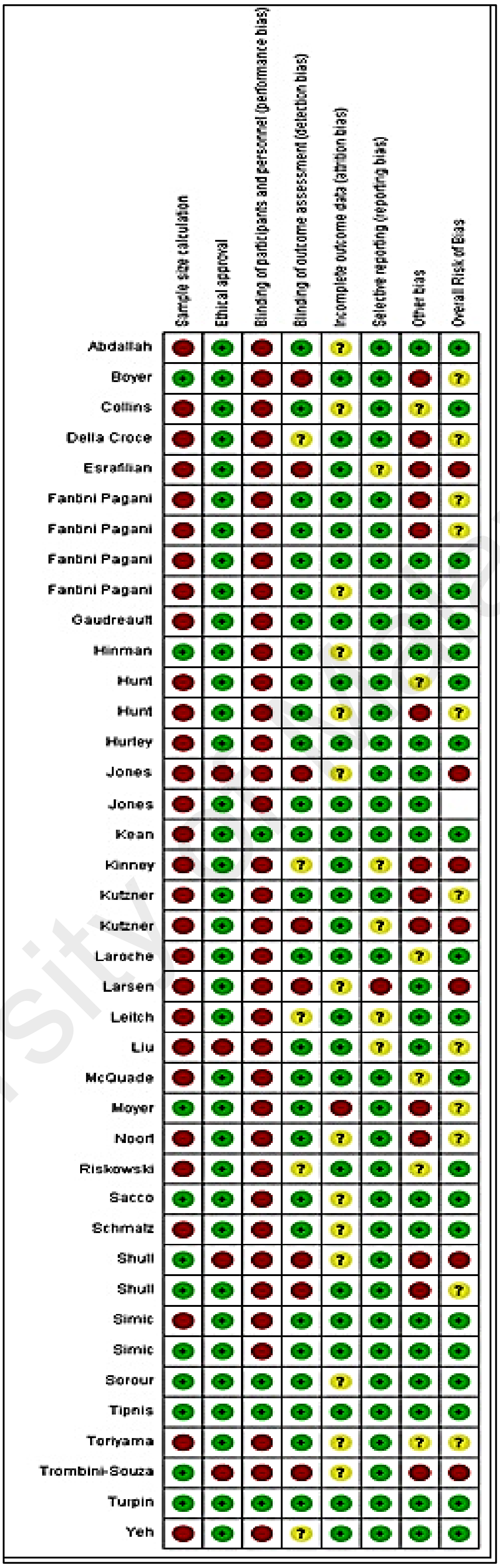


Figure 2.4: Risk of bias summary for non-randomized studies.

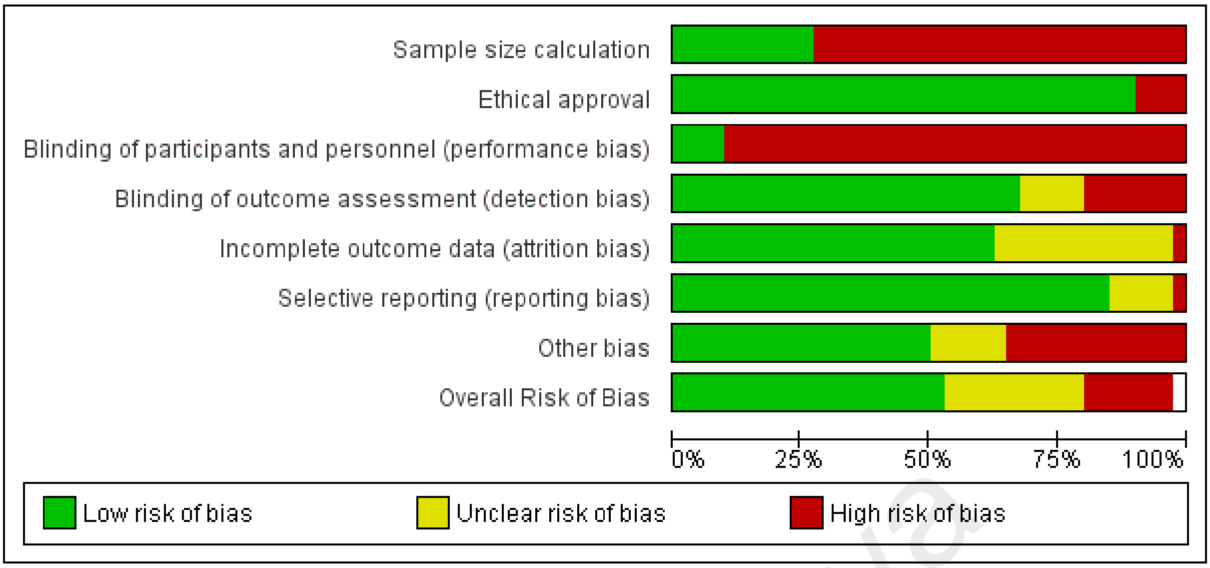


Figure 2.5: Risk of bias graph for non-randomized studies

2.4.7 Knee Adduction Moment (KAM)

KAM was reported as net, first peak or second peak in different studies. As they are clinically different, their forest plots were drawn separately (Figures 2.6, 2.7 and 2.8).

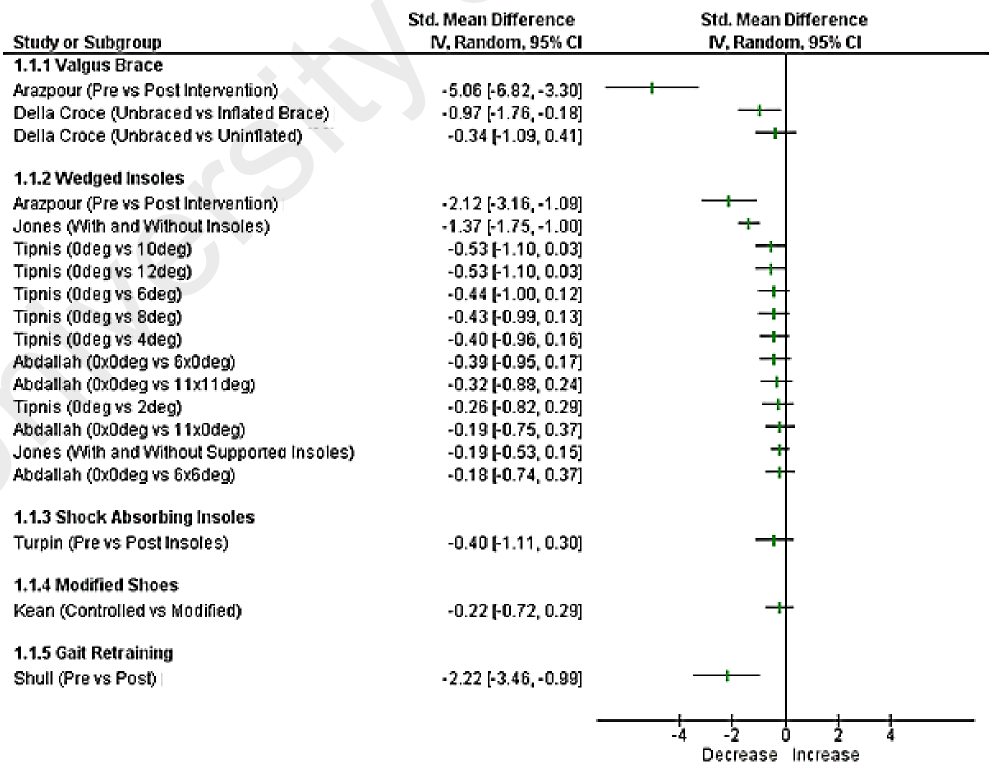


Figure 2.6: Forest plot for net knee adduction moment for the selected studies.

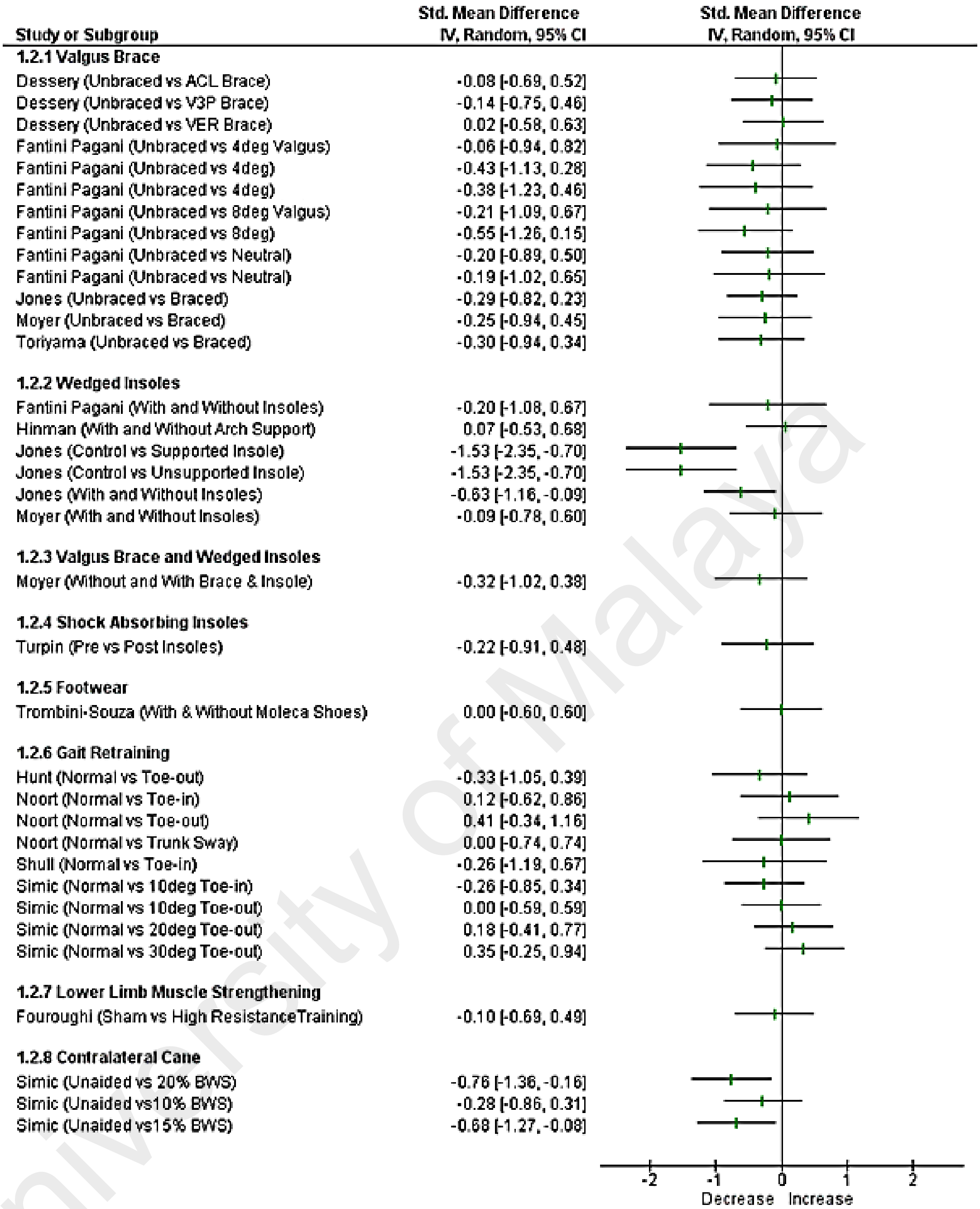


Figure 2.7: Forest plot for first peak KAM.

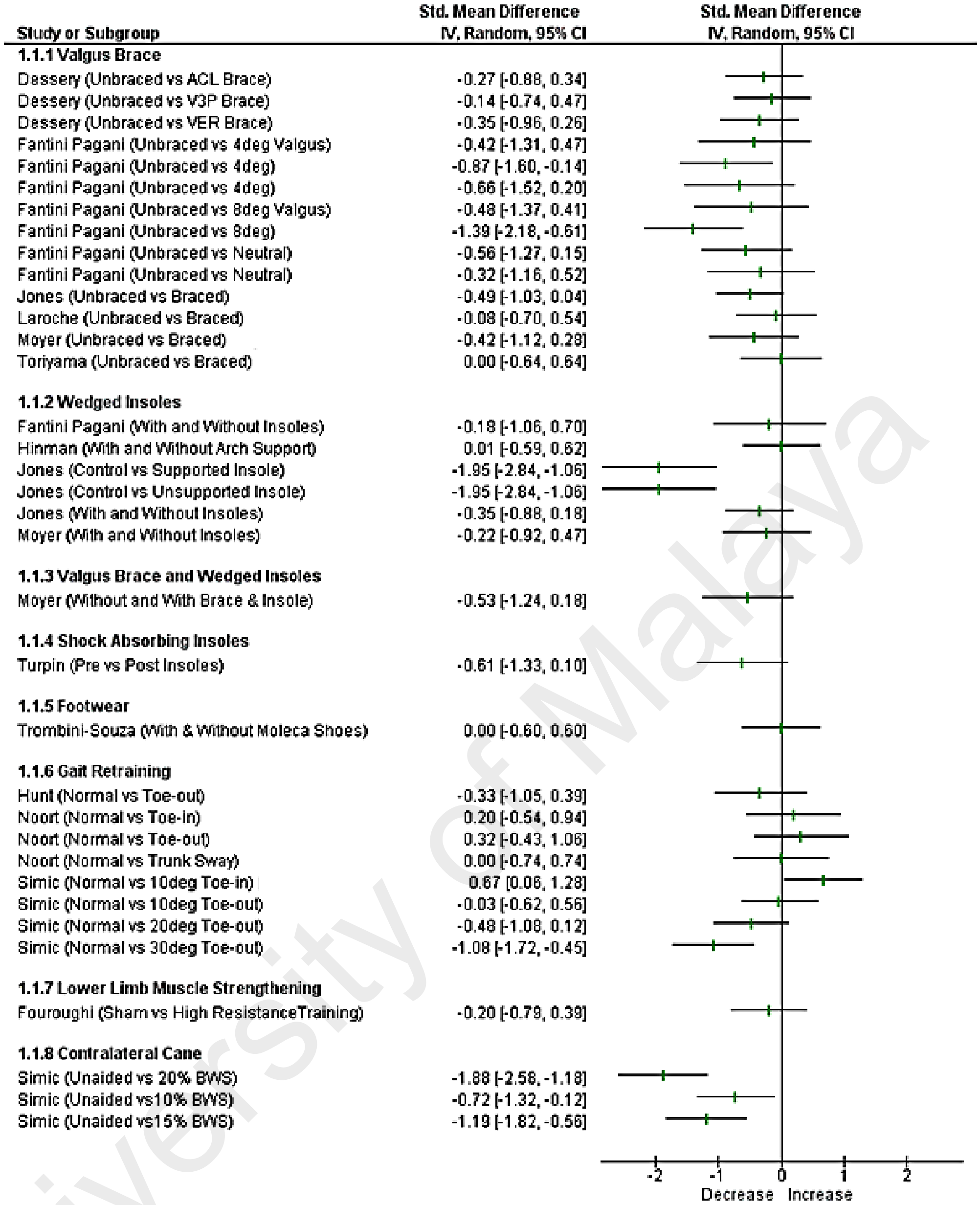


Figure 2.8: Forest plot for second peak KAM.

2.4.7.1 Knee Brace

A total of 13 studies reported the effects of KAM by knee braces (Arazpour, Bani, Maleki *et al.*, 2013; Della Croce, Crapanzano, & Li, 2013; Dessery, Belzile, Turmel *et al.*, 2014; Esrafilian, Karimi, & Eshraghi, 2012; Fantini Pagani, Böhle, Potthast *et al.*, 2010; Fantini Pagani, Hinrichs, & Brüggemann, 2012; Fantini Pagani, Potthast, & Brüggemann, 2010; Jones, Nester, Richards *et al.*, 2013; Laroche, Morisset, Fortunet *et* *al.*, 2014; Larsen, Jacofsky, Brown *et al.*, 2013; Moyer, Birmingham, Dombroski *et al.*, 2013; Riskowski, 2010; Toriyama, Deie, Shimada *et al.*, 2011). Out of these studies, 7 considered net KAM (Arazpour, Bani, Maleki *et al.*, 2013; Della Croce, Crapanzano, & Li, 2013; Esrafilian, Karimi, & Eshraghi, 2012; Fantini Pagani, Böhle, Potthast *et al.*, 2010; Fantini Pagani, Hinrichs, & Brüggemann, 2012; Fantini Pagani, Potthast, & Brüggemann, 2010; Toriyama, Deie, Shimada *et al.*, 2011), 7 considered first peak KAM (Dessery, Belzile, Turmel *et al.*, 2014; Fantini Pagani, Böhle, Potthast *et al.*, 2010; Fantini Pagani, Hinrichs, & Brüggemann, 2012; Fantini Pagani, Potthast, & Brüggemann, 2010; Jones, Nester, Richards *et al.*, 2013; Moyer, Birmingham, Dombroski *et al.*, 2013; Toriyama, Deie, Shimada *et al.*, 2011), 8 considered second peak KAM (Dessery, Belzile, Turmel *et al.*, 2014; Fantini Pagani, Böhle, Potthast *et al.*, 2010; Fantini Pagani, Hinrichs, & Brüggemann, 2012; Fantini Pagani, Potthast, & Brüggemann, 2010; Jones, Zhang, Laxton *et al.*, 2013; Laroche, Morisset, Fortunet *et al.*, 2014; Moyer, Birmingham, Dombroski *et al.*, 2013; Toriyama, Deie, Shimada *et al.*, 2011), 1 considered mid-stance KAM (Laroche, Morisset, Fortunet *et al.*, 2014), 1 considered peak knee abductor moment (Riskowski, 2010) (Riskowski, 2010) while 1 study considered peak knee abductor moment in stance and swing phases (Larsen, Jacofsky, Brown *et al.*, 2013). Significant decrease in net KAM was observed when using unloader (Arazpour, Bani, Maleki *et al.*, 2013), pneumatic (Della Croce, Crapanzano, & Li, 2013) and V3P valgus braces (Fantini Pagani, Böhle, Potthast *et al.*, 2010) in single-visit studies as well as those with follow-ups. Further reduction in KAM was observed with valgus brace of 4º adjustment (as compared to neutral setting) (Fantini Pagani, Böhle, Potthast *et al.*, 2010) and valgus brace with 7psi inflation (as compared to uninflated brace) (Della Croce, Crapanzano, & Li, 2013). Up to 26% reduction in KAM was observed by knee braces. No effects of unloader knee brace (Toriyama, Deie, Shimada *et al.*, 2011) and V3P knee brace (Fantini Pagani, Potthast, & Brüggemann, 2010) were found on net KAM in two single visit studies.

First peak KAM was reported to be reduced by unloader brace (Toriyama, Deie, Shimada *et al.*, 2011) and V3P brace (Fantini Pagani, Potthast, & Brüggemann, 2010). On the other hand it was reported to be unaffected by unloader brace with external rotation function and V3P brace (Dessery, Belzile, Turmel *et al.*, 2014). Second peak KAM was reported to be unaffected by unloader brace (Toriyama, Deie, Shimada *et al.*, 2011). While it was reported to be significantly affected by V3P brace (Fantini Pagani, Potthast, & Brüggemann, 2010; Moyer, Birmingham, Dombroski *et al.*, 2013), unloader brace with external rotation function (Dessery, Belzile, Turmel *et al.*, 2014), functional knee brace (used in ligament injuries) (Dessery, Belzile, Turmel *et al.*, 2014) and distraction rotation brace (Laroche, Morisset, Fortunet *et al.*, 2014) by three studies.

KAM and knee abduction moment in swing were reported to increase immediately after wearing knee brace. This effect was found to be insignificant after 2 months follow-up (Larsen, Jacofsky, Brown *et al.*, 2013). In other study that used a feedback based gait monitoring brace, it was reported that the knee abductor moment increased from 13.8% to 22% after 30 minutes training (Riskowski, 2010).

2.4.7.2 Insoles

Twelve studies investigated the effects of insoles on KAM (Abdallah & Radwan, 2011; Arazpour, Bani, Maleki *et al.*, 2013; Fantini Pagani, Hinrichs, & Brüggemann, 2012; Hinman, Bardin, Simic *et al.*, 2013; Jones, Chapman, Forsythe *et al.*, 2014; Jones, Nester, Richards *et al.*, 2013; Jones, Zhang, Laxton *et al.*, 2013; Kinney, Besier, Silder *et al.*, 2013; Leitch, Birmingham, Jones *et al.*, 2011; Moyer, Birmingham, Dombroski *et al.*, 2013; Tipnis, Anloague, Laubach *et al.*, 2014; Turpin, De Vincenzo, Apps *et al.*, 2012). Seven of them took net KAM as outcome measure (Abdallah & Radwan, 2011; Arazpour, Bani, Maleki *et al.*, 2013; Fantini Pagani, Hinrichs, & Brüggemann, 2012; Jones, Chapman, Forsythe *et al.*, 2014; Leitch, Birmingham, Jones *et al.*, 2011; Tipnis, Anloague, Laubach *et al.*, 2014; Turpin, De Vincenzo, Apps *et al.*, 2012) while six took the first and second peak KAM values (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Hinman, Bardin, Simic *et al.*, 2013; Jones, Nester, Richards *et al.*, 2013; Jones, Zhang, Laxton *et al.*, 2013; Moyer, Birmingham, Dombroski *et al.*, 2013; Turpin, De Vincenzo, Apps *et al.*, 2012) .Two studies also considered mid-stance KAM (Jones, Nester, Richards *et al.*, 2013; Jones, Zhang, Laxton *et al.*, 2013).

Several studies reported a significant reduction of net KAM (Arazpour, Bani, Maleki *et al.*, 2013; Fantini Pagani, Hinrichs, & Brüggemann, 2012; Leitch, Birmingham, Jones *et al.*, 2011; Tipnis, Anloague, Laubach *et al.*, 2014), peak KAM values (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Hinman, Bardin, Simic *et al.*, 2013; Jones, Zhang, Laxton *et al.*, 2013) by using LWI with (Hinman, Bardin, Simic *et al.*, 2013; Jones, Zhang, Laxton *et al.*, 2013; Tipnis, Anloague, Laubach *et al.*, 2014) or without (Arazpour, Bani, Maleki *et al.*, 2013; Fantini Pagani, Hinrichs, & Brüggemann, 2012; Hinman, Bardin, Simic *et al.*, 2013; Jones, Zhang, Laxton *et al.*, 2013) medial arch support. One study tested the effects for shock absorbing insoles for one month and found differences only in second peak KAM, while first peak KAM and net KAM remained the same (Turpin, De Vincenzo, Apps *et al.*, 2012). Similar difference was found by another study which tested LWI without medial arch support, while first peak KAM remained the same (Moyer, Birmingham, Dombroski *et al.*, 2013). A randomized cross-over study tested LWI and reported reduction in first peak KAM only (among first, second and mid-stance peak KAM values), after 2 week follow-up (Jones, Nester, Richards *et al.*, 2013). Two studies compared LWI with arch support to the one without support, and found both to be effective in reducing first and second peak KAM values. No differences were found between the effects of the two interventions (Hinman, Bardin, Simic *et al.*, 2013; Jones, Zhang, Laxton *et al.*, 2013). A single visit study compared the effects of three conditions: control shoes, LWI with support, LWI without support (Jones, Chapman, Forsythe *et al.*, 2014). The study reported that 54% of the participants had similar reduction for the two interventions, 20% had increased KAM for both type of insoles while 25% had inconsistent results among them. An experimental study with cross-sectional analysis considered unilateral and bilateral supported LWI effects on KAM with different inclinations (0ºx0º, 6ºx0º, 6ºx6º, 11ºx0º, 11ºx11º) (Abdallah & Radwan, 2011). No significant reduction was found for any of the experimental conditions against control.

2.4.7.3 LWI and Knee Brace

Four studies compared LWI and valgus knee brace for KAM reduction and found no significant difference between the effects of these two interventions (Arazpour, Bani, Maleki *et al.*, 2013; Fantini Pagani, Hinrichs, & Brüggemann, 2012; Jones, Nester, Richards *et al.*, 2013; Moyer, Birmingham, Dombroski *et al.*, 2013). Simultaneous use of LWI and valgus brace was found to be effective in reducing KAM as compared to individual use (Moyer, Birmingham, Dombroski *et al.*, 2013).

2.4.7.4 Gait Modification

Five studies related to gait modification considered KAM as outcome measure (Hunt & Takacs, 2014; Shull, Lurie, Cutkosky *et al.*, 2011; Shull, Shultz, Silder *et al.*, 2013; Simic, Wrigley, Hinman *et al.*, 2013; van den Noort, Schaffers, Snijders *et al.*, 2013a). One study investigated net KAM (Shull, Lurie, Cutkosky *et al.*, 2011) one investigated mid-stance KAM (van den Noort, Schaffers, Snijders *et al.*, 2013a) while four investigated first and second peak KAM values (Hunt & Takacs, 2014; Shull, Shultz, Silder *et al.*, 2013; Simic, Wrigley, Hinman *et al.*, 2013; van den Noort, Schaffers, Snijders *et al.*, 2013a). One study incorporated data driven models along with haptic feedback system that modified gait to reduce KAM (Shull, Lurie, Cutkosky *et al.*, 2011).

This modification includes increased toe-out (13º-25º), toe-in (13º-25º), trunk sway (7º-17º) and tibia angle (5º-13º). They found at least 30% KAM reduction in 9 out of 10 participants. Another single-visit study tested the effects of toe-in (10º), toe-out (10º, 20º, 30º) and FPA (0º) (Simic, Wrigley, Hinman *et al.*, 2013). They found no change in first and second peak KAM values as compared to natural gait. In contrast, two studies investigated the effects of 5º toe-in gait (Shull, Shultz, Silder *et al.*, 2013) and 10 week toe-out gait (11.5º) (Hunt & Takacs, 2014) and found considerable reduction in first peak KAM only and second peak KAM only respectively, while other peaks remained the same. Van den Noort et al considered the effects of slow (15% reduced) and fast (14% increased) walking speeds, toe-in (19º), toe-out (16º) and trunk sway (14º) angles separately as compared to the natural gait (van den Noort, Schaffers, Snijders *et al.*, 2013a). They reported significant reduction in early stance peak for toe-in, toe-out, and reduction in mid-stance peak for slow walking, toe-in and trunk sway, reduction in late stance peak for toe-out only. Maximum reductions in first peak (45%), second peak (56%) and mid-stance peak (40%) for toe-in, toe-out and slow walking speed respectively. Fast walking speed led to increase in early and late stance peak by 30% and 22% respectively.

2.4.7.5 Footwear

The effects of footwear were tested by five studies (Boyer, Federolf, Lin *et al.*, 2012; Kean, Bennell, Wrigley *et al.*, 2013; Kutzner, Küther, Heinlein *et al.*, 2011; Sacco, Trombini-Souza, Butugan *et al.*, 2012; Trombini-Souza, Kimura, Ribeiro *et al.*, 2011). Two studies used the variable stiffness shoe and found significant reduction in net KAM (Kean, Bennell, Wrigley *et al.*, 2013) and first peak KAM (Boyer, Federolf, Lin *et al.*, 2012). Other two studies tested inexpensive footwear Moleca® and heeled shoes against barefoot in normal walking and stair descent. The hypothesis for these studies was that Moleca® would mimic barefoot gait but it increased first and second peak KAM values insignificantly during stair descent. Heeled shoes increased KAM throughout the stance phase as compared to Moleca® and barefoot walking (Sacco, Trombini-Souza, Butugan *et al.*, 2012; Trombini-Souza, Kimura, Ribeiro *et al.*, 2011). (Kutzner, Küther, Heinlein *et al.*, 2011) et al tested five types of footwear (basic running shoes, high level running shoes, men/ women dress shoes, Masai Barefoot Technology (MBT) shoes) and reported that all these shoes increased KAM by 7-12% (Kutzner, Stephan, Dymke *et al.*, 2013).

2.4.7.6 Physiotherapy/ RT/ Muscle Strengthening

Three of the included studies investigated the effects of physiotherapy, RT and muscle strengthening in KAM (Foroughi, Smith, Lange *et al.*, 2011; Gaudreault, Mezghani, Turcot *et al.*, 2011; McQuade & de Oliveira, 2011). No effect was found for these interventions on KAM. The exercises included: muscle strengthening and stretching, proprioceptive exercises, aerobic training, knee extension/ flexion, hip abduction/ adduction, leg press, plantar-flexion for 8 week (McQuade & de Oliveira, 2011), 12 week (Gaudreault, Mezghani, Turcot *et al.*, 2011) and 6 month (Foroughi, Smith, Lange *et al.*, 2011)follow-up.

2.4.7.7 Contralateral Cane Use

Simic, Bennell, Hunt *et al.* (2011) asked the participants to use cane contralaterally with 10%,15% and 20% body weight support in order to observe the effects on KAM. First and second peak KAM values decreased in all the experimental groups as compared to unaided walking. A dosage-response was also found in the study, that increasing body weight support decreased KAM values.

2.4.8 Knee Adduction Angular Impulse (KAAI)

A total of 20 studies considered KAAI as outcome measure. 4 studies were related to knee brace (Dessery, Belzile, Turmel *et al.*, 2014; Fantini Pagani, Böhle, Potthast *et al.*, 2010; Fantini Pagani, Potthast, & Brüggemann, 2010; Laroche, Morisset, Fortunet *et al.*, 2014), 5 were related to insoles (Hinman, Bardin, Simic *et al.*, 2013; Jones, Chapman, Forsythe *et al.*, 2014; Jones, Zhang, Laxton *et al.*, 2013; Tipnis, Anloague, Laubach *et al.*, 2014; Turpin, De Vincenzo, Apps *et al.*, 2012), 3 to braces and wedged insoles combined (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Jones, Nester, Richards *et al.*, 2013; Moyer, Birmingham, Dombroski *et al.*, 2013), 3 studies each were related to footwear (Kean, Bennell, Wrigley *et al.*, 2013; Sacco, Trombini-Souza, Butugan *et al.*, 2012; Trombini-Souza, Kimura, Ribeiro *et al.*, 2011)and gait modifications (Hunt & Takacs, 2014; Simic, Wrigley, Hinman *et al.*, 2013; van den Noort, Schaffers, Snijders *et al.*, 2013a)and 1 study each was related to physiotherapy (Gaudreault, Mezghani, Turcot *et al.*, 2011) and contralateral cane use (Simic, Bennell, Hunt *et al.*, 2011).

Significant reduction in KAAI was found using V3P knee brace for all adjustments (neutral, 4° and 8°) (Fantini Pagani, Böhle, Potthast *et al.*, 2010; Fantini Pagani, Potthast, & Brüggemann, 2010), external rotation unloader brace (Dessery, Belzile, Turmel *et al.*, 2014), LWI with and without arch support (Hinman, Bardin, Simic *et al.*, 2013; Jones, Chapman, Forsythe *et al.*, 2014; Jones, Zhang, Laxton *et al.*, 2013), variable stiffness shoe (Kean, Bennell, Wrigley *et al.*, 2013) & Moleca® shoe (Sacco, Trombini-Souza, Butugan *et al.*, 2012; Trombini-Souza, Kimura, Ribeiro *et al.*, 2011). Similar reduction in KAAI was found with contralateral cane use (Simic, Bennell, Hunt *et al.*, 2011) and physiotherapy treatment (Gaudreault, Mezghani, Turcot *et al.*, 2011).

Conversely, no effects of shock absorbing insoles (Turpin, De Vincenzo, Apps *et al.*, 2012), V3P brace (Dessery, Belzile, Turmel *et al.*, 2014; Moyer, Birmingham, Dombroski *et al.*, 2013), functional knee brace (Dessery, Belzile, Turmel *et al.*, 2014), and distraction rotation knee brace (Laroche, Morisset, Fortunet *et al.*, 2014) were found by the included studies. Figure 2.9 represents the forest plot for KAAI for the selected studies.

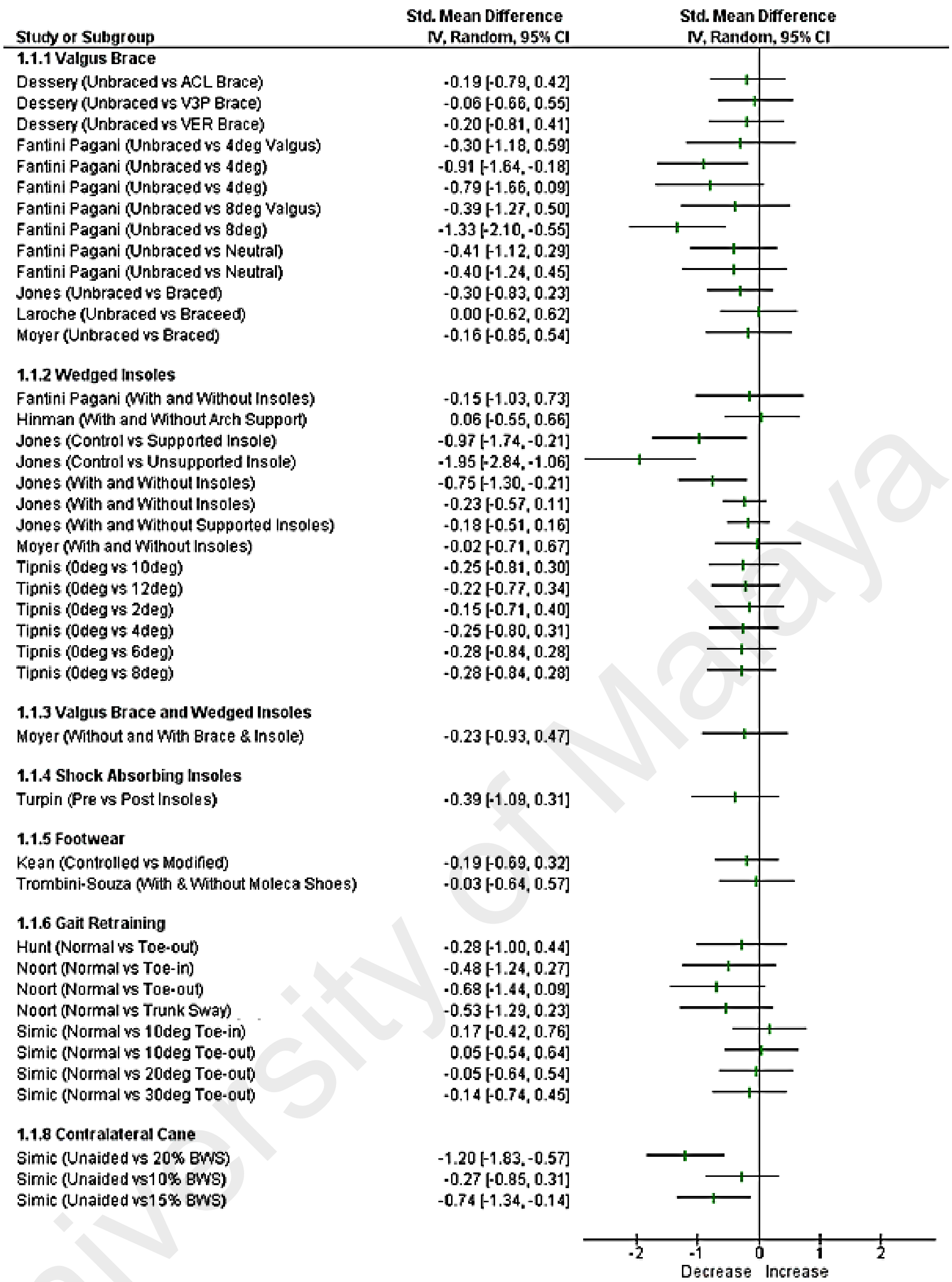


Figure 2.9: Forest plot for the knee adduction angular impulse for the selected studies.

Out of the three that studies compared valgus knee brace with LWI, two of these studies reported a significant reduction in KAAI by both the interventions (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Jones, Nester, Richards *et al.*, 2013). (Jones, Nester, Richards *et al.*, 2013) reported LWI to have more reduction (12%) in KAAI than brace (7%), while (Fantini Pagani, Hinrichs, & Brüggemann, 2012) reported knee brace to have more reduction (14-18%) than LWI (7%) from baseline. On the other hand,(Moyer, Birmingham, Dombroski *et al.*, 2013) reported no significant reduction by both the interventions, however, their simultaneous use could have a considerable effect on KAAI [47].

As for gait modification, two studies reported insignificant change in KAAI with toe-out gait modification (Hunt & Takacs, 2014; van den Noort, Schaffers, Snijders *et al.*, 2013a), while one reported significant decrease (Simic, Wrigley, Hinman *et al.*, 2013). (van den Noort, Schaffers, Snijders *et al.*, 2013a) reported significant decrease in KAAI with 19° toe-in gait while (Simic, Wrigley, Hinman *et al.*, 2013) reported an increase in KAAI with 10° toe-in gait. van den Noort, Schaffers, Snijders *et al.* (2013a) found trunk sway to be decreasing KAAI and slow walking speed to be increasing it.

2.4.9 Knee Flexor Moment (KFM) & Knee Extensor Moment (KEM)

Thirteen studies reported effects of interventions on flexor/ extensor moments. Four of these studies were related to knee brace (Laroche, Morisset, Fortunet *et al.*, 2014; Riskowski, 2010; Schmalz, Knopf, Drewitz *et al.*, 2010; Toriyama, Deie, Shimada *et al.*, 2011), four were related to gait modifications(Hunt & Takacs, 2014; Shull, Shultz, Silder *et al.*, 2013; Simic, Wrigley, Hinman *et al.*, 2013; van den Noort, Schaffers, Snijders *et al.*, 2013b), three were related to LWIs (Hinman, Bardin, Simic *et al.*, 2013; Jones, Chapman, Forsythe *et al.*, 2014; Jones, Zhang, Laxton *et al.*, 2013) and two were related to physiotherapy/ muscle strengthening (Foroughi, Smith, Lange *et al.*, 2011; Gaudreault, Mezghani, Turcot *et al.*, 2011). No change in KFM was found for V3P brace (Schmalz, Knopf, Drewitz *et al.*, 2010), distraction rotation knee brace (Laroche, Morisset, Fortunet *et al.*, 2014), LWI with and without medial arch support (Hinman, Bardin, Simic *et al.*, 2013; Jones, Chapman, Forsythe *et al.*, 2014; Jones, Zhang, Laxton *et al.*, 2013), toe-in gait (Shull, Shultz, Silder *et al.*, 2013) and toe-out gait modifications (Hunt & Takacs,

2014) . Two studies reported a significant difference in KFM at first peak by unloading brace (Toriyama, Deie, Shimada *et al.*, 2011) and significant increase in both KFM and KEM by feedback based gait monitoring knee brace (Riskowski, 2010). (Simic, Wrigley, Hinman *et al.*, 2013) reported that early stance KEM decreased with toe-in and increased with toe-out, while late stance peak KFM increased with toe-in and decreased with toe-out. KFM was found to be reduced significantly with slow and fast walking speeds, with slow walking speed being more effective van den Noort, Schaffers, Snijders *et al.* (2013a). Two studies reported no effect of physiotherapy/ muscle strengthening on KFM (Foroughi, Smith, Lange *et al.*, 2011; Gaudreault, Mezghani, Turcot *et al.*, 2011). (Gaudreault, Mezghani, Turcot *et al.*, 2011), however, when performed Principal Component Analysis (PCA), found that first peak KFM increased significantly.

2.4.10 Knee Range of Motion (Knee Flexion/ Extension Angles)

Twelve studies reported effects of interventions on knee range of motion. Three of these studies were related to knee brace (Esrafilian, Karimi, & Eshraghi, 2012; Larsen, Jacofsky, Brown *et al.*, 2013; Riskowski, 2010), Two related to LWI (Jones, Zhang, Laxton *et al.*, 2013; Tipnis, Anloague, Laubach *et al.*, 2014), two compared knee brace and LWI (Arazpour, Bani, Maleki *et al.*, 2013; Jones, Nester, Richards *et al.*, 2013), four were related to physical therapy (Gaudreault, Mezghani, Turcot *et al.*, 2011; Hiyama, Yamada, Kitagawa *et al.*, 2012; Khademi-Kalantari, Mahmoodi Aghdam, Akbarzadeh Baghban *et al.*, 2014; Wang, Lee, Liang *et al.*, 2011) and one was related to knee sleeve (Collins, Blackburn, Olcott *et al.*, 2011). Two studies reported significant reduction of knee flexion angle during stance phase by brace usage (Esrafilian, Karimi, & Eshraghi, 2012; Larsen, Jacofsky, Brown *et al.*, 2013). (Riskowski, 2010) reported significant increase of knee flexion angle at initial contact by brace usage. While (Jones, Nester, Richards *et al.*, 2013) reported significant reduction of knee flexion during swing phase by the use of knee brace and reported no effects at knee flexion angle during stance phase, loading response and at initial contact. Increase in knee flexion/ extension angles with brace usage was reported by only one study (Arazpour, Bani, Maleki *et al.*, 2013).

No effect of LWI was found on knee flexion angle during early stance (Jones, Nester, Richards *et al.*, 2013; Jones, Zhang, Laxton *et al.*, 2013; Tipnis, Anloague, Laubach *et al.*, 2014)} and initial contact (Jones, Nester, Richards *et al.*, 2013). (Tipnis, Anloague, Laubach *et al.*, 2014) reported significant increase of knee flexion when wedging increased up to 10° and reduction of peak knee flexion at 12° wedging. The comparison between knee brace and LWI showed that both of these increased knee range of motion significantly, but LWI was found to be more effective (Arazpour, Bani, Maleki *et al.*, 2013).

No effects of standard physiotherapy techniques were found on knee flexion angles (Gaudreault, Mezghani, Turcot *et al.*, 2011; Khademi-Kalantari, Mahmoodi Aghdam, Akbarzadeh Baghban *et al.*, 2014; Wang, Lee, Liang *et al.*, 2011). However, non-surgical joint distraction technique and walking exercise had significant effect on knee flexion but no effect on knee extension (Hiyama, Yamada, Kitagawa *et al.*, 2012; Khademi-Kalantari, Mahmoodi Aghdam, Akbarzadeh Baghban *et al.*, 2014). Aquatic and land-based exercises significantly reduced knee extension angle as compared to control. Knee sleeves with and without stochastic resonance electrical stimulation reduced knee flexion angle at initial contact (Collins, Blackburn, Olcott *et al.*, 2011).

2.4.11 Knee Adduction/ Abduction Angle (Lower Limb Malalignment)

Eleven studies investigated knee adduction/ abduction angle. Three studies were related to knee brace (Esrafilian, Karimi, & Eshraghi, 2012; Laroche, Morisset, Fortunet *et al.*, 2014; Larsen, Jacofsky, Brown *et al.*, 2013)and LWI (Jones, Zhang, Laxton *et al.*, 2013; Tipnis, Anloague, Laubach *et al.*, 2014; Yeh, Chen, Hsu *et al.*, 2014) each. Three studies compared brace and LWI (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Jones, Nester, Richards *et al.*, 2013; van Raaij, Reijman, W. *et al.*, 2010). One study each was related to variable stiffness shoe (Boyer, Federolf, Lin *et al.*, 2012) and physiotherapy (Gaudreault, Mezghani, Turcot *et al.*, 2011). No change in adduction/ abduction angle was observed during stance phase by the use of distraction rotation knee brace (Laroche, Morisset, Fortunet *et al.*, 2014) and LWI (Jones, Nester, Richards *et al.*, 2013; Jones, Zhang, Laxton *et al.*, 2013; Yeh, Chen, Hsu *et al.*, 2014). Two studies reported decrease in knee adduction by the use of LWI with inclination of 4° and above (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Tipnis, Anloague, Laubach *et al.*, 2014). Three studies reported significant change in knee adduction angle by the use of valgus knee brace (Esrafilian, Karimi, & Eshraghi, 2012; Jones, Nester, Richards *et al.*, 2013; Larsen, Jacofsky, Brown *et al.*, 2013). Variable stiffness shoe was found to be slightly increasing knee adduction/ abduction angle during loading response (Boyer, Federolf, Lin *et al.*, 2012). Standard physiotherapy treatment had no effect on peak knee adduction/ abduction angle (Gaudreault, Mezghani, Turcot *et al.*, 2011). The comparison between brace and LWI, by a 6 month follow-up RCT, showed that both the interventions were unable to correct malalignment as compared to the baseline (van Raaij, Reijman, Brouwer *et al.*, 2010; van Raaij, Reijman, W. *et al.*, 2010).

2.4.12 Ground Reaction Force (GRF)

Twelve studies investigated the effects of interventions on GRF. Four studies were related to knee brace (Dessery, Belzile, Turmel *et al.*, 2014; Esrafilian, Karimi, & Eshraghi, 2012; Larsen, Jacofsky, Brown *et al.*, 2013; Schmalz, Knopf, Drewitz *et al.*, 2010), two each were related to modified walking shoe (Boyer, Federolf, Lin *et al.*, 2012; Kean, Bennell, Wrigley *et al.*, 2013) and the comparison between brace and LWI (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Moyer, Birmingham, Dombroski *et al.*, 2013), while one study each was related to LWI (Yeh, Chen, Hsu *et al.*, 2014), toe-in gait (Shull, Shultz, Silder *et al.*, 2013), knee sleeves (Collins, Blackburn, Olcott *et al.*, 2011) and quadriceps muscle strengthening (Hunt, Hinman, Metcalf *et al.*, 2010). No change in GRF was observed by the use of LWI [46, 84], V3P knee brace (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Yeh, Chen, Hsu *et al.*, 2014), toe-in gait (Shull, Shultz, Silder *et al.*, 2013), modified walking shoe (Kean, Bennell, Wrigley *et al.*, 2013), quadriceps muscle strengthening (Hunt, Hinman, Metcalf *et al.*, 2010) and knee sleeve with and without stochastic resonance electrical stimulation (Collins, Blackburn, Olcott *et al.*, 2011) during stance phase. However, knee sleeve with and without stochastic resonance electrical stimulation significantly reduced heel strike transient peak (Collins, Blackburn, Olcott *et al.*, 2011).

Reduction in mediolateral GRF was found by the use of modified walking shoe (Boyer, Federolf, Lin *et al.*, 2012; Kean, Bennell, Wrigley *et al.*, 2013) and VER brace (Dessery, Belzile, Turmel *et al.*, 2014) at first and second peak KAM respectively. V3P knee brace (8º angulation) and a new type of brace were found to be reducing mean mediolateral GRF (Dessery, Belzile, Turmel *et al.*, 2014). No effects of V3P brace (0º angulation) and ACL brace were found on mediolateral GRF (Dessery, Belzile, Turmel *et al.*, 2014). Increase in mediolateral GRF was reported by the use of V3P brace with 4º and 8º angulation.

Increase in vertical GRF (Abdallah & Radwan, 2011) and second peak GRF (Yeh, Chen, Hsu *et al.*, 2014) was observed by the use of a new type of brace design and LWI with arch support respectively. Two studies reported increased vertical GRF and weight acceptance by the use of knee brace on arthritic limb during early stance (Larsen, Jacofsky, Brown *et al.*, 2013; Schmalz, Knopf, Drewitz *et al.*, 2010). The horizontal component of GRF was found to be increased in with brace condition as compared to without brace condition Schmalz, 2010 #271}.

2.4.13 Ground Reaction Force Lever Arm

A total of 5 studies reported GRF lever arm. One study each was related to LWI (Yeh, Chen, Hsu *et al.*, 2014), modified walking shoe (Kean, Bennell, Wrigley *et al.*, 2013) and toe-in gait modification (Shull, Shultz, Silder *et al.*, 2013). Two studies compared LWI and valgus knee brace (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Moyer, Birmingham, Dombroski *et al.*, 2013). Significant reduction of lever arm was reported at first peak KAM by the use of LWI with arch support, modified walking shoe and toe-in gait (Kean, Bennell, Wrigley *et al.*, 2013; Shull, Shultz, Silder *et al.*, 2013; Yeh, Chen, Hsu *et al.*, 2014). Conversely, no change of lever arm was reported at first peak by the use of LWI and valgus knee braces by two studies (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Moyer, Birmingham, Dombroski *et al.*, 2013). Significant reduction of lever arm was reported at second peak KAM by the use of LWI and valgus knee brace (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Yeh, Chen, Hsu *et al.*, 2014). Mean lever arm was also found to be reduced by modified walking shoe (Kean, Bennell, Wrigley *et al.*, 2013).

Comparison between V3P knee brace and LWI showed that valgus brace reduced lever arm at second peak, during 20-30% of stance phase and 70-80% of stance phase with 8º valgus angulation (Fantini Pagani, Hinrichs, & Brüggemann, 2012). Same effect was found with LWI and brace with 4º angulation except during 20-30% of stance phase. Also, valgus brace was found to be more effective than LWI. No change was reported for lever arm at second peak KAM by the use of both LWI and brace when used individually as well as when used simultaneously (Moyer, Birmingham, Dombroski *et al.*, 2013).

2.4.14 Muscle Co-contraction

Three studies reported lower limb muscle co-contraction activities, related to V3P knee brace (0º & 4º angulation) (Fantini Pagani, Willwacher, Kleis *et al.*, 2013) knee sleeves with stochastic resonance electrical stimulation (Collins, Blackburn, Olcott *et al.*, 2011) and RT (McQuade & de Oliveira, 2011). Hamstrings-quadriceps muscle co-contraction ratios tended to increase after RT, but this change was not statistically significant. Significant decrease in Vastus Lateralis/ Lateral Hamstrings muscle co-contraction ratios was found during the whole stance phase by knee sleeves with and without stochastic resonance electrical stimulation as compared to controls. Further significant decrease was observed with electrical stimulation along with knee sleeve as compared to knee sleeve alone (Collins, Blackburn, Olcott *et al.*, 2011). Significant differences for medial/ lateral muscle co-contraction ratios were found during late stance. With 4º valgus adjustment muscle co-contraction was observed to be decreasing in 10 participants out of 12 (in remaining 2 it was increased) (Fantini Pagani, Willwacher, Kleis *et al.*, 2013). With neutral flexible adjustment, muscle co-contraction increased in 4 participants, decreased in 6 participants and remained unchanged in 2 participants out of 12. No changes were found in the remaining phases of gait.

2.4.15 Knee Joint Centre-Centre of Pressure (CoP)

Seven of the included studies reported knee center of pressure offset. 3 studies were related to LWI (Jones, Zhang, Laxton *et al.*, 2013; Leitch, Birmingham, Jones *et al.*, 2011; Yeh, Chen, Hsu *et al.*, 2014), two were related to modified walking shoe (Boyer, Federolf, Lin *et al.*, 2012; Kean, Bennell, Wrigley *et al.*, 2013) and one each to knee brace (Dessery, Belzile, Turmel *et al.*, 2014) and toe-in gait (Shull, Shultz, Silder *et al.*, 2013). CoP was found to be shifting laterally (Jones, Zhang, Laxton *et al.*, 2013; Leitch, Birmingham, Jones *et al.*, 2011; Yeh, Chen, Hsu *et al.*, 2014) and anteriorly (Leitch, Birmingham, Jones *et al.*, 2011) during early stance, mid-stance and at second peak by the use of LWI. During late stance, only LWI with arch support was found to be shifting CoP laterally (Jones, Zhang, Laxton *et al.*, 2013). Significant reduction in CoP excursion was found by modified walking shoes (Boyer, Federolf, Lin *et al.*, 2012; Kean, Bennell, Wrigley *et al.*, 2013).

Dessery, Belzile, Turmel *et al.* (2014), in a cross-over study, compared V3P brace, functional brace (ACL brace) and unloader brace with VER brace and found significantly reduced knee-CoP distance only by the use of VER brace. Toe-in gait modification shifted knee joint centre medially and CoP laterally at first peak (Shull, Shultz, Silder *et al.*, 2013).

2.4.16 Knee Joint Loads

Five studies measured knee compartmental loads directly via computational modelling and telemetric implants (Kinney, Besier, Silder *et al.*, 2013; Kutzner, Küther, Heinlein *et al.*, 2011; Kutzner, Stephan, Dymke *et al.*, 2013; Liu & Zhang, 2013; Messier, Mihalko, Miller *et al.*, 2013). These studies observed the effects of valgus brace (Kutzner, Küther, Heinlein *et al.*, 2011), LWI (Liu & Zhang, 2013), gait modification (Kinney, Besier, Silder *et al.*, 2013), footwear (Kutzner, Stephan, Dymke *et al.*, 2013), and intensive diet plus exercise (Messier, Mihalko, Miller *et al.*, 2013).

Two valgus braces that worked on 3 point bending system were tested with neutral, 4° and 8° adjustments (Liu & Zhang, 2013). One was MOS brace (bilateral frame) and other was GA (unilateral brace). Through telemetric implants the total axial force transferred via medial compartment was measured at first and second peaks. For first peak (second peak), MOS brace reduced knee joint loading by 10% (9%), 18% (24%) and 23% (30%) for neutral, 4° and 8° adjustments respectively. Conversely, GA brace only reduced 7% at second peak for 8° valgus adjustment.

Finite Element Analysis (FEA) was done to study the von Mises stress and medial contact force for LWI of inclinations 0°, 5° and 10°(Kutzner, Küther, Heinlein *et al.*, 2011). They found significant reduction in von Mises stress and medial contact force with either 5° or 10° as compared to 0° insole.

Effects of nine types of gait modifications (involved 4 different hiking pole configurations) were found on knee joint loads at 25%, 50% and 75% of the stance phase on a single subject with a force measuring implant at knee (Kinney, Besier, Silder *et al.*, 2013). There was observed to be significant reduction in knee forces at both medial and lateral compartment through bilateral widely placed hiking poles (18% in overall stance phase). Maximum reduction in joint forces was found to be 34% at 75% of stance phase.

(Kutzner, Stephan, Dymke *et al.*, 2013) used telemetric knee implants to study the effects of four types of shoes (basic running shoe, advanced running shoe, dress shoe and MBT shoe) on knee joint loads. All these shoes increased resultant joint loads by 2-5% and medial compartment loads by 3-5%.

An RCT that was conducted to study the effects of exercise only, diet only and exercise plus diet group, modelled tibiofemoral contact forces (Messier, Mihalko, Miller *et al.*, 2013). The study reported that maximum reduction (10%) in knee loads was found in diet only group, followed by exercise plus diet group (9%) and exercise only group (5%).

2.4.17 Pain and Discomfort

A variety of pain scores were used in the selected studies, namely: WOMAC pain score, VAS pain score, KOOS pain score, NRS pain score, NHP pain score and JKOM pain score (Figure 2.10 to 2.14). An increase in pain score means increase in pain in these scoring systems except KOOS in which an increasing score means decrease in pain.

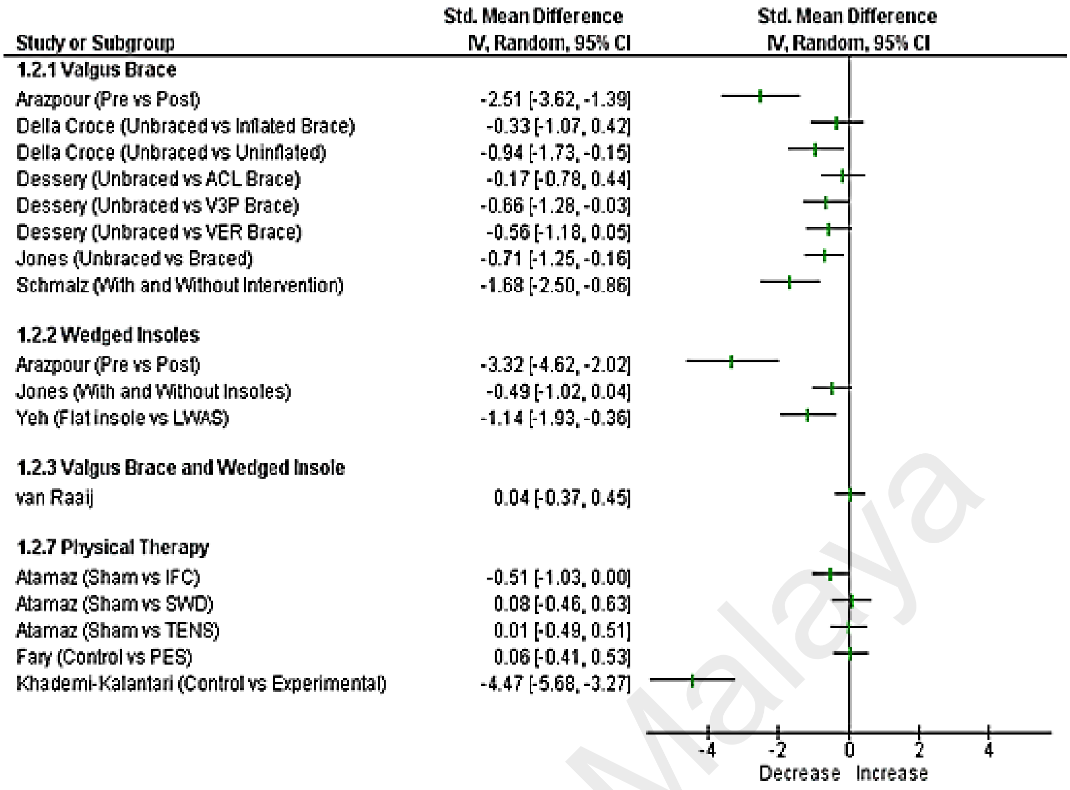


Figure 2.10: Forest plot for VAS pain score

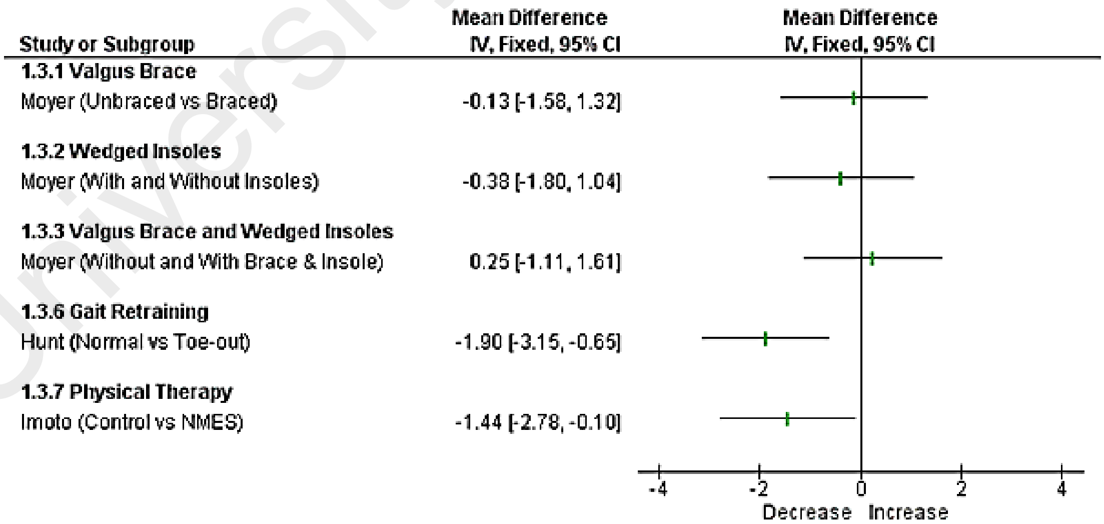


Figure 2.11: Forest plot for NRS pain score

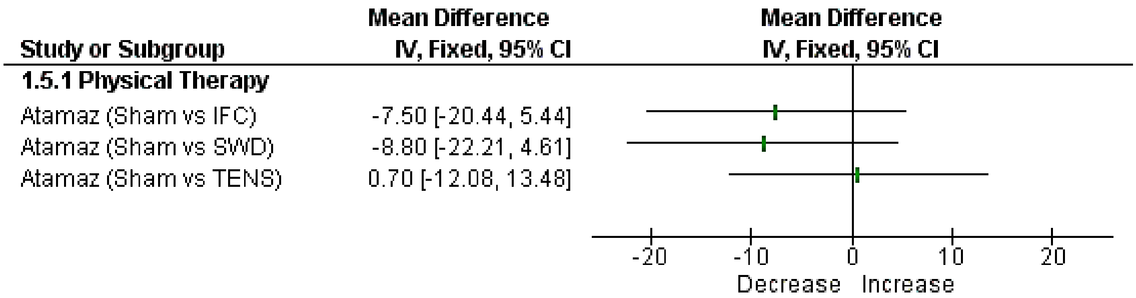


Figure 2.12: Forest plot for NHP pain score.

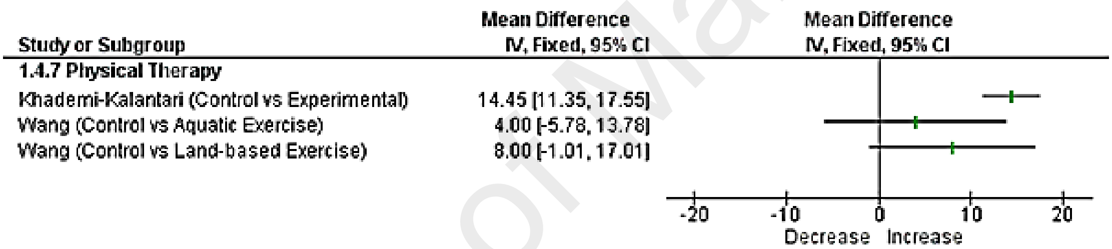


Figure 2.13: Forest plot for KOOS pain score.

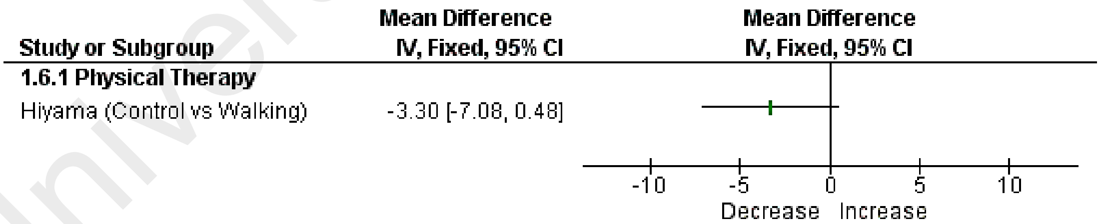


Figure 2.14: Forest plot for JKOM pain score.

2.4.17.1 Knee Brace

Eleven studies used pain score as outcome while using knee brace (Arazpour, Bani, Maleki *et al.*, 2013; Cherian, Bhave, Kapadia *et al.*; Della Croce, Crapanzano, & Li, 2013; Dessery, Belzile, Turmel *et al.*, 2014; Fantini Pagani, Böhle, Potthast *et al.*, 2010; Hunter, Harvey, Gross *et al.*, 2011; Hurley, Hatfield Murdock, Stanish *et al.*, 2012; Jones, Nester, Richards *et al.*, 2013; Laroche, Morisset, Fortunet *et al.*, 2014; Moyer, Birmingham, Dombroski *et al.*, 2013; van Raaij, Reijman, W. *et al.*, 2010). Eight studies reported an immediate reduction in pain after using knee brace. These studies include both single-visit and follow-up studies (Arazpour, Bani, Maleki *et al.*, 2013; Cherian, Bhave, Kapadia *et al.*; Dessery, Belzile, Turmel *et al.*, 2014; Fantini Pagani, Böhle, Potthast *et al.*, 2010; Hunter, Harvey, Gross *et al.*, 2011; Jones, Nester, Richards *et al.*, 2013; Laroche, Morisset, Fortunet *et al.*, 2014; van Raaij, Reijman, W. *et al.*, 2010). (Della Croce, Crapanzano, & Li, 2013) tested a novel pneumatic knee brace with three conditions: unbraced, uninflated brace, inflated brace with 7psi inflation. It was reported that there was significant pain relief in uninflated condition as compared to unbraced condition. While, no significant difference was found between unbraced and 7psi inflation brace. Also, discomfort was reported in wearing the brace with 7psi inflation. Another cross-over study tested knee orthosis with 4° and 8° angulation as opposed to unbraced condition for two weeks (Fantini Pagani, Böhle, Potthast *et al.*, 2010). Both the angulated braces proved to be minimizing pain as compared to unbraced condition and no discomfort was reported for the braces. Two studies did not report any significant improvement in pain while using knee brace (Hurley, Hatfield Murdock, Stanish *et al.*, 2012; Moyer, Birmingham, Dombroski *et al.*, 2013). One of these studies was a cohort study (Hurley, Hatfield Murdock, Stanish *et al.*, 2012) and the other was a cross-over trial (Moyer, Birmingham, Dombroski *et al.*, 2013). In both these studies, no improvement in pain was observed after 6-month follow-up. In contrast, another study (an RCT) reported significant improvement with knee brace after a 6-month follow-up. (Hunter, Harvey, Gross *et al.*, 2011) conducted RCT to test a patellar knee brace with realigning strap against a brace without realigning strap and found the same improvement in pain for the two conditions against baseline.

2.4.17.2 Insoles

Seven studies assessed pain score when using LWI (both supported and unsupported) and shock absorbing insoles (Arazpour, Bani, Maleki *et al.*, 2013; Jones, Chapman, Forsythe *et al.*, 2014; Jones, Nester, Richards *et al.*, 2013; Moyer, Birmingham, Dombroski *et al.*, 2013; Turpin, De Vincenzo, Apps *et al.*, 2012; van Raaij, Reijman, W. *et al.*, 2010; Yeh, Chen, Hsu *et al.*, 2014), while one measured comfort level for wedged inclinations (Tipnis, Anloague, Laubach *et al.*, 2014). Six studies reported decrease in pain when wearing insoles (Arazpour, Bani, Maleki *et al.*, 2013; Jones, Chapman, Forsythe *et al.*, 2014; Jones, Nester, Richards *et al.*, 2013; Turpin, De Vincenzo, Apps *et al.*, 2012; van Raaij, Reijman, W. *et al.*, 2010; Yeh, Chen, Hsu *et al.*, 2014), while one did not (Moyer, Birmingham, Dombroski *et al.*, 2013). (Turpin, De Vincenzo, Apps *et al.*, 2012) conducted pre-post intervention test with one-month follow-up and reported that normal flat shock absorbing insoles significantly reduced pain. In a case-control trial. (Yeh, Chen, Hsu *et al.*, 2014), found LWI with medial arch support to reduce pain significantly when compared with flat insole. Similarly, reduction in pain was observed with supported LWI as compared to unsupported LWI by (Jones, Nester, Richards *et al.*, 2013). Three other studies (a quasi-experimental study (Arazpour, Bani, Maleki *et al.*, 2013), a randomized cross-over study (Jones, Nester, Richards *et al.*, 2013) and an RCT with 6 month follow-up (van Raaij, Reijman, W. *et al.*, 2010)) investigated the effects of unsupported LWI and found significant decrease in pain.

(Moyer, Birmingham, Dombroski *et al.*, 2013) reported no significant decrease in pain while wearing LWI when compared with no LWI condition.

The relationship between wedge angulation and comfort level was investigated in an experimental design with cross-sectional analysis (Tipnis, Anloague, Laubach *et al.*, 2014). The investigators reported that no decrease in comfort level was found for 0° to 8° inclination, but it decreased significantly for inclination beyond 8° (i.e. 10° and 12°).

2.4.17.3 Knee Brace and LWI

Four studies that compared knee brace with LWI reported that there is no notable difference in pain scores between the two conditions (Arazpour, Bani, Maleki *et al.*, 2013; Laroche, Morisset, Fortunet *et al.*, 2014; Moyer, Birmingham, Dombroski *et al.*, 2013; van Raaij, Reijman, W. *et al.*, 2010).

2.4.17.4 Gait Modification

Two studies measured pain in gait modification programs (Hunt & Takacs, 2014; Simic, Wrigley, Hinman *et al.*, 2013). (Hunt & Takacs, 2014) studied the effect of toe-out gait of 11.4° with 10-week follow-up and found 44% decrease in pain as compared to baseline. In contrast, (Simic, Wrigley, Hinman *et al.*, 2013) performed single-visit gait modification with fixed modification (10º toe-in, and 10º, 20º, 30º toe-out) and reported no significant difference in pain for all four gait modifications as compared to natural gait.

2.4.17.5 Physiotherapy/ RT/ Muscle Strengthening

Six studies investigated the effects of physiotherapy, RT and muscle strengthening on pain (Farr, Going, McKnight *et al.*, 2010; Foroughi, Smith, Lange *et al.*, 2011; Gaudreault, Mezghani, Turcot *et al.*, 2011; Khademi-Kalantari, Mahmoodi Aghdam, Akbarzadeh Baghban *et al.*, 2014; McQuade & de Oliveira, 2011; Sayers, Gibson, &

Cook, 2012). Two of these studied the effects of lower limb muscle strengthening and found significant reduction in pain after 8-week and 3-month follow-ups. Lower limb muscle strengthening includes progressive resistive exercises for knee extensors and flexors (Gaudreault, Mezghani, Turcot *et al.*, 2011; McQuade & de Oliveira, 2011). Another RCT, in which one group was allocated high resistance training and other was sham group, reported significant reduction in pain in both groups after 6-month follow-up. High resistance training included knee extension/ flexion, leg press, plantar flexion and hip abduction/ adduction, while the sham group had all these except hip abduction/ adduction and had minimal resistance set on the exercise machines (Foroughi, Smith, Lange *et al.*, 2011). For an RCT, three groups (HSPT, SSST and control) were tested and it was found that HSPT and SSST had the same level of pain improvement as compared to control group. Control group had to do stretching and warm-up exercises only (Sayers, Gibson, & Cook, 2012).

Self-management (SM) did not appear to have considerable effect in pain reduction in an RCT that compared RT only, SM only and RT + SM groups with a 9 month follow-up (Farr, Going, McKnight *et al.*, 2010). RT only group, that included muscle strengthening and stretching, aerobics, range of motion, balance and flexibility, was found to have highest reduction in pain. SM only group was trained for educational and behavioural techniques for pain and stress management, physical function and healthy lifestyle practices.

Non-surgical knee joint distraction had maximum immediate reduction in pain when it was combined with standard physiotherapy and compared with standard physiotherapy only group (Khademi-Kalantari, Mahmoodi Aghdam, Akbarzadeh Baghban *et al.*, 2014). Both the groups showed reduction in pain after one month, with knee distraction plus standard physiotherapy group having greater reduction than physiotherapy only group.

Standard physiotherapy included hot packs, 1MHz ultrasound, TENS and lower limb muscle strengthening. Knee joint distraction was applied for 20 minutes in 30° flexion in supine flexion.

2.4.17.6 Electrical Stimulation

Four studies investigation the effects of electrical stimulation along with some physical therapy agents on pain reduction (Atamaz, Durmaz, Baydar *et al.*, 2012; Fary, Carroll, Briffa *et al.*, 2011; Imoto, Peccin, Teixeira, Silva, Abrahao *et al.*, 2013; Tok, Aydemir, Peker *et al.*, 2011). Out of these, three reported no significant improvement of pain by electrical stimulation (Atamaz, Durmaz, Baydar *et al.*, 2012; Fary, Carroll, Briffa *et al.*, 2011; Tok, Aydemir, Peker *et al.*, 2011) while one did not (Imoto, Peccin, Teixeira, Silva, Abrahao *et al.*, 2013). (Atamaz, Durmaz, Baydar *et al.*, 2012) conducted an RCT to test the effects of TENS, IFC and SWD along with exercise training for 3 weeks as compared to their sham groups. All groups received same set of lower extremity and muscle strengthening exercises. While the sham groups received sham electrical stimulations. The investigators found reductions in pain to be similar for all the experimental groups as compared to their sham groups. (Tok, Aydemir, Peker *et al.*, 2011) in an RCT, formed two groups: one received electrical stimulation with continuous passive motion while other received same electrical stimulation with isometric exercise for 3 weeks. Both the groups showed improvement in pain as compared to baseline but did not differ from each other. A 26 week follow-up RCT compared PES with placebo and found that PES was not more effective than placebo (Fary, Carroll, Briffa *et al.*, 2011). The only study that reported an improvement in pain by electrical stimulation compared NMES group versus control group for 8 weeks (Imoto, Peccin, Teixeira, Silva, Abrahao *et al.*, 2013). NMES group received educational guidance, quadriceps strengthening exercises and NMES, while the control group received educational guidance and could use ice-packs and hot-packs based on their own decision.

2.4.17.7 Radiation Therapy

In an RCT, Hsieh, Lo, Liao *et al.* (2012b) compared radiation therapy group with a placebo group and baseline data for 2 weeks and found no effect of radiation therapy on pain

2.4.17.8 EMF Therapy

Özgüçlü, Çetin, Çetin *et al.* (2010) conducted an RCT to investigate the effects of EMF therapy on pain. The study compared EMF therapy group and a sham group, both the groups performed isometric knee exercises. Both the groups showed improvement in pain as compared to baseline, but no difference was found between them after 2 weeks.

2.4.17.9 Acupressure versus Isometric Exercise

A quasi-experimental study compared acupressure against isometric exercise for 3 months (Sorour, Ayoub, & Abd El Aziz, 2014). Both the groups showed improvement in pain with their baseline data. Acupressure was found to be slightly and insignificantly better at reducing pain than isometric exercise.

2.4.17.10 Aquatic versus Land-based Exercises

Wang, Lee, Liang *et al.* (2011), in an RCT, compared acupressure against isometric exercise for 12 weeks. Both the groups showed improvement in pain as compared to baseline, but no difference was found between them after 12 weeks. Both groups received aerobic and flexibility training classes, one group received the training at a basketball court (land-based), while the other received it at a public swimming pool (aquatic).

2.4.17.11 Walking Exercise

(Hiyama, Yamada, Kitagawa *et al.*, 2012) tested the effects of walking exercise for four weeks via RCT. The experimental group was asked to increase their number of steps up to 3000 steps daily. There was found to be a significant improvement in pain in the experimental group as compared to control.

2.4.17.12 Contralateral Cane Use

In a single visit study, (Simic, Bennell, Hunt *et al.*, 2011) investigated the effects of contralateral cane use on pain. The participants were asked to use cane with 10%, 15% and 20% body weight support. 15% reduction in pain was found by cane usage but it was independent of the percentage of body weight support.

2.4.17.13 Intensive Diet and Exercise

The effect of diet plus exercise was found to be maximum in pain reduction when compared with diet only and exercise only groups in an RCT done for 18 months (Messier, Mihalko, Miller *et al.*, 2013). For the diet plus exercise group, 38% of the participants reported very low and no pain. Improvement in pain was found in all three groups as compared to baseline. The exercises included aerobics and muscle strengthening. The diet plan aimed at reducing about 800-1000kcal per day, setting the minimum calorie intake for women to be 1100kcal and for men to be 1200kcal per day.

2.4.18 Performance Measure

Several studies assessed performance measure which include walking speed, TUG test, 6 minute walk test, timed stair climb, 20 steps on 6" step, 5º chair rise, 2 minute walk test, timed up and go test, rise from a chair and walking test, trail making test, gait time, transfer to and from chair, ascending/ descending stairs, postural stability, 400m self-paced walk, stair climbing, daily step count, 10m fast speed test, time to 15m test, use of accelerometer in measurement of daily activities, measurement of IL-6 and Paracetamol® intake.

2.4.18.1 Walking Speed

Walking speed is considered the most important performance measure and one of the TSPs. Some studies reported significant increase in walking speed after wearing knee brace (Arazpour, Bani, Maleki *et al.*, 2013; Fantini Pagani, Potthast, & Brüggemann, 2010; Jones, Nester, Richards *et al.*, 2013; Laroche, Morisset, Fortunet *et al.*, 2014; Schmalz, Knopf, Drewitz *et al.*, 2010; Toriyama, Deie, Shimada *et al.*, 2011) and LWI (Arazpour, Bani, Maleki *et al.*, 2013; Jones, Nester, Richards *et al.*, 2013), while some reported no significant change with either knee brace (Dessery, Belzile, Turmel *et al.*, 2014; Hurley, Hatfield Murdock, Stanish *et al.*, 2012; Moyer, Birmingham, Dombroski *et al.*, 2013; Riskowski, 2010) or LWI (Jones, Zhang, Laxton *et al.*, 2013; Moyer, Birmingham, Dombroski *et al.*, 2013), see Figure 2.15. Quadriceps strengthening (Hunt, Hinman, Metcalf *et al.*, 2010), HSPT (Sayers, Gibson, & Cook, 2012) and diet plus exercise (Messier, Mihalko, Miller *et al.*, 2013) also lead to significant increase in walking speed. In contrast, in some studies, no significant change in walking speed was found after wearing shock absorbing insoles (Turpin, De Vincenzo, Apps *et al.*, 2012), gait modification (Hunt & Takacs, 2014; Simic, Wrigley, Hinman *et al.*, 2013), modified walking shoes (Riskowski, 2010), contralateral cane use (Simic, Bennell, Hunt *et al.*, 2011) and use of hiking poles (Kinney, Besier, Silder *et al.*, 2013). Diet only and exercise only (consisted of 15 minutes aerobic walking, 20 minute strength training, a second aerobic phase of 15 minutes and a cool-down of 10 minutes) groups showed no significant increase in walking speed (Messier, Mihalko, Miller *et al.*, 2013).

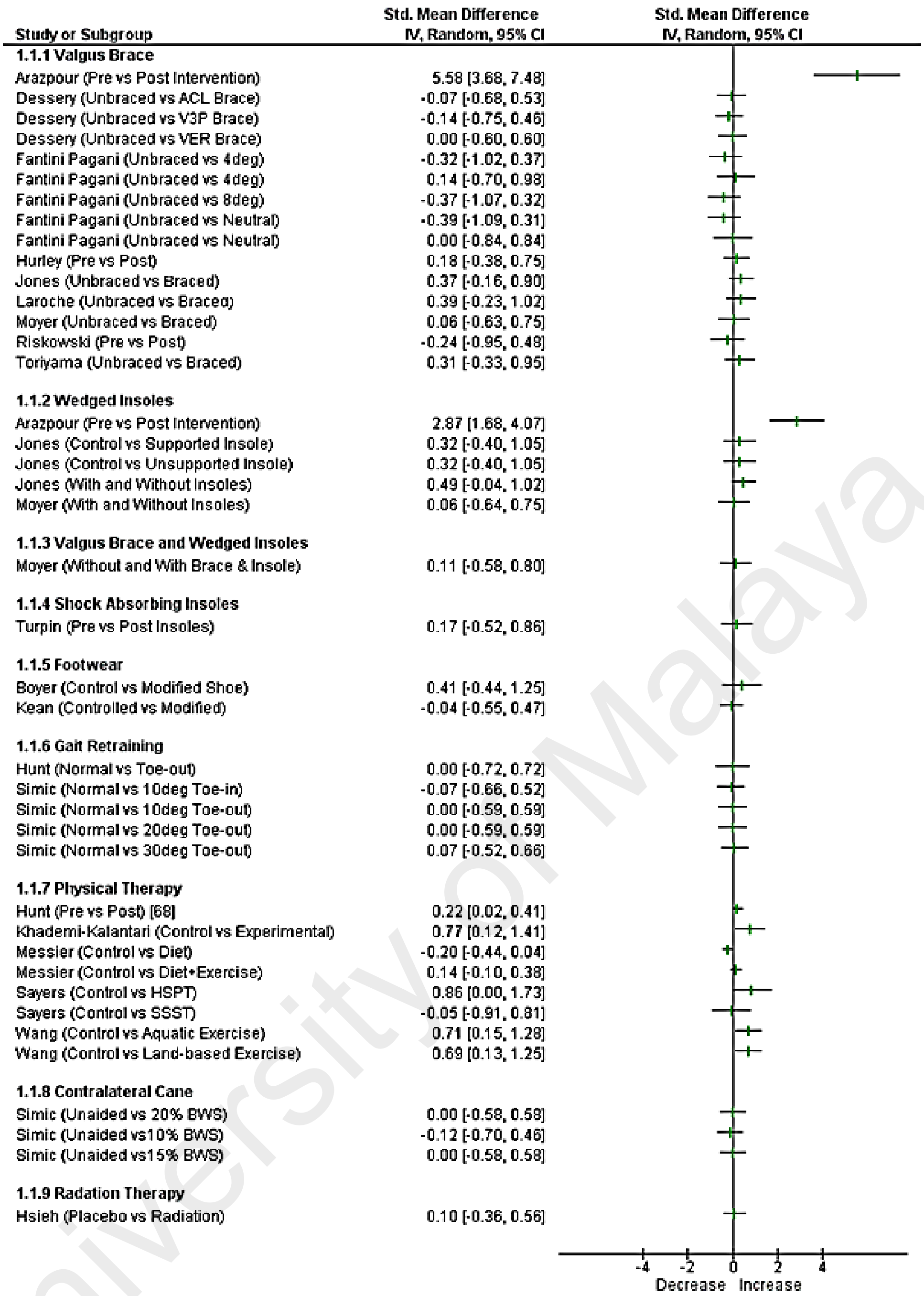


Figure 2.15: Forest plot for walking speed for the selected studies.

2.4.18.2 Daily Step Count

One study measured daily step count and found no significant difference between baseline and follow-up of knee brace usage (Hurley, Hatfield Murdock, Stanish *et al.*, 2012).

2.4.18.3 Timed Stair Ascent and Descent

Time required to climb specific numbers of stairs was found to be significantly lower after wearing knee brace (Cherian, Bhave, Kapadia *et al.*; Fantini Pagani, Böhle, Potthast *et al.*, 2010; Turpin, De Vincenzo, Apps *et al.*, 2012), after 10 weeks toe-out gait modification (Hunt & Takacs, 2014) and after having standard physiotherapy treatment for 12 weeks (Gaudreault, Mezghani, Turcot *et al.*, 2011). No effect of radiation therapy was found (Hsieh, Lo, Liao *et al.*, 2012b). While the time required for stair descent was found to be lower in standard physiotherapy treatment for 12 weeks and remained unchanged for radiation therapy (Gaudreault, Mezghani, Turcot *et al.*, 2011; Hsieh, Lo, Liao *et al.*, 2012b).

2.4.18.4 6-minute Walk Test

Physiotherapy along with non-surgical knee join distraction (Khademi-Kalantari, Mahmoodi Aghdam, Akbarzadeh Baghban *et al.*, 2014), aquatic exercise and land-based exercises (Wang, Lee, Liang *et al.*, 2011) significantly increased the distance covered in 6 minutes. No effect of knee brace was found (Fantini Pagani, Böhle, Potthast *et al.*, 2010.) Small improvement was observed in diet only and exercise only groups, while maximum significant change was found for diet plus exercise group (Messier, Mihalko, Miller *et al.*, 2013).

2.4.18.5 Timed Chair Rise

Standard physiotherapy had significant effect in reducing time for transfer to and from chair (Gaudreault, Mezghani, Turcot *et al.*, 2011), while no effect was seen with HSPT, SSST (Sayers, Gibson, & Cook, 2012), radiation therapy (Hsieh, Lo, Liao *et al.*, 2012a) and pneumatic knee brace (Cherian, Bhave, Kapadia *et al.*) use.

2.4.18.6 Walking

HSPT (Sayers, Gibson, & Cook, 2012) and pneumatic brace (Cherian, Bhave, Kapadia *et al.*) had significant effect in reducing time of 400m self-paced walk test and 10m fast speed walk test respectively. No significant effect was seen of radiation therapy in 10m fast speed walk test (Hsieh, Lo, Liao *et al.*, 2012a). Also, no significant effects of electrical nerve stimulation, IFCs and SWD groups were found when compared with their sham groups in time to 15m test (Atamaz, Kirazli, & Akkoc, 2006). Standard physiotherapy was found to be significant in improving walk test results (Gaudreault, Mezghani, Turcot *et al.*, 2011).

2.4.18.7 Postural Stability

No significant effects were seen of HSPT, SSST (Sayers, Gibson, & Cook, 2012) and radiation therapy (Hsieh, Lo, Liao *et al.*, 2012a) on increasing postural stability.

2.4.18.8 TUG Test

NMES (Imoto, Peccin, Teixeira, Silva, Abrahão *et al.*, 2013), four week walking exercise (Cherian, Bhave, Kapadia *et al.*) and the use of pneumatic knee brace (Cherian, Bhave, Kapadia *et al.*) significantly reduced time for TUG.

2.4.18.9 20 Steps on 6" Steps

Only one study used this test for pneumatic knee brace and found significant reduction in time against the control group (Cherian, Bhave, Kapadia *et al.*).

2.4.18.10 Gait Time

A four week walking exercise program did not report significant differences as compared to controls in single task gait time but significant differences were reported in dual task gait time (Hiyama, Yamada, Kitagawa *et al.*, 2012).

2.4.18.11 Trail Making Test

Walking group improved significantly in automaticity after having four week exercise program (Hiyama, Yamada, Kitagawa *et al.*, 2012).

2.4.18.12 Accelerometry

One study measured accelerometer data to assess light, moderate and hard activities on daily basis in minutes and found to significant difference between PES group and placebo group in moderate to severe knee OA (Fary, Carroll, Briffa *et al.*, 2011). Another study calculated time spent in moderate-intensity physical activity, vigorous-intensity physical activity and combined moderate and vigorous intensity physical activities and found significant improvement in the combined moderate and vigorous intensity physical activities in RT group and also in self-management management group up to 3 months. But RT group was also able to sustain these changes at 9 month follow-up (Farr, Going, McKnight *et al.*, 2010).

2.4.18.13 IL-6

Only one study measured IL-6 for 18 months. The exercise only group did not show any significant difference in IL-6 level, while both the diet only and diet plus exercise groups showed same level of improvement (Messier, Mihalko, Miller *et al.*, 2013).

2.4.19 Paracetamol® Intake

Paracetamol® intake was found to be lower in TENS, IFC and SWD groups when compared to their sham groups after 3 months. But only IFC group showed reduced Paracetamol® intake after 6 months (Atamaz, Kirazli, & Akkoc, 2006).

2.4.20 Physical Function

The questionnaires used to measure self-reported physical function were: WOMAC function, VAS activity, KOOS sports and recreation, KOOS quality of life, KOOS activity, SF-36 physical activity, LEAS scores, LEFS score, NHP physical mobility and Human activity profile score (Atamaz, Durmaz, Baydar *et al.*, 2012; Cherian, Bhave, Kapadia *et al.*; Fantini Pagani, Böhle, Potthast *et al.*, 2010; Fary, Carroll, Briffa *et al.*, 2011; Gaudreault, Mezghani, Turcot *et al.*, 2011; Hsieh, Lo, Liao *et al.*, 2012b; Hunter, Harvey, Gross *et al.*, 2011; Hurley, Hatfield Murdock, Stanish *et al.*, 2012; Jones, Nester, Richards *et al.*, 2013; Khademi-Kalantari, Mahmoodi Aghdam, Akbarzadeh Baghban *et al.*, 2014; Laroche, Morisset, Fortunet *et al.*, 2014; Larsen, Jacofsky, Brown *et al.*, 2013; McQuade & de Oliveira, 2011; Messier, Mihalko, Miller *et al.*, 2013; Özgüçlü, Çetin, Çetin *et al.*, 2010; Sayers, Gibson, & Cook, 2012; Sorour, Ayoub, & Abd El Aziz, 2014; Teixeira, Piva, & Fitzgerald, 2011; Tok, Aydemir, Peker *et al.*, 2011; van Raaij, Reijman, W. *et al.*, 2010; Wang, Lee, Liang *et al.*, 2011). Three studies reported that immediate use of brace can improve function significantly (Fantini Pagani, Böhle, Potthast *et al.*, 2010; Jones, Nester, Richards *et al.*, 2013; Laroche, Morisset, Fortunet *et al.*, 2014), while one study reported the same for wedged insoles in early knee OA (Jones, Nester, Richards *et al.*, 2013). (Larsen, Jacofsky, Brown *et al.*, 2013) measured short-term solution across walking and sit-to-stand activities in lower grade OA patients with knee brace. In this study no improvement in function was found prior to two month usage. (Cherian, Bhave, Kapadia *et al.*), in an RCT, investigated the effects of brace as compared to control on function for 3 months and reported that significant improvement was found in SF-36 physical and KSS functional scores, while no improvement was recorded via LEFS and KSS objective scores. Another RCT compared the effects of valgus knee brace and LWI for up to 6 months usage, both the interventions showed improvement in function but none exceeded the other (van Raaij, Reijman, W. *et al.*, 2010). In contrast, (Hurley, Hatfield Murdock, Stanish *et al.*, 2012), in a cohort study using unloader brace, reported that there was no improvement in function for 6 months usage, only an insignificant trend in improvement could be observed.

Very high effect on physical function improvement of physiotherapy and resistance exercise (Gaudreault, Mezghani, Turcot *et al.*, 2011; McQuade & de Oliveira, 2011; Sorour, Ayoub, & Abd El Aziz, 2014), aquatic and land-based exercises (Wang, Lee, Liang *et al.*, 2011), high speed and slow speed power training (Sayers, Gibson, & Cook, 2012)was observed. Comparatively lower but significant improvement was also seen in physical function scores with acupressure (Sorour, Ayoub, & Abd El Aziz, 2014).

Electrical stimulation (Atamaz, Durmaz, Baydar *et al.*, 2012; Fary, Carroll, Briffa *et al.*, 2011; Tok, Aydemir, Peker *et al.*, 2011), PEMF (Özgüçlü, Çetin, Çetin *et al.*, 2010) and radiation therapy (Hsieh, Lo, Liao *et al.*, 2012b) did not show any additive effects. An RCT conducted for impairment-based (lower extremity muscle strengthening and stretching and aerobic activities) exercise with and without perturbation training (side-stepping, braiding, cross-over steps etc.) (Teixeira, Piva, & Fitzgerald, 2011). The study, after 2 months follow-up, reported that there is no effect of perturbation training on physical function. Another study which compared the effects of exercise only, diet only and diet plus exercise for 18 months observed that improvement in physical function was found in diet plus exercise group only (Messier, Mihalko, Miller *et al.*, 2013).

2.4.21 Mental Health

Four studies assessed the effects of intervention on self-reported mental health using SF-36 mental score (Cherian, Bhave, Kapadia *et al.*; Fary, Carroll, Briffa *et al.*, 2011; Messier, Mihalko, Miller *et al.*, 2013; Tok, Aydemir, Peker *et al.*, 2011). No mental improvement was seen in participants after 3 months of brace use (Cherian, Bhave, Kapadia *et al.*). Also, no mental improvement was seen after 18 months follow-up in all three groups of exercise, diet and diet plus exercise (Messier, Mihalko, Miller *et al.*, 2013) [94]. Very small and insignificant differences were seen in both PES and placebo groups (Fary, Carroll, Briffa *et al.*, 2011). Only one study reported significant improvement in mental health in a group which received electrical stimulation along with isometric exercise after 3 weeks (Tok, Aydemir, Peker *et al.*, 2011).

2.4.22 Disability

Four studies measured physical disability using KOOS ADL and Lequesne index (Imoto, Peccin, Teixeira, Silva, Abrahão *et al.*, 2013; McQuade & de Oliveira, 2011; Teixeira, Piva, & Fitzgerald, 2011; Wang, Lee, Liang *et al.*, 2011). ADLs was found to be improved significantly by land-based exercises (Wang, Lee, Liang *et al.*, 2011) and resistance training (McQuade & de Oliveira, 2011). Comparatively lower improvement could be achieved by aquatic exercises (Wang, Lee, Liang *et al.*, 2011) and impairment-based exercises (Teixeira, Piva, & Fitzgerald, 2011). NMES was found to be very significant in improving ADL, Lequesne test and reducing disability (Imoto, Peccin, Teixeira, Silva, Abrahão *et al.*, 2013).

2.4.23 Adverse Events

A total of 15 studies reported adverse events or complaints for the interventions used (Atamaz, Durmaz, Baydar *et al.*, 2012; Cherian, Bhave, Kapadia *et al.*; Della Croce, Crapanzano, & Li, 2013; Fary, Carroll, Briffa *et al.*, 2011; Hunt & Takacs, 2014; Hunter, Harvey, Gross *et al.*, 2011; Imoto, Peccin, Teixeira, Silva, Abrahão *et al.*, 2013; Jones, Zhang, Laxton *et al.*, 2013; Kutzner, Küther, Heinlein *et al.*, 2011; Laroche, Morisset, Fortunet *et al.*, 2014; Messier, Mihalko, Miller *et al.*, 2013; Schmalz, Knopf, Drewitz *et al.*, 2010; Turpin, De Vincenzo, Apps *et al.*, 2012; van Raaij, Reijman, W. *et al.*, 2010; Wang, Lee, Liang *et al.*, 2011). Seven studies reported complaints about use of valgus braces (Cherian, Bhave, Kapadia *et al.*; Della Croce, Crapanzano, & Li, 2013; Hunter, Harvey, Gross *et al.*, 2011; Kutzner, Küther, Heinlein *et al.*, 2011; Laroche, Morisset, Fortunet *et al.*, 2014; Schmalz, Knopf, Drewitz *et al.*, 2010; van Raaij, Reijman, W. *et al.*, 2010; Wang, Lee, Liang *et al.*, 2011), three about insoles(Jones, Zhang, Laxton *et al.*, 2013; Turpin, De Vincenzo, Apps *et al.*, 2012; van Raaij, Reijman, W. *et al.*, 2010), three about electrical stimulation (Atamaz, Durmaz, Baydar *et al.*, 2012; Imoto, Peccin, Teixeira, Silva, Abrahão *et al.*, 2013; Schmalz, Knopf, Drewitz *et al.*, 2010) and one each for gait modification (Hunt & Takacs, 2014), aquatic & land based exercises (Wang, Lee, Liang *et al.*, 2011) and exercises (Messier, Mihalko, Miller *et al.*, 2013).

The complaints and discomfort reported by participants include: skin irritation (Cherian, Bhave, Kapadia *et al.*; van Raaij, Reijman, W. *et al.*, 2010), skin reaction (Cherian, Bhave, Kapadia *et al.*; Fary, Carroll, Briffa *et al.*, 2011), increased knee pain (Cherian, Bhave, Kapadia *et al.*; Hunter, Harvey, Gross *et al.*, 2011; Wang, Lee, Liang *et al.*, 2011) pain/ swelling in ankle/ subtalar joint (Hunter, Harvey, Gross *et al.*, 2011; Jones, Zhang, Laxton *et al.*, 2013), discomfort (Hunt & Takacs, 2014; Jones, Zhang, Laxton *et al.*, 2013; Kutzner, Küther, Heinlein *et al.*, 2011; Turpin, De Vincenzo, Apps *et al.*, 2012), fitting problem (Hunter, Harvey, Gross *et al.*, 2011; van Raaij, Reijman, W. *et al.*, 2010), slipping (Schmalz, Knopf, Drewitz *et al.*, 2010), skin blisters (van Raaij, Reijman, W. *et al.*, 2010), dizziness (Wang, Lee, Liang *et al.*, 2011), soreness (Messier, Mihalko, Miller *et al.*, 2013), bruising (Messier, Mihalko, Miller *et al.*, 2013), muscle strain (Messier, Mihalko, Miller *et al.*, 2013), hyper-extensive crisis (Imoto, Peccin, Teixeira, Silva, Abrahão *et al.*, 2013), abnormal electrical events (Cherian, Bhave, Kapadia *et al.*) and worsening of symptoms (Atamaz, Durmaz, Baydar *et al.*, 2012).

2.5 Summary of Main Results

This review included 61 studies, published between the years 2010 and 2014, investigating the effects of different types of interventions on symptomatic treatment of knee OA. The included studies differed widely according to the type of intervention provided, study design, sample size, severity of OA and duration of follow-up. This review aimed at performing a comparative study among the recent advancements in knee OA relief, some major findings from the results obtained are summarized in this section.

One observation that was made while performing this review was that the studies involving gait modification and biomechanical interventions (valgus brace, LWI and modified shoes) were mostly single visit, had smaller sample sizes and took healthy participants as subjects thus had lower quality of evidence and inconsistent results. On the other hand, the studies involving physical therapy agents were mostly RCT, had lager sample sizes, adequate follow-up periods and thus had high quality of evidence and consistent results.

Biomechanical interventions (knee brace, LWI, modified walking shoes, cane) significantly alter knee biomechanics through multiple mechanisms. Valgus knee brace and LWI can significantly decrease direct measures of medial compartment loads (KAM, KAAI) and indirect measures of medial compartment loads (muscle co-contraction). However, the adverse effects of knee braces were reported to be high and improvement in pain could also be achieved by flat insoles instead of LWI (Parkes, Maricar, Lunt *et al.*). The results of these studies were inconsistent, and the clinical importance of these interventions remains ambiguous. Another major finding was that most of the studies which used KAM as outcome measure, did not report KFM along with it, while reduction in KAM is not significantly effective until increase in KFM does not occur (Walter, D'Lima, Colwell *et al.*, 2010). Contralateral cane and hiking poles were found to be effective in reducing KAM, KAAI and knee joint loads in general, but the number of studies investigating their effects is very low and cane & hiking poles are not aesthetically pleasant. It is also evident that knee osteoarthritic patients tend to prefer conservative techniques over any invasive and pharmaceutical technique. However, the experiments conducted on conservative techniques are limited to only biomechanics of a patient. Other parameters like physical performance measures, postural stability and risk of fall assessment for conservative techniques thus remain neglected. Therefore, there is a need of testing knee brace, lateral wedged insole, gait modification methods and other conservative techniques on parameters of physical performance measures and balance.

Standard physiotherapy exercises showed consistently that they can effectively reduce pain and improve functionality and overall quality of life. The clinical benefits of these interventions are well-established. Their effects on KAM reduction however, could not be validated and their pathophysiology remains unclear.

Based on the results of included studies, electrical nerve stimulation, radiation therapy and EMF therapy do not have any additional effects on knee OA management. The only study claiming that neuro-muscular electrical stimulation can improve functionality and reduce pain used electrical stimulation on experimental group as well as isometric exercise. While the control group only used hot/ cold therapy. Therefore, the improvement in experimental group may be due to isometric exercise (Imoto, Peccin, Teixeira, Silva, Abrahão *et al.*, 2013). Conversely, electric stimulation may have effects on reduction in muscle co-contraction, but this effect is not investigated for these interventions.

Intensive diet was found to be extremely significant in improvement of joint load reduction. These results however, were reported for overweight and obese OA patients only (Messier, Mihalko, Miller *et al.*, 2013). Further investigations are needed to find its effects on non-obese participants.

2.6 Summary

This comparative review of interventions for knee OA for the past five years concludes that quality of evidence is highest for intensive diet and physiotherapy exercises. These interventions improve physical function and quality of life and pain most efficiently.

On the other hand, conservative techniques are found effective in knee joint load reduction, but are not tested for parameters other than knee biomechanics. These techniques are cheaper and have minimal side effects as compare to the invasive ones and are thus preferred by patients who tend to avoid pharmaceutical or surgical solutions.

There is a paucity of studies that compare the effectiveness of all these individual conservative treatment techniques. Furthermore, there has not been much performance-oriented data on all these techniques which could help the healthcare professionals to make evidence-based decisions on which technique to choose or recommend for the patients.

CHAPTER 3: EFFECTS OF DIFFERENT FOOT PROGRESSION ANGLES AND PLATFORM SETTINGS ON POSTURAL STABILITY AND FALL RISK IN HEALTHY AND MEDIAL KNEE OSTEOARTHRITIC ADULTS

3.1 Introduction

The chapter addresses objective 1 as stated in section 1.3. This study presented in this chapter aims at investigating the effects of varying toe angles at different platform settings on Overall Stability Index (OSI) of postural stability and fall risk using Biodex Balance System (BBS) in healthy participants and medial knee osteoarthritis patients. The chapter begins with a brief review of previous works dealing with foot progression angles and different methodologies used to assess postural stability and risk of fall. It also states the hypothesis for the research. Further on, a methodology is presented defining sampling procedure, experimental setting, study protocol and statistical methods. Following this, is the presentation of results of the experiment. The chapter ends with a discussion of the results and the conclusions drawn from the study.

3.2 Study Background

Maintaining static and dynamic balance is a key factor in performing Activities of Daily Living (ADL). Failing to do so, risks the postural stability (a person's control over their body's orientation in space(Woollacott & Shumway-Cook, 2002), making them vulnerable to perturbations and increasing their risk of fall. The elderly are especially prone to fall related injuries (Alamgir, Muazzam, & Nasrullah, 2012; Kim, 2016; Ku, Abu Osman, & Wan Abas, 2014), mainly because of the deterioration of the body systems responsible for maintaining posture, such as vision, somatosensory input and muscle strength with age (Bemben, Massey, Bemben *et al.*, 1991; Fernie, Gryfe, Holliday *et al.*, 1982; Frontera, Hughes, Lutz *et al.*, 1991). Around 11% of the falls among adults result in fatalities (Gilbert, Todd, May *et al.*, 2009). Falls are also reported to have a major contribution in injury-related hospitalization in different parts of the world such as the

U.S.A. (Orces & Alamgir, 2014) , Canada (Jin, Lalonde, Brussoni *et al.*, 2015), Finland (Kannus, Palvanen, Niemi *et al.*, 1999) and Iran (Saadat, Hafezi-Nejad, Ekhtiari *et al.*, 2016).

An external (vestibulo-ocular) input and a spontaneous internal (motor) output are the two crucial ends of maintaining stability (Hill, Williams, Chen *et al.*, 2013). Biomechanics defines it in terms of the conscious and subconscious shifting of the body's centre of mass (CoM) through swaying the body or changing the foot position (Son, Lee, Yang *et al.*, 2014). If this CoM shifts out of the ground contact area of the body (feet, in standing position), the individual tends to return it to this area. Since the Centre of Pressure (CoP) is the representative point of average distribution of the pressure over the entire contact area, its excursion over this area can represent the balance of a person. There is a wide range of tools used to assess postural stability and balance of a person. Functional tools such as timed up and go test (TUG) (Podsiadlo & Richardson, 1991), step test (Hill, Williams, Chen *et al.*, 2013), and star excursion balance test (SEBT) (Hyong & Kang, 2016) aim to measure stability by observational recording. While instrumental tools such as Kistler Force Plates (Stodolka[1], Golema, & Migasiewicz, 2016), Biodex Balance System (BBS; Biodex Medical System Inc., Shirley, NY, USA) (Milanese, Ku, Abu Osman *et al.*, 2012) and Balance Master- NeuroCom (BalanceMaster®, NeuroCom International Inc., Oregon) (Baert, Mahmoudian, Nieuwenhuys *et al.*, 2013) provide digital measures of postural stability and risk of fall deriving through CoP excursion.

The foot progression angle (FPA) is defined as the angle between the line joining the centre of the ankle joint to the second metatarsal head and the progression axis of the walk. A deviation in FPA has been observed to shift the CoP mediolaterally (van den Noort, Schaffers, Snijders *et al.*, 2013a). This shifting reduces the moment arm of the ground reaction force, in result decreasing the knee adduction moment (a widely acknowledged measure of the knee joint load) (van den Noort, Schaffers, Snijders *et al.*, 2013a). There can be two types of deviations in the natural FPA during gait: (1) toe-out gait: shifting the foot externally while walking (2) toe-in gait: shifting the foot internally while walking. These two gait modifications have been focused as a treatment for knee load dependent disorders such as medial knee osteoarthritis (Khalaj, Abu Osman, Mokhtar *et al.*, 2014). It has been reported that knee osteoarthritis patients already have impaired balance and increased risk of fall as compared to healthy individuals (Khalaj, Osman, Mokhtar *et al.*, 2014).

So far, studies have reported the effects of changing foot position on balance in quiet standing with double stance and single stance. The variations in foot position include changing the heel width (inter-calcaneal distance), the angle between the feet and anteroposterior or mediolateral position of the feet relative to each other (Kirby, Price, & MacLeod, 1987; McIlroy & Maki, 1997; Mouzat, Dabonneville, & Bertrand, 2004; Schneiders, Gregory, Karas *et al.*, 2016). The earliest of these studies measured the standing balance of ten healthy participants through a force platform by varying the angle and distance between their feet by uneven increments (Kirby, Price, & MacLeod, 1987). Later on, another study taking a female only sample, tested the effects of different foot positions on orthostatic posture (Mouzat, Dabonneville, & Bertrand, 2004). They suggested a heel width in the range of 0.1- 0.2m and feet angle of 15-45º for better stability. A more recent study observed the effects of self-selected and pre-determined foot positions on single limb stance postural sway through BalanceMaster® with both eyes open and eyes closed (Schneiders, Gregory, Karas *et al.*, 2016). All these studies however, have only observed static balance. In real-life, there are situations where a person has to encounter uneven terrains (pebbles, gravels etc.), ramps, stairs and slippery or wet floor in which the person has to regain balance. To the best of our knowledge, the effects of changing FPA while standing on an unstable platform with varying degrees of tilt have not been observed. Furthermore, no such experiment has been done for knee osteoarthritis patients. If toe-in or toe-out gait modifications compromise the postural stability of the patient and/ or increase the risk of fall, then these gait modifications need to be considered with caution. Another limitation in our knowledge from the existing literature is that so far, we do not know the interaction of the changing FPAs and platform settings with the presence of knee osteoarthritis.

This study aims to investigate the effects of varying toe angles at different platform settings on Overall Stability Index (OSI) of postural stability and the risk of fall using BBS in healthy participants and participants having moderate knee osteoarthritis. It is hypothesized that changing the foot progression angles will affect the postural stability and risk of fall in both the participant groups for static and dynamic conditions. It is also hypothesized that the different platform settings will affect the postural stability and risk of fall in both of the participant groups.

3.3 Methods

3.3.1 Participants

20 participants were recruited for the healthy control group (CG) from the general community having no known symptoms of any degenerative lower limb joint deformity. 20 participants with bilateral symptomatic medial compartment knee OA, comprising the OA Group (OAG), were recruited from the Department of Sports Medicine, University of Malaya Medical Centre. Medial compartment knee OA was confirmed through anteroposterior weight-bearing radiographic evidence and was graded according to Kellgren-Lawrence scoring system. The experiment was conducted at the Body Performance Lab, University of Malaya.

3.3.2 Inclusion and Exclusion Criteria

The inclusion criteria for both the CG and OAG were age: 50 to 70 years, BMI of less than 30 kg/ m^2 (non-obese (Organization, 2000)). The OAG were of Kellgren-Lawrence grade II and III and required to ascend and descend a 10-steps flight of stairs and jog 5m safely. The participants were excluded on the basis of any neurological or musculoskeletal disorder, cardiovascular or respiratory disease, lower limb fracture/ surgery in the past 12 months or inability to adopt toe-in and toe-out gait pattern. The patients were also excluded if they had other deformities like knee extension lag, excessive internal/ external tibial rotation or mid-tarsal abduction deformity.

3.3.3 Sample Size

The sample power calculation was based on the overall stability index of physical balance, and considered an F-test statistical design for repeated measures (between and within effects), with a moderate effect size of 0.25, a power of 80%, and an alpha error of 5% suggesting each group should contain at least 20 participants.

3.3.4 Ethical Approval

Ethical approval was obtained from UMMC Medical Research Ethics Committee (MREC), MECID.NO: 20161- 2070. All participants provided written informed consent for the study (see Appendix A).

3.3.5 Protocol of Balance Assessment

The Biodex Balance System (BBS; Biodex Medical System Inc., Shirley, NY, USA) assesses a person’s neuromuscular control over balance. The machine consists of a circular platform and a display unit, see Figure 3.1. The participant stands on the circular platform which tilts up to 20º in each direction (360º range of motion). The platform tilts according to the level set through the display unit. There are 12 levels of platform tilt, with 12 being the easiest and 1 being the most difficult. By varying the platform level, the force exerted by the springs attached to the underside of the platform is changed. The force of each platform level is pre-set by the manufacturer by using 8 springs placed underneath the perimeter of the balance platform. Each spring, having an uncompressed length of .14 m, when compressed to 0.75 m, exerts a force of 88.9 N to the platform. The resistance level declines from most resistant (level 1) to least resistant (level 12), with each resistance lasting 3.75 seconds.

Figure 3.1 Biodex Balance System, Biodex Medical Systems, Inc. Courtesy: operation/ service manual.

For this study, the following set of platform settings was used in random order:

3.3.5.1 Postural Stability

(1) Static: having a static platform.

(2) PS8: Dynamic platform setting 8: dynamic platform of level 8 difficulty

3.3.5.2 Risk of Fall

(1) FR12: Each test trial starts from dynamic level 12 and keeps on decreasing to level 8

(2) FR8: Each test trial starts from dynamic level 8 and keeps on decreasing to level 2

The platform can move in anterior-posterior (AP) and medial-lateral (ML) axes simultaneously, giving three types of measurements: anterior/posterior stability index, medial/lateral stability index and overall stability index (OSI). This study focused on OSI only (calculated as in Equation 3.1), because it is reported to be the most reliable parameter for assessing balance (Arnold & Schmitz, 1998). A higher control over balance is indicated by a lower OSI score.

$$\boldsymbol{OSI} = \sqrt{\frac{\sum(\mathbf{0}-\boldsymbol{X})^{\mathbf{2}} + \sum(\mathbf{0}-\boldsymbol{Y})^{\mathbf{2}}}{\boldsymbol{No.\ of\ samples}}} \qquad \textbf{Equation 3.1}$$

At the centre of balance (the position at which the participant is standing balanced, represented by the dot in the middle of the cross-hair on screen), the x and y variables are (0,0). As the user deviates from the centre of balance in sagittal plane, the value of x increases, while when they deviate from this centre of balance in frontal plane, the value of y increases. In other words, it can be said x and y represent the co-ordinates of the centre of gravity on the platform, whose values is (0,0) at time t = 0. Number of samples is the number of test recordings for each test protocol.

3.3.6 Data Collection

In this single-visit study, the participants were briefed about the study protocol and introduced to the BBS. Before starting the experiment, they filled out the WOMAC (Western Ontario and McMaster Universities Index of Osteoarthritis) version VA3 questionnaire.1. It is a self-reported questionnaire containing 3 sections for pain, stiffness, and difficulty performing daily activities. Each of the 24 questions is represented by a score of 0 to 10, (2 points each for none, mild, moderate, severe and extreme pain levels) with a higher score indicating worse pain, stiffness or physical function.

The participants were asked to stand on the BBS facing the monitor, barefoot with eyes open and their hands on their hips. Trials were discarded if they supported themselves with handlebars. The distance between the heels was kept constant at 0.16m in order to avoid the adaptability effects on the stabilizing response due to different heel distances (Khalaj, Osman, Mokhtar *et al.*, 2014; McIlroy & Maki, 1997). The data were taken with the following FPAs: (1) participant's natural FPA (*N*) (2) 10º (3) 20º (4) 30º (5) 40º (6) -10º (7) -20º (see Figure 3.2). They were asked to stand straight and sway without changing their foot positions, in order to keep the moving black dot at the centre of the crosshair displayed on the monitor. For each platform setting and each toe angle two trials were

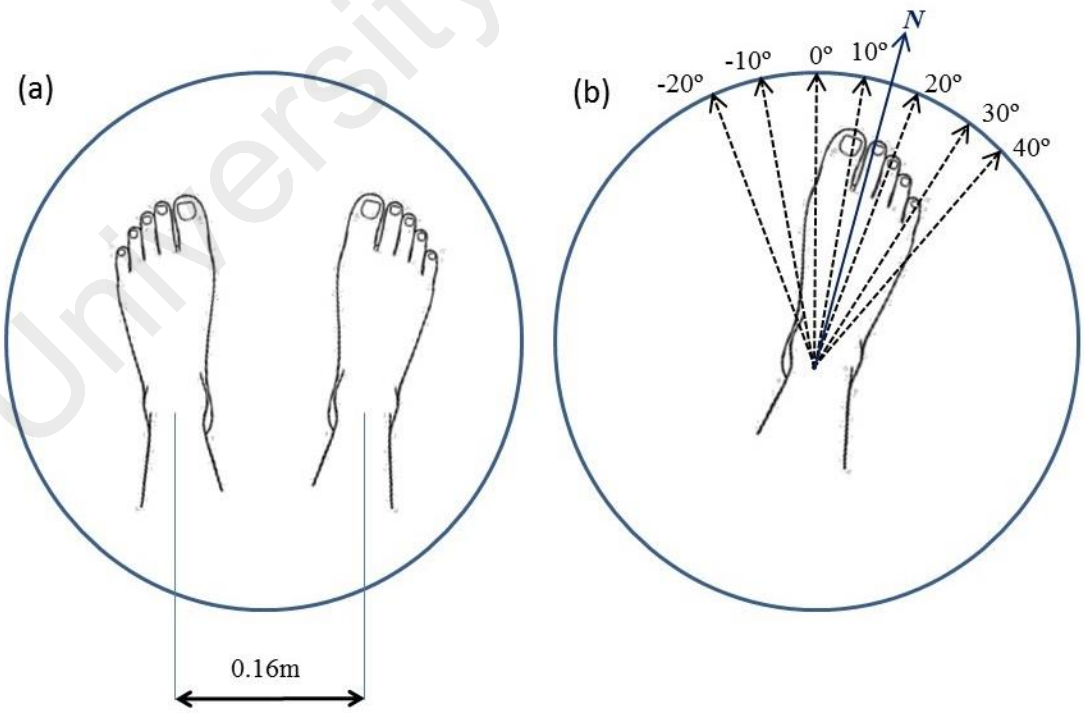


Figure 3.2 (a) Heel distance was kept constant at 0.16m (b) schematic showing different foot progression angles from -20º to 40º, where N represents natural foot angle (5.6º for healthy group and 6.4º for osteoarthritis group).

obtained, each of 30-seconds duration and separated by a 10-seconds rest period. For each participant, 28 data points were obtained (4 platform settings x 7 toe angles). These settings and toe angles were randomized through www.randomisation.com.

3.3.7 Statistics

Shapiro-Wilk test was applied to the data to assess normality. One-way repeated measures ANOVA with Bonferroni corrected post- hoc tests was applied to do pairwise comparisons for each of the participants group. Three-way mixed repeated measures ANOVA was applied keeping Group (CG or OAG) as the between-participants variable and platform settings and toe angles as the within-participants variables. Bonferroni corrections were applied for post- hoc analyses. Simple contrasts were observed for the significant interaction effects. Mann–Whitney test ($\alpha = 0.05$ was applied to compare WOMAC scores using IBM SPSS version 20 (SPSS Inc., USA).

3.4 Results

3.4.1 Natural Foot Progression Angle

The natural FPA (N) for CG was found to be 5.6º ± 2.1º, while for OAG it was found to be 6.4º ± 3.6º, with no significant difference between the two natural FPAs.

3.4.2 Demographics, WOMAC Scores and Stability Indices:

Table 3.1 represents the demographic data and WOMAC scores of the two participant groups. No significant differences were found between the two groups for age, height, body mass and BMI. As for WOMAC pain, stiffness, physical function and total scores, significant differences were found between the groups ($p < 0.001$).

Table 3.1 summarizes the mean stability indices for all test conditions. It was observed that the highest OSI values were observed with an FR8 platform setting for the OAG, going up to 2.74 ± 1.25.

Table 3.1: Demographic data of the CG (Control Group) and OAG (Osteoarthritis Group).

Attributes	CG	OAG	*p*-Value
n *(male, female)*	20 (11,9)	20 (8,12)	
Age *(years)*	59.5 ± 7.33	61.5 ± 8.63	0.49
Height *(m)*	1.64 ± 0.04	1.63 ± 0.03	0.64
Body Mass *(kg)*	69.95 ± 9.86	70.45 ± 8.80	0.95
BMI *(kg/m^2)*	26.00 ± 4.21	26.40 ± 4.20	1
Duration of OA (years)	N/A	6.87 ± 2.89	
Kellgren-Lawrence Grade			
II		10	
III		10	
Femoro-tibial angles	N/A	180.41º ± 3.95º	
WOMAC			
Pain *(0-50)*	1.60 ± 0.89	13.5 ± 5.65	< 0.001
Stiffness *(0-20)*	1.50 ± 0.54	7.25 ± 7.16	< 0.001
Physical function *(0-170)*	5.8 ± 3.11	61.75 ± 31.45	< 0.001
Total *(0-240)*	8.8 ± 3.49	82.5 ± 39.85	< 0.001

3.4.3 Between- Participants Effects (Effects of the presence of kOA)

Three-way mixed repeated measure ANOVA showed that there was a significant main effect of Group, $F(1, 38) = 15.605$, $p < 0.01$. The OAG group, having an estimated marginal mean of (EMM) of 1.23 ± 0.08 had significantly higher OSIs than the CG group with an EMM of 0.743 ± 0.06.

Table 3.2: Mean values of overall stability indices at different foot progression angles for OAG (osteoarthritis group) and CG (control group). Where N represents natural toe angle (5.6º for CG and 6.4º for OAG) and the bold *p*-values represent significant differences from mean.

		Control Group (CG)					Osteoarthritis Group (OAG)				
Platform Setting	Toe Angle	Mean	SD	Upper Bound	Lower Bound	CV	Mean	SD	Upper Bound	Lower Bound	CV
Static	-20º	0.45	0.22	0.54	0.36	0.48	0.66	0.23	0.76	0.56	0.34
	-10º	0.39	0.19	0.47	0.31	0.49	0.51	0.24	0.62	0.40	0.47
	0º	0.42	0.22	0.52	0.32	0.53	0.58	0.27	0.70	0.46	0.46
	N	0.40	0.22	0.49	0.31	0.54	0.62	0.21	0.71	0.53	0.33
	10º	0.37	0.15	0.43	0.31	0.39	0.59	0.30	0.72	0.46	0.50
	20º	0.33	0.15	0.39	0.27	0.44	0.49	0.20	0.58	0.40	0.40
	30º	0.32	0.14	0.38	0.26	0.44	0.50	0.20	0.59	0.41	0.39
	40º	0.34	0.17	0.41	0.27	0.49	0.70	0.29	0.82	0.58	0.41
FR12	-20º	0.68	0.27	0.80	0.56	0.40	1.03	0.44	1.22	0.84	0.43
	-10º	0.60	0.29	0.73	0.47	0.48	0.90	0.38	1.07	0.73	0.42
	0º	0.63	0.27	0.75	0.51	0.42	0.98	0.42	1.16	0.80	0.43
	N	0.60	0.24	0.71	0.49	0.40	0.99	0.36	1.15	0.83	0.37
	10º	0.55	0.17	0.62	0.48	0.31	1.00	0.14	1.06	0.94	0.14
	20º	0.54	0.13	0.60	0.48	0.24	0.96	0.34	1.11	0.81	0.35
	30º	0.50	0.22	0.60	0.40	0.44	0.85	0.42	1.04	0.66	0.50
	40º	0.52	0.16	0.59	0.45	0.30	**1.09**	0.37	1.25	0.93	0.34
PS8	-20º	0.42	0.19	0.50	0.34	0.44	**1.22**	0.48	1.43	1.01	0.39
	-10º	0.26	0.08	0.29	0.23	0.29	1.08	0.39	1.25	0.91	0.37
	0º	0.34	0.15	0.41	0.27	0.44	1.14	0.62	1.41	0.87	0.54
	N	0.36	0.04	0.38	0.34	0.12	1.06	0.52	1.39	0.93	0.45
	10º	0.35	0.02	0.36	0.34	0.06	1.15	0.42	1.33	0.97	0.36
	20º	0.30	0.11	0.35	0.25	0.38	1.17	0.56	1.42	0.92	0.48

Table 3.2: continued

		Control Group (CG)					Osteoarthritis Group (OAG)				
	30º	0.27	0.10	0.31	0.23	0.37	1.05	0.46	1.25	0.85	0.44
	40º	0.29	0.12	0.34	0.24	0.42	**1.20**	0.50	1.42	0.98	0.42
FR8	-20º	**1.74**	0.04	1.76	1.72	0.02	**2.74**	1.31	3.31	2.17	0.48
	-10º	**1.49**	0.36	1.65	1.33	0.24	1.99	0.95	2.41	1.57	0.48
	0º	1.23	0.41	1.61	1.25	0.29	**2.38**	1.18	2.90	1.86	0.49
	N	1.19	0.45	1.59	1.19	0.32	2.04	1.11	2.53	1.55	0.55
	10º	1.31	0.48	1.52	1.10	0.36	**2.31**	1.18	2.83	1.79	0.51
	20º	1.21	0.11	1.26	1.16	0.09	**2.49**	1.22	3.03	1.95	0.49
	30º	1.25	0.34	1.40	1.10	0.27	**2.28**	1.16	2.79	1.77	0.51
	40º	**1.37**	0.43	1.56	1.18	0.32	**2.27**	1.25	2.82	1.72	0.55

Where N represents natural toe angle (5.6º for CG and 6.4º for OAG) and the bold p-values represent significant differences from N.

3.4.5 Effect of Platform Settings

There was a significant main effect of platform setting, $F(3, 114) = 42.685$, $p < 0.01$. Pairwise comparisons showed that all the settings differed from Static (0.51 ± 0.02) in the following order of increasing estimated marginal mean (EMM): FR12 (EMM ± SE = 0.72 ± 0.04, $p < 0.01$), PS8 (0.98 ± 0.06, $p < 0.01$) and FR8 (1.71 ± 0.16, $p < 0.01$), where SE is the standard error. Furthermore, the FR8 setting had significantly higher OSI values than PS8 ($p < 0.01$) and FR12 ($p < 0.01$). The PS8 setting had significantly higher OSIs than FR12 ($p < 0.01$).

3.4.6 Effects of Toe-angles

There was a significant main effect of the toe angles, $F(7, 266) = 2.48$, $p = 0.02$. Natural toe angle (N) was found to produce OSI values having an EMM of 0.96 ± 0.07. Pairwise comparisons showed significant differences from N for the toe angles of -20º (1.07 ± 0.07, $p = 0.03$), -10º (0.85 ± 0.04, $p = 0.04$), 30º (1.56 ± 0.06, $p = 0.02$) and 40º (1.89 ± 0.08, $p = 0.01$). Furthermore, 40º had significantly higher OSI values than -10º ($p = 0.02$) and 0º ($p = 0.03$). Similarly, 30º toe angle had significantly higher OSI values than -10º ($p = 0.03$) and 0º ($p = 0.03$).

3.4.7 Group × Settings Interactions:

There was a significant interaction between the type of platform setting and whether the participant was from CG or OAG, $F(3, 144) = 6.97$, $p < 0.01$.

This effect shows that the profile of the stability indices across different platform settings was different for OAG than CG. In general, the interaction graph (Figure 3.3) suggests that the balance indices of OAG are more influenced by the increasingly difficult platform setting than the balance indices of CG. Although OSIs of both CG and OAG increased with increasing platform, difficulty, this increase was more pronounced for

OAG. To investigate this effect, the investigators looked into the within-participant contrasts.

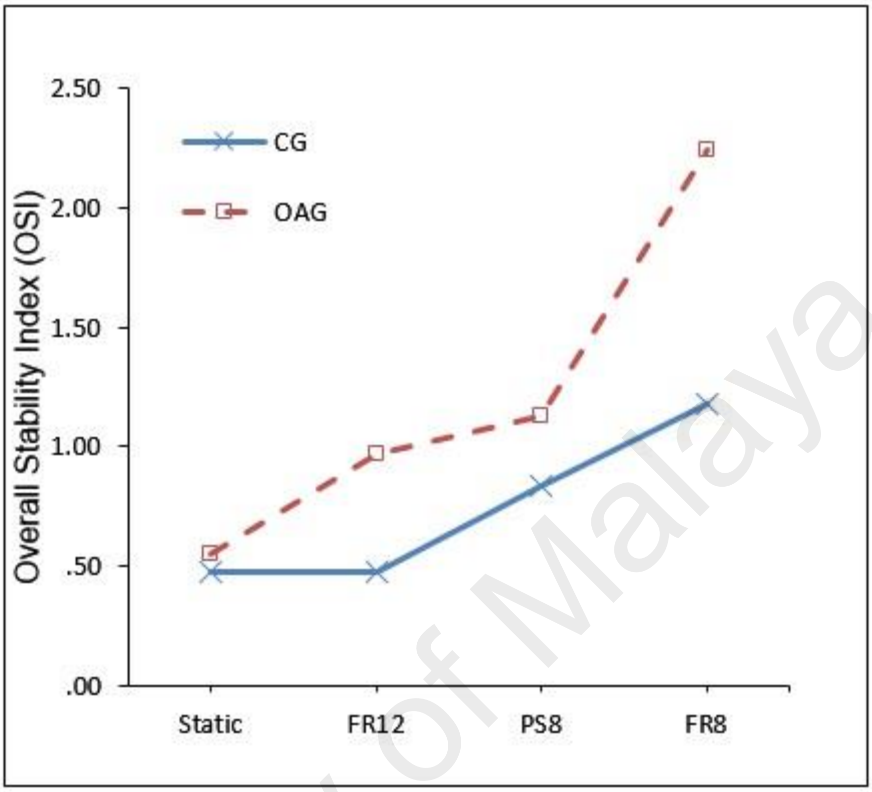


Figure 3.3: Interaction effects of Group x Settings. The two lines represent two participant groups CG (Control Group) and OAG (Osteoarthritis Group). The horizontal axis represents platform settings in an order of increasing difficulty, where FR12: Fall Risk test with dynamic platform level 12 to 8, PS8: Postural Stability test with dynamic level 8 and FR8: Fall Risk test with dynamic platform level 8 to 2.

3.4.7.1 Contrasts (Group × Settings)

The contrasts of static versus all other platform settings (FR12, PS8 and FR8) were found to be significant. The respective F values for FR12, PS8 and FR8 were found to be $F(1, 38) = 30.07$, $p < 0.01$, $F(1, 38) = 4.12$, $p < 0.04$ and $F(1, 38) = 8.77$, $p < 0.01$. The results indicate that OSIs for FR12, PS8 and FR8, when compared to static platform setting for OAG were significantly higher than for CG.

3.4.8 Group × Toe-angles Interactions:

There was a non-significant interaction between the toe angles and whether the participant was from CG or OAG, $F(7, 266) = 0.89$, $p = 0.50$.

3.4.9 Toe angles × settings Interactions:

There was a significant interaction between the type of platform setting and the toe angle, F (21, 798) = 2.83, $p < 0.01$. The interaction graph (Figure 3.4) shows that the behaviour of platform settings static, FR12 and PS8 resembled each other while FR8 behaved differently. For further clarification, within participants contrasts were investigated.

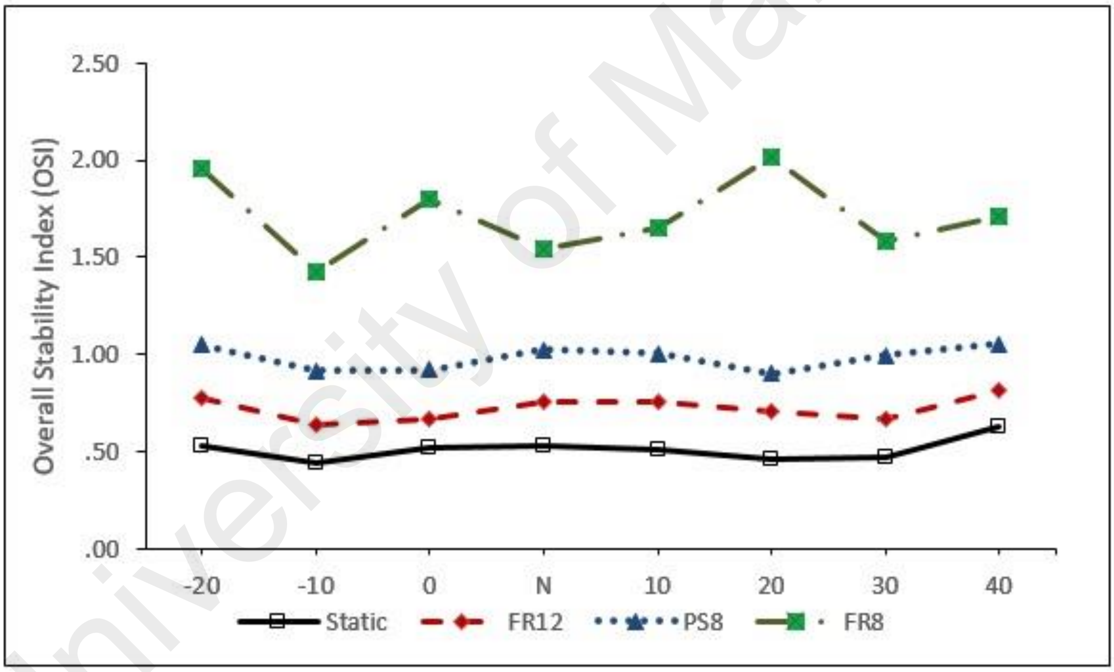


Figure 3.4: Interaction effects of Settings × Toe angles. The four lines represent the platform settings, where FR12: Fall Risk test with dynamic platform level 12 to 8, PS8: Postural Stability test with dynamic level 8 and FR8: Fall Risk test with dynamic platform level 8 to 2. . The horizontal axis represents toe angles in an increasing order.

3.4.9.1 Contrasts (Toe-angles × Settings)

Within-participants contrasts showed that the only significant interactions were found between platform settings FR8 and static. The increased OSI at -20°, -10° and 40° was found to be significantly higher at FR8 than at static.

3.4.10 Group × Toe angles × Settings Interactions:

There was a non-significant interaction between the type of platform setting, the toe angle and whether the participant was from CG or OAG, F (21, 798) = 1.07, p = 0.36.

3.5 Discussion

The human body is an inherently stable system in terms of balance despite of non-uniform mass and load distribution (Woollacott & Shumway-Cook, 2002). However, balance can be lost due to prolonged dizziness, impaired vestibular apparatus, physical injury to the head/ limbs or visual impairment. Therefore, any postural modification aimed at treating a disorder should be designed as such that it does not compromise the balance of the person. The aim of this study was to assess postural stability and risk of fall at different foot progression angles under static standing and dynamic standing conditions. By introducing varying degrees of platform tilt, the investigators aimed to simulate the challenges offered by different types of terrains to the static and dynamic standing balance of a person. The results showed that for static and fall risk level 12 conditions, there was no effect of changing the foot progression angles in either of the participant groups (healthy and knee osteoarthritis groups). The postural stability of the healthy participants was not affected by the changing foot progression angles at level 8 condition, while at this condition, there was a decrease in stability at extreme toe-in and extreme toe-out angles among the participants with knee osteoarthritis. Fall risk increased significantly for both the participant groups at level 8 condition, for higher degrees of toe angle deviations from the natural toe angle. Our first hypothesis, that the changing foot progression angles will bring a change in balance parameters for both the participant groups holds true only for the highly unstable dynamic platform settings.

In general, it was observed that the healthy population is so stable by nature that variations in the toe angles did not affect it for static and highly unstable platforms. The only angle at which the healthy group was found to be unstable was -20º and 40º only for FR8 setting. A possible explanation of this behaviour may be that the foot's natural progression angle is inherently toe-out (Shull, Shultz, Silder *et al.*, 2013; Simic, Wrigley, Hinman *et al.*, 2013), hence there are inherent abilities of balancing mechanisms for a range of toe-out angles. While when we make this angle opposite to the natural, the body loses its stability.

The study also checked the individual effects of our three primary factors (presence/ absence of knee osteoarthritis, platform settings and toe angles) one by one, keeping the other two variables irrelevant. The results showed that if we ignore the platform settings and the toe angles (pooling data from all the platform settings and toe angles and categorizing them into healthy and knee osteoarthritis group), the presence of knee osteoarthritis had a considerable effect in decreasing the postural stability and increasing the risk of fall of the participant. Similarly, changing toe angles produced significantly different stability indices if we ignore the platform setting applied and the presence/ absence of knee osteoarthritis (pooling data from both the participant groups and all the platform settings and categorizing them into 8 toe angles). Stability indices increased significantly at the two ends of our tested spectrum of foot progression angles (-20º and 40º).

The platform settings significantly affected balance when we ignored the toe angle applied and the presence/ absence of knee osteoarthritis (combining data from both the participant groups and all the toe angles and categorizing them into 4 platform settings). The stability of the participants, in general, deteriorated as we move in an order of increasingly unstable platform setting. The interaction between participant groups and platform settings showed that the presence of knee osteoarthritis increased the sensitivity to the terrain in terms of balance. Simply put, the balance of the participants with knee osteoarthritis gets affected to the highly unstable platforms more than the balance of healthy individuals. There was also a significant interaction between toe angles and platform settings. The results indicated that the differences of stability indices at natural toe angle and -20°, -10° and 40° toe angles at the fall risk level 8 condition (highly unstable platform) were significantly higher than the static platform setting. Our second hypothesis, hence holds true that the changing platform settings will affect balance for both participant groups.

A similar study by Nafiseh *et al*, took three participant groups (healthy, mild knee osteoarthritis patients and moderate knee osteoarthritis patients), and found the differences in overall stability index through one-way analysis of variance (Khalaj, Osman, Mokhtar *et al.*, 2014). They reported that the healthy participants differed from both the osteoarthritis groups at static standing and dynamics standing settings. Our results also support this finding that the knee osteoarthritis participants have poorer balance as compared to healthy participants. These results were obtained from a different statistical approach (three-way mixed analysis of variance) which also gave us the interactions between the independent variables. This interaction was not addressed before and fills the gap in the literature.

An interesting finding from the interactions is that the foot progression angles affect the two participant groups and, more importantly, this effect is similar in both the groups. While the platform settings affect the knee osteoarthritis group significantly more than the healthy participants. These findings suggest that the knee osteoarthritis syndrome does not relate to changing foot progression angles, while it affects the balance of a person when they change the terrain they are treading or climbing. This greater fall risk is the reason that the persons with knee osteoarthritis feel more pain and discomfort while performing physical activities other than normal level-walking (Jadelis, Miller, Ettinger *et al.*, 2001; Pandya, Draganich, Mauer *et al.*, 2005).

A notable finding from our analyses is that the effect of changing foot progression angles became more evident as the platform became more unstable for both participant groups. This means that the stability index values for each toe-angle varied more at a more unstable platform as compared to the platforms with lesser degree of tilt. One may infer from this that for highly unstable terrains a person needs to be cautious in altering the foot progression angle, as this alteration may result in more pronounced effects on stability compared to concrete, stable terrains.

An application of our findings is in the prescription of toe-out and toe-in angles for knee osteoarthritis treatment which are gaining popularity as practically feasible and cost-less non-surgical and non-pharmacological treatment options for knee osteoarthritis (Khalaj, Abu Osman, Mokhtar *et al.*, 2014).

3.6 Conclusion

The participants having moderate medial knee osteoarthritis have a poorer postural stability and increased risk of fall as compared to healthy participants. Changing platform settings had a profound effect on balance, and this effect was more pronounced for the participants with knee osteoarthritis than healthy participants. Changing toe angles produced similar effects on both the participant groups, with decreased stability and increased fall risk at extreme toe-in and extreme toe-out angles. Future studies should develop balance enhancement strategies for osteoarthritis patients at higher foot progression angles and for highly unstable terrains.

CHAPTER 4: ORTHOSES VS GAIT MODIFICATIONS: IMMEDIATE RESPONSE IN IMPROVING PHYSICAL PERFORMANCE MEASURES IN HEALTHY AND MEDIAL KNEE OSTEOARTHRITIC ADULTS

4.1 Introduction

The chapter addresses objective 2 as stated in section 1.3. The chapter presents the study that aimed to assess the immediate effects of two types of conservative techniques: orthoses (knee braces and wedged insoles) and gait modification methods (toe-in and toe-out gait) in improving physical performance of healthy and knee osteoarthritis participants. The tests used to assess the physical function of the participants were those recommended by the Osteoarthritis Research Society International (OARSI) for knee osteoarthritis patients. These tests were not performed previously on any of the conservative treatment techniques except knee brace. The chapter begins with a brief review of previous works that report how knee osteoarthritis affects physical performance of the patients, different tool to assess physical function and conservative treatment techniques for knee osteoarthritis. It also states the hypothesis for the research. Further on, a methodology is presented defining sampling procedure, experimental setting, study protocol and statistical methods. Following this, is the presentation of results of the experiment. The chapter presents a discussion of the results and the conclusions drawn from the study. This chapter assesses the efficiency of the orthoses and gait modification techniques in terms of physical performance of the participants, while the chapter following this (Chapter 5), assesses these techniques in terms of joint kinetics and balance.

4.2 Study Background

Physical functional is crucial in performing the activities of daily living, and in degenerative joint diseases like osteoarthritis, this can be impaired and affects the quality of life. Hence, a major outcome variable for the treatment of degenerative joint diseases is the physical function of the patients. Knee osteoarthritis (kOA), the most commonly occurring type of osteoarthritis in the world, largely because of its wearisome mobility and load-bearing characteristics during gait (Badley, 2005; Lawrence, Felson, & Helmick, 2008), is known to impair lower limb muscle strength, physical function, joint mobility and joint range of motion (Bączkowicz & Majorczyk, 2014; Bijlsma, Berenbaum, & Lafeber, 2011; Knoop, Steultjens, Van der Leeden *et al.*, 2011; Walker, 2011). Owing to these characteristics, a kOA patient experiences varying degrees of difficulty in performing even the simplest of tasks such as standing up from a chair, standing at ease and ascending or descending stairs. Stair ascent, in particular, can be extremely challenging because of the compromised proprioception in kOA patients (Hicks-Little, Peindl, Fehring *et al.*, 2012; Startzell, Owens, Mulfinger *et al.*, 2000). For older adults (the dominant population for kOA), stair ascent and descent is already considered a risky activity, with 10% of the deaths caused by falls occurring during stair climb (Lee & Chou, 2007). A diseased knee joint can only increase this percentage because of decreased proprioception and increased knee joint moments. Unfortunately, the conservative treatment techniques aimed at treating mild and moderate levels of kOA are not extensively tested for improving the physical function of the patients.

The conservative treatment techniques encompass orthoses and gait modification techniques. Orthoses, which include knee braces and laterally wedged insoles, are the mechanical devices that are designed to affect the biomechanical parameters of the kOA patient by decreasing the load at the medial compartment of the knee joint (Fantini Pagani, Hinrichs, & Brüggemann, 2012; Hinman, Bardin, Simic *et al.*, 2013; Jones, Nester, Richards *et al.*, 2013; Kutzner, Küther, Heinlein *et al.*, 2011; Turpin, De Vincenzo, Apps *et al.*, 2012). On the other hand, gait modification methods rely on decreasing the knee joint load through postural change (trunk sway, alteration of the foot progression angle, knee thrust etc.) (Hunt & Takacs, 2014; Simic, Hunt, Bennell *et al.*, 2012; Simic, Wrigley, Hinman *et al.*, 2013). Toe-out gait is one of the two methods of altering the foot progression angle (the angle between the line passing through the centre of the ankle joint the second metatarsal head and the progression axis of the walk) (Shull, Silder, Shultz *et al.*, 2013). It involves external rotation of the foot more than a natural 8-10º angle (Simic, Hinman, Wrigley *et al.*, 2011). Toeing-out is believed to laterally shift the GRF vector thus reducing the moment arm of the force. Since the knee adduction moment is a product of GRF and its lever arm, toe-in gait reduces the knee adduction moment. In contrast to toe-out gait, the toe is moved inwards (internal rotation of the foot) during toe-in gait. Toe-in gait is relatively less studied than toe-out gait modification, with foot progression angles ranging from 2.1º (Chen, Kuo, & Andriacchi, 1997; Shull, Silder, Shultz *et al.*, 2013) to 19.9º (Rosenbaum, 2013). However, it is still debatable as to which of the gait retraining methods is the most efficient in terms of providing symptomatic relief for kOA.

To the best of our knowledge, the only conservative treatment technique ever to be tested for performance-based tests is the knee brace. The brace is reported to either improve or have no effect on the physical function of the kOA patients during activities such as walking, stair ascent and descent, and sit-to-stand activity (Cherian, Bhave, Kapadia *et al.*; Dessery, Belzile, Turmel *et al.*, 2014; Hurley, Hatfield Murdock, Stanish *et al.*, 2012; Larsen, Jacofsky, Brown *et al.*, 2013; Wang, Yu, Hashish *et al.*, 2013). Unfortunately, for other conservative techniques, no such information is available. A need, therefore, exists for testing the conservative treatment techniques, which are non-invasive and cheaper than the surgical and pharmacological techniques and with no reported side-effects, for kOA on the physical function of the patient.

Physical performance is categorically measured through either the self-reported tests or performance-based tests, with the former being less preferred for their higher risk of biases (Parent & Moffet, 2002; Stratford & Kennedy, 2004, 2006; Stratford, Kennedy, &

Riddle, 2009). The physical performance tests, on the other hand, report the actual physical abilities of a person, rather than a perceived notion of the patient. The study has included the OARSI (Osteoarthritis Research Society International) recommended performance-based tests to measure the physical function of kOA patients (Dobson, Hinman, Roos *et al.*, 2013). They are universally accepted, easy to conduct and very much daily activity-oriented. Three of these five tests (30-second chair test, 40m fast-paced walk test and stair climb test) are the core tests, while the other two (timed up and go test and 6-minute walk test) are additional tests. These tests evaluate the lower body strength, dynamic balance, agility, ambulatory transition and aerobic capacity of a person.

The objectives of the study were (1) evaluating the immediate effects of knee brace, lateral wedged insole, toe-in gait and toe-out gait on standard physical performance measures in healthy participants and kOA patients and (2) comparing the effects of these interventions with each other to find the most efficient treatment technique in terms of physical function.

4.3 Methods

4.3.1 Subjects

20 participants were recruited for the healthy control group (CG) from the general community having no known symptoms of any degenerative lower limb joint deformity. Twenty participants with bilateral symptomatic medial compartment knee OA, comprising the OA Group (OAG), were recruited from the Department of Sports Medicine, University of Malaya Medical Centre. Symptomatic was defined as having knee pain or stiffness and/or difficulty performing daily activities. Medial compartment knee OA was confirmed through anteroposterior radiographic evidence and was graded according to Kellgren-Lawrence grade system. The experiment was conducted at the Body Performance Lab, University of Malaya.

4.3.2 Inclusion and Exclusion Criteria

The inclusion criteria for both the CG and OAG were age: 50 to 70 years, BMI of less than 30 kg/ m^2 (non-obese (Organization, 2000)). The OAG were of Kellgren-Lawrence grade II and III and required to ascend and descend a 10-steps flight of stairs and jog 5m safely. The participants were excluded on the basis of any neurological or musculoskeletal disorder, cardiovascular or respiratory disease, lower limb fracture/ surgery in the past 12 months or inability to adopt toe-in and toe-out gait pattern. In addition, participants who had had knee intraarticular injection within the last 6 months, or taking joint supplements like glucosamine and/or chondroitin for the last 3 months were also excluded.

4.3.3 Sample Size

The sample power calculation was based on the physical performance variables, and considered an F-test statistical design for repeated measures (between and within effects), with a moderate effect size of 0.25, a power of 80%, and an alpha error of 5% suggesting each group should contain at least 20 participants.

4.3.4 Ethical Approval

Approval was obtained from University of Malaya Medical Centre (UMMC). All participants provided written informed consent for the study.

4.3.5 Interventions

4.3.5.1 Orthoses

The orthoses used in this study were knee brace (KB) and lateral wedged insole (LWI). The knee brace (Donjoy OA Adjuster™ 3, USA) works on 4 points of leverage system, see Figure 4.1. The lateral wedged insole (Salfordinsole™, UK) was full-length with 5º inclination. Both orthoses are specifically designed for medial compartment knee osteoarthritis.

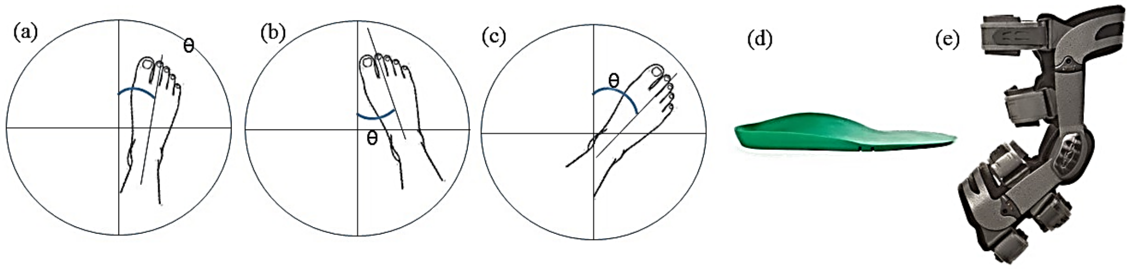


Figure 4.1: (a) Natural foot progression angle (b) toe-in gait modification (c) toe-out gait modification (d) knee brace (Donjoy OA AdjusterTM 3, USA), (e) laterally wedged insole (SalfordinsoleTM, UK),

4.3.5.2 Gait Modifications

The study deals with the effects of two gait modification techniques that deal with foot progression angle (FPA). The participants walked with straight foot, self-selected toe-out angle (TO: making V shape with their feet) and toe-in angle (TI: making A shape with their feet), see Figure 4.1.. The participants were given practice sessions for these gait modifications with the minimum toe-out angle of natural FPA plus 15º and minimum toe-in angle of natural FPA minus 15º.

4.3.6 Data Collection

The study was a single visit study. The participants were briefed about the study protocol, introduced to the interventions. Before the starting the experiment, they filled out the WOMAC (Western Ontario and McMaster Universities Index of Osteoarthritis) version VA3.1 (see Appendix C). It is a self-reported questionnaire containing 3 sections for pain, stiffness, and difficulty performing daily activities. Each of the 24 questions is represented by a score of 0 to 10, with a higher score indicating worse pain, stiffness or physical function.

The participants were then provided with shoes (Supercloud, Adidas, UK) in order to minimize the influence of different shoes. Each participant was trained with the interventions especially for toe-out and toe-in gait with adequate practice by the mutual discretion of the participant and the investigator. The OARSI-recommended performance-based test protocols were followed to assess the physical function in people

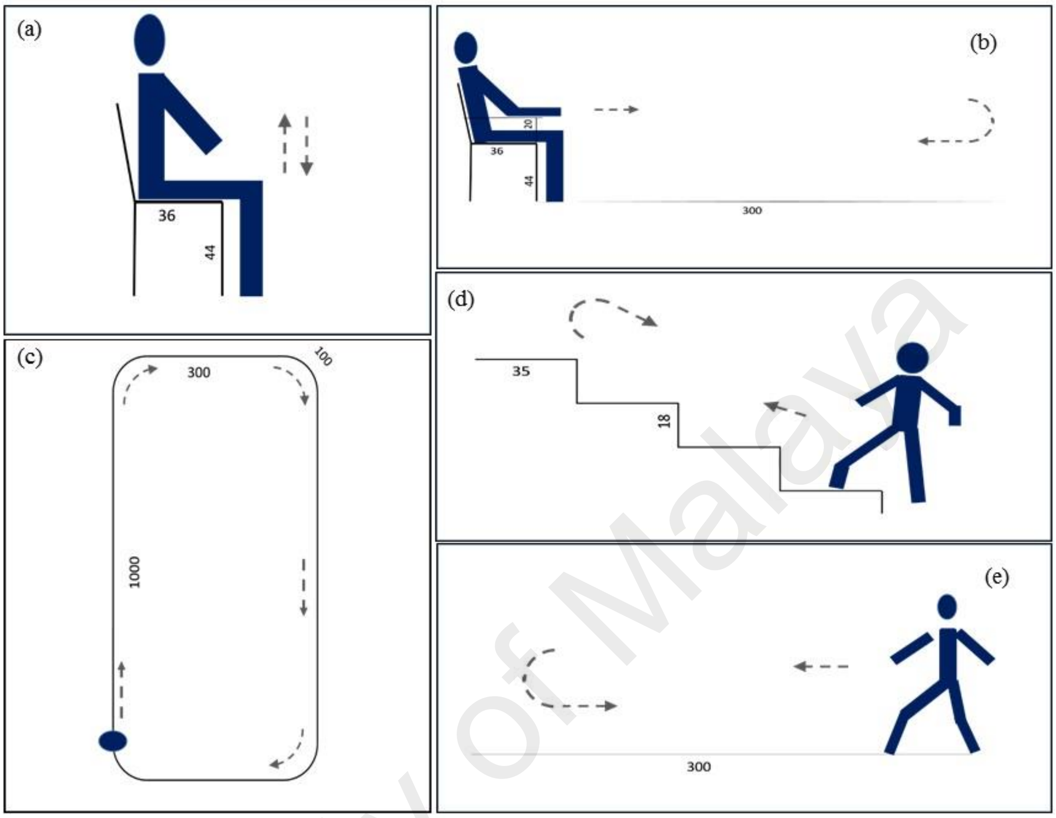


Figure 4.2: Schematics of performance-based tests (a) 30-second chair stand test (b) time up and go (TUG) test (c) 6-minute walk test (d) stair climb test (e) 40m fast-paced walk test. Grey arrows show direction of movement or progression. All dimensions are given in centimetres.

with kOA, described briefly through Table 4.1 and Figure 4.2. The five tests and the five test conditions (natural walk-N, TO, TI, KB and LWI) were randomized using random permutations through http://randomization.com/. The data set for each participant comprised of 5 tests x 5 test conditions = 25 data points. During the experiment, one investigator conducted the experiment, noteding down the required readings, (see Appendix B), while the other observed the foot progression angles of the participant, prompting for any deviations from the test protocol. The participants gave subjective feedback about pain and discomfort in between the trials.

Table 4.1: Brief description of the five standard performance-based tests used in the study.

Performance Test	Protocol	Equipment Used	Outcome Variable
30-second Chair Stand Test	The participant is asked to perform a sit-to-stand activity for a period of 30sec without any support	Chair without arms with a seat height of 44cm	Number of chair stands
Timed Up and Go (TUG) test	The participants are asked to stand up from a sitting position, walk 3 meters at normal walking speed, turn around, walk the same path to the chair and sit down on it.	Chair with arm rest. Seat height of the chair was 44cm and arm-rest height was 20cm from seat.	Time in seconds
6-minute walk test	Participant is asked to walk on a defined path in 6 minutes.	Flat walking area with length = 10m, width = 3m and arc-length =1m. Total perimeter = 30m	Distance in metre
Stair Climb Test	Participant is asked to ascend and descend a staircase, without using handrails.	Staircase with 10 steps. Each step with height = 18cm and width =35cm	Time in seconds
40m (4 x 10m) Fast-paced walk Test	Participants are asked to walk 4 times on a 10m walkway as fast as they can.	Walkway with a length of 10m	Walking speed in metres/ second

4.3.7 Statistics

Shapiro-Wilk test was applied to the data to assess normality. Repeated measure ANOVA was used to find within-effects in each group while Independent sample t-test was used to find differences between groups at $\alpha = 5\%$. The Bonferroni corrections were applied during the post hoc pairwise comparisons, to avoid false positives. Student's independent sample t-test was used to compare anthropometric and demographic parameters between the two groups, while Mann–Whitney test ($\alpha = 5\%$) was applied to compare WOMAC scores using IBM SPSS version 20 (SPSS Inc., USA).

4.4 Results

4.4.1 Demographics and WOMAC Scores

Table 4.2 represents the demographic data and WOMAC scores of the two participant groups. No significant differences were found between the two groups for age, height, body mass and BMI. As for WOMAC pain, stiffness, physical function and total scores, significant differences were found between the groups ($p < 0.001$).

Table 4.2: Demographic data of the CG (Control Group) and OAG (Osteoarthritis Group).

Attributes		CG	OAG	*p*-Value
n *(male, female)*		20 (11,9)	20 (8,12)	
Age *(years)*		59.5 ± 7.33	61.5 ± 8.63	0.49
Height *(m)*		1.64 ± 0.04	1.63 ± 0.03	0.64
Body Mass *(kg)*		69.95 ± 9.86	70.45 ± 8.80	0.95
BMI *(kg/m^2)*		26.00 ± 4.21	26.40 ± 4.20	1
Duration of OA		N/A	6.87 ± 6.89	
Kellgren-Lawrence Grade				
	II		10	
	III		10	
WOMAC				
	Pain *(0-50)*	1.60 ± 0.89	13.5 ± 5.65	<0.001
	Stiffness *(0-20)*	1.50 ± 0.54	7.25 ± 7.16	<0.001
	Physical function *(0-170)*	5.8 ± 3.11	61.75 ± 31.45	<0.001
	Total *(0-240)*	8.8 ± 3.49	82.5± 39.85	<0.001

4.4.2 Within Group (CG)

Within the group, the differences among TUG test and 30-second chair stand test scores for all the test conditions were found insignificant, see Table 3. TO was found to be affecting the outcome variables the most, hence had significantly higher values from N, TI and LWI for 6-minute walk test and stair climb test. While for 40m fast-paced walk test, the only difference found was between TO and LWI. There was also a difference between TO and KB for stair climb test and 6-minute walk test. For stair climb test only, TI was found significantly different than N.

4.4.3 Within Group (OAG)

Within the group, the differences among TUG scores and 30-second chair stand test scores for all the test conditions were found insignificant, see Table 4.3. KB and TI were found significantly different from TO in 6-minute walk test. For stair climb test, TO seemed to be affecting the observed parameter (time) the most, having the largest value, while KB seemed to be taking the least amount of time. Consequently, TO was found significantly different from N, LWI and KB, while KB was found significantly different from N, TO, TI and LWI. TI and LWI also differed significantly from each other. For 40m fast-paced walk test, KB was observed to be the most efficient (having the highest walking speed), while TO decreased the speed the most. As a result, TO differed significantly from N, TI and KB, while KB differed significantly from N, TO, TI and LWI. TI also differed significantly from N.

4.4.4 Between Groups (CG x OAG)

The outcome variables for the OAG group were found to be significantly different (higher for 40m fast-paced walk test and stair climb test while lower for 30-second chair test and 6-minute walk test) for all the test conditions (N, TO, TI, LWI, KB), Table 3. However, for TUG test scores, the difference between test conditions TO and TI was found to be insignificant between groups. For rest of the test conditions, TUG scores remained significantly different between the two groups. Figure 4.3 represents mean and standard deviation values for the physical performance measures for the two groups.

4.4.5 Subjective Feedback for OAG

Five OAG participants reported increased pain in medial part of the symptomatic knee joint with TO during 6-minute walk test. During stair climb test, 6 participants reported pain in the symptomatic knee joint. Three patients reported that TI is more difficult than TO for stair ascent and descent, reporting pain in the lateral part of the symptomatic knee joint (they had to take the support of the hand rails). They also reported stretching at the back of the thigh. Walking with TO, one patient reported pain in the whole leg at the end of the 40m fast-paced walk test, while a pain in the shank during the middle of the test. Four participants reported heel discomfort with TO during 40m fast-paced walk test. Two patients reported pain in the left pelvis (non-symptomatic side) with TI at the start of the

Table 4.3: Results of independent sample t-test and pair-wise comparison of repeated measures ANOVA with mean ± standard deviation values of Control Group (CG) and Osteoarthritis Group (OAG). Only significant p-values are mentioned ($p < 0.05$). The upwards arrow (↑) represents an improvement, while downwards arrow (↓) represents impairment in the physical function parameter.

Physical Performance Test	Test Condition	CG (n = 20)	% Improvement from N	OAG (n = 20)	% Improvement from N	*p* CG x OAG	*p* CG	*p* OAG
30-second Chair Stand Test *(number of chair stands)*	Normal (N)	17.00 ± 1.49		13.00 ± 3.25		< 0.001		
	Toe-out (TO)	16.00 ± 1.47	↓5.88	13.00 ± 3.48	0	0.010		
	Toe-in (TI)	16.00 ± 1.70	↓5.88	12.00 ± 2.95	↓7.69	< 0.001		
	Wedged insole (LWI)	16.00 ± 1.13	↓5.88	12.00 ± 2.65	↓7.69	< 0.001		
	Knee Brace (KB)	16.00 ± 2.06	↓5.88	11.00 ± 1.80	↓7.69	< 0.001		
Timed Up and Go (TUG) test *(time in seconds)*	Normal (N)	7.93 ± 0.76		8.38 ± 1.80		0.007		
	Toe-out (TO)	8.72 ± 1.57	↓9.96	8.86 ± 2.90	↓5.73			
	Toe-in (TI)	8.17 ± 1.01	↓3.03	9.08 ± 1.70	↓8.35			
	Wedged insole (LWI)	7.60 ± 0.46	↑4.16	8.67 ± 1.67	↓3.46	0.041		
	Knee Brace (KB)	7.95 ± 0.59	↓0.25	9.62 ± 1.33	↓14.80	< 0.001		
6-minute Walk Test *(distance in metres)*	Normal (N)	561.67 ± 15.05		420.54 ± 36.56		< 0.001		
	Toe-out (TO)	513.00 ± 9.86	↓8.67	390.7 ± 49.36	↓7.10	< 0.001	<0.001 $^{\text{TO x N}}$	0.001 $^{\text{TO x KB}}$
	Toe-in (TI)	565.10 ± 18.12	↑0.61	384.14 ± 36.73	↓8.66	< 0.001	0.048 $^{\text{TI x TO}}$	0.001 $^{\text{TO x TI}}$
	Wedged insole (LWI)	559 ± 16.37	↓0.48	436.2 ± 36.64	↑3.72	< 0.001	<0.001 $^{\text{LWI x TO}}$	
	Knee Brace (KB)	554.40 ± 19.67	↓1.29	485.33 ± 7.19	↑15.41	< 0.001	<0.001 $^{\text{KB x TO}}$	

Table 4.3: continued

Physical Performance Test	Test Condition	CG (n = 20)	% Improvement from N	OAG (n = 20)	% Improvement from N	*p* CG x OAG	*p* CG	*p* OAG
Stair Climb Test *(time in seconds)*	Normal (N)	7.72 ± 0.44		17.91 ± 6		< 0.001	< 0.001 $^{\text{N x TO}}$	0.014 $^{\text{N x TO}}$, 0.017 $^{\text{N x TI}}$
	Toe-out (TO)	9.69 ± 0.89	↓25.52	22.89 ± 7	↓27.81	< 0.001	0.009 $^{\text{TO x TI}}$	0.015 $^{\text{TO x LWI}}$
	Toe-in (TI)	8.38 ± 0.66	↓8.55	21.74 ± 7.36	↓21.38	< 0.001	0.003 $^{\text{TI x N}}$	0.007 $^{\text{TI x LWI}}$
	Wedged insole (LWI)	7.70 ± 0.55	↑0.26	18.23 ± 4.07	↓1.79	< 0.001	< 0.001 $^{\text{LWI x TO}}$	
	Knee Brace (KB)	8.11 ± 0.79	↓5.05	15.71 ± 3.50	↑12.28	< 0.001	0.044 $^{\text{KB x TO}}$	0.001 $^{\text{KB x TO, KB x TI}}$ 0.037 $^{\text{KB x N}}$ 0.041 $^{\text{KB x LWI}}$
40m (4 x 10m) Fast-paced walk Test *(walking speed in metres per second)*	Normal (N)	1.96 ± 0.11		1.22 ± 0.31		0.001		0.005 $^{\text{N x TO}}$
	Toe-out (TO)	1.88 ± 0.08	↓4.08	1.03 ± 0.27	↓15.57	<0.001	0.025 $^{\text{TO x LWI}}$	0.001 $^{\text{TO x TI}}$
	Toe-in (TI)	1.94 ± 0.09	↓1.02	1.04 ± 0.28	↓14.75	<0.001		0.035 $^{\text{TI x N}}$
	Wedged insole (LWI)	1.97 ± 0.08	↑0.51	1.16 ± 0.28	↓4.92	<0.001		0.013 $^{\text{LWI x KB}}$
	Knee Brace (KB)	1.89 ± 0.07	↓3.57	1.28 ± 0.064	↑4.92	0.001		0.001 $^{\text{KB x TO, KB x TI,}}$ 0.041 $^{\text{KB x N}}$

40m fast-paced walk test. One patient felt more comfortable with TI than TO during the level walk (6-minute walk test and 40m TO was reported to be more comfortable than TI by two patients during 30-second chair test. KB was reported to be heavy and wearisome as compared to other interventions by eight patients. No adverse effects were reported for LWI.

4.4.6 Subjective Feedback for CG

Six CG participants reported that the brace felt heavier and discomforting during all the tests. The participants did not report any adverse effects for any of the interventions. No other adverse effects were reported by the participants for any of the test conditions.

4.5 Discussion

One of the primary outcomes of knee osteoarthritis is the loss of knee joint motion which affects their ability to perform day to day activities efficiently. A patient, therefore, opts for the treatment techniques that have immediate effects on improving their physical function. This may be the rationale behind opting for knee joint replacement (Kennedy, Stratford, Wessel et al., 2005). This need of improving physical performance should be considered while devising other treatment and prevention protocols for kOA also. The prime objective of the study was to evaluate the immediate effects of the conservative treatment techniques for kOA (knee brace, lateral wedged insole, toe-in gait and toe-out gait) through standard physical performance tests recommended by OARSI on healthy participants and kOA patients. The study also aimed at comparing these interventions with each other to identify which of them has the most profound effects on the physical function of the healthy and osteoarthritis sample, while simultaneously comparing the two samples with each other.

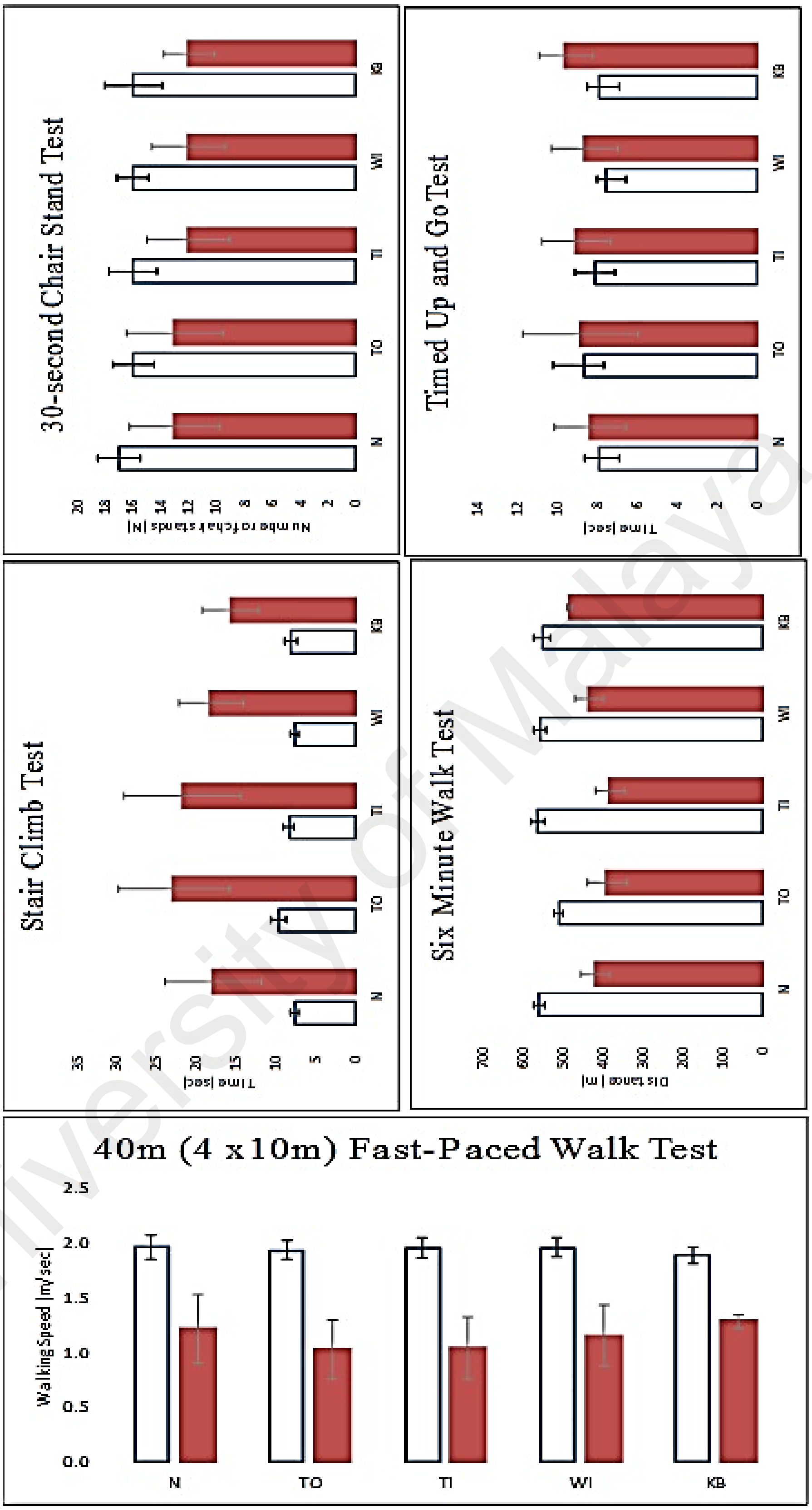


Figure 4.3: Mean values representing outcome variables of performance-based tests for all test conditions. Where N is natural gait, TO is toe-out gait, TI is toe-in gait, WI is lateral wedged insoles and KB is knee brace. The hollow bars represent the data for Control Group (CG), while the solid bars represent the data for Osteoarthritis Group (OAG)

fast-paced walk test). For TUG test, one patient reported fear of falling over with TO.

The values for the physical performance test parameters for normal walk obtained through our experiments are in range with those found from the literature for healthy and kOA both. It was observed that the tested interventions produced considerable effects even with immediate application. Out of the tested interventions, one had maximum effect for both the participant groups, i.e. toe-out. This effect was more pronounced in kOA patients. The underlying mechanics of toe-out gait may explain some of its effects on physical function. Toe-out gait shifts the center of mass (CoM) posteriorly in a static condition, as a result of this shift, the balance of the body is compromised, and the person tends to regain balance out of the fear of falling. This fear of fall combined with shifting in the CoM and change in tibia angle by toe-ing out may explain the significant effect of this gait modification on physical function (Shull, Lurie, Cutkosky *et al.*, 2011). The effect is the most evident from the stair climb test, in which a 25.56% increase in time taken to ascend and descend stairs is observed in healthy adults and 27. 81% increase in kOA patients. This may be due to the fact that more muscle force required in ascending/ descending stairs than level walking means more CoM excursion [Koyama *et al*]. Another test which is often related to balance is the TUG test for which the same fear of fall was reported by the participants. Due to the dynamic posterio-medial shift of CoM, the body weight is more concentrated on the heels, which can cause heel pain (as reported by four patients in 40m fast-paced walk). On the other hand, when we decrease the foot progression angle from the natural value (toe-in gait) the CoM shifts anteriorly in a static condition. This encourages the person to move faster, crossing their legs slightly while doing so which induces a fear of fall and slight discomfort. This affects their physical function but not as much as toe-out. This may be the reason that patients reported that climbing stairs with toe-in gait is more difficult than other interventions.

The knee brace, reported to be improving physical function of knee osteoarthritis patients in a follow-up period during level walking, did not seem to have much immediate effect from our experiment (Cherian, Bhave, Kapadia *et al.*; Larsen, Jacofsky, Brown *et al.*, 2013). However, it significantly improved the stair climb activity (12.28%) and the fast-paced walk time (4.92%) in osteoarthritis patients. The adverse effects of the weight and slight discomfort of wearing an external device on the leg may have affected the test parameters, resulting in a much less improvement than anticipated. Wedged insoles, although reported to increase the postural stability of a person, did not appear to be influencing the overall physical function of the participants in our study (Ganesan, Lee, & Aruin, 2014). Another important thing to note is that the considerable effects of any of the interventions are not found in short-term activities i.e. 30-second chair stand test and TUG test. It is the longer-duration activities that are being considerably influenced by the interventions.

Overall, among all the interventions, wedged insoles seemed to be affecting the physical performance measures the least. Also, no adverse effects were reported for the insoles by the participants. TI and TO should not be recommended for kOA patients and LWI and KB must also be recommended cautiously. The gait modification methods (toe-out gait and toe-in gait) need further research and improvement before being prescribed to the patients as they are severely impairing the physical function of both healthy and knee osteoarthritis patients. Changing the foot progression angle also changes the pennate angle of the foot muscles, potentially increasing the overall mechanical work done of the lower limb. It is hence suggested to develop strategies to overcome the inherent adverse issues created by the postural change from natural posture. Afterward, the patients would be required to properly train as per the developed strategies in order to target the symptomatic relief of knee osteoarthritis.

4.6 Conclusion

The study concludes that the all the tested conservative techniques except laterally wedged insoles have immediate effects on physical performance measures in both healthy and medial knee osteoarthritis participants. The valgus knee brace is found to have the most favorable effects, while toe-out gait is found to have the most impairing effects on physical function. Future studies can develop strategies for improving gait modification methods on the basis of issues identified by this study.

CHAPTER 5: COMBINED EFFECTS OF KNEE BRACE, LATERALLY WEDGED INSOLES AND TOE-IN GAIT ON KNEE ADDUCTION MOMENT AND RISK OF FALL FOR MODERATE MEDIAL KNEE OSTEOARTHRITIS PATIENTS

5.1 Introduction

The chapter addresses the toe-in aspect of objective 3 of this thesis, as stated in section 1.3. This study presented in this chapter tests the hypothesis that toe-in gait (TI) will further reduce first peak KAM and increase fall risk when combined with a knee brace (KB) and laterally wedged insoles (LWI) in medial knee osteoarthritis (kOA) patients. The previous chapters (Chapters 3 & 4) presented a comparison of orthoses and gait modifications in terms of physical function, knee joint load and balance, while this chapter presents a synergistic effect of orthoses and TI on knee joint kinetics and balance. The chapter begins with a brief review of previous works dealing with knee joint load, altering the foot progression angles (toe-in gait modification), and their effects on knee joint kinetics and overall balance. It also states the hypothesis for the research. Further on, a methodology is presented defining sampling procedure, experimental setting, study protocol and statistical methods. Following this, is the presentation of results of the experiment. The chapter presents a discussion of the results and the conclusions drawn from the study.

5.2 Study Background

Knee osteoarthritis (kOA) is the most commonly occurring type of osteoarthritis in the world (Lawrence, Felson, Helmick *et al.*, 2008) largely because of the knee joint's load-bearing characteristics during gait. kOA inflicts an irreversible damage to the joint structures, including bone, cartilage and joint capsule (Felson, 2004). The considerably higher tendency of affecting the medial compartment of the knee joint in this disease, as compared to the lateral compartment, is the prime outcome of an enormous load share (

~70%) born by the medial compartment (Jones, Nester, Richards *et al.*, 2013). A resulting varus alignment of the knee joint is not only a major risk factor in medial compartment kOA progression but it also further aggravates the aforementioned imbalance of load distribution between the medial and lateral compartments of the knee joint (Sharma, Song, Dunlop *et al.*, 2010). The knee adduction moment (KAM), when calculated through 3D gait analysis of kOA patients, has proven this imbalanced load distribution across the joint (Andriacchi, 1994; Zhao, Banks, Mitchell *et al.*, 2007). Across these analyses, KAM has been accepted as a fairly reliable and accurate surrogate measure of the load exerted on the medial compartment of the knee joint (Bennell, Bowles, Wang *et al.*, 2011; Birmingham, Hunt, Jones *et al.*, 2007; Miyazaki, Wada, Kawahara *et al.*, 2002; Zhao, Banks, Mitchell *et al.*, 2007). It is also reported to be highly related to kOA severity and progression, and as a result, to the knee joint damage (Miyazaki, Wada, Kawahara *et al.*, 2002; Sharma, Hurwitz, Thonar *et al.*, 1998). Due to this reliability, the aim of most of the conservative treatment techniques for kOA is to reduce KAM during gait. Generally, conservative treatments include the use of a knee brace (KB), laterally wedged insoles (LWI) and gait modification methods. The KB is designed to apply 3- or 4-point pressure systems around the knee joint to either push or pull the joint into a lesser-degree varus position during both stance and swing phases of the gait (Arazpour, Bani, Maleki *et al.*, 2013). The LWI attempts to reduce KAM by laterally shifting the center of pressure (CoP) at the base of the foot and increasing the subtalar joint valgus moment. This lateral shifting of CoP and the counteractive moment lead to a decrease in the ground reaction force (GRF) lever arm, thereby decreasing KAM (Kakihana, Akai, Nakazawa *et al.*, 2007; Kakihana, Akai, Nakazawa *et al.*, 2005; Maly, Culham, & Costigan, 2002).

Currently, it is a matter of interest among researchers that an alteration in gait may result in a reduced joint load and a symptomatic relief among kOA patients (Shull, Silder, Shultz *et al.*, 2013; Simic, Hinman, Wrigley *et al.*, 2011; Tokunaga, Nakai, Matsumoto *et al.*, 2016; van den Noort, Schaffers, Snijders *et al.*, 2013a). The gait alterations include mediolateral trunk sway (Hunt, Birmingham, Bryant *et al.*, 2008; Mundermann, Asay, Mundermann *et al.*, 2008; Simic, Hunt, Bennell *et al.*, 2012), reducing the walking speed (Robbins & Maly, 2009; van den Noort, Schaffers, Snijders *et al.*, 2013a), increasing the step-width (Paquette, Klipple, & Zhang, 2015) and an alteration in the foot progression angle (FPA) (Chang, Hurwitz, Dunlop *et al.*, 2007; Lynn, Kajaks, & Costigan, 2008; Shull, Silder, Shultz *et al.*, 2013). A mediolateral trunk sway of up to 13.8º is reported to efficiently reduce peak KAM values (Simic, Hunt, Bennell *et al.*, 2012). This gait modification, however, is not prioritized by the participants, as reported by studies reporting multi-parameter gait modification programs (Hunt, Simic, Hinman *et al.*, 2011; Mündermann, Asay, Mündermann *et al.*, 2008; Shull, Lurie, Cutkosky *et al.*, 2011). The reported adverse effects of trunk sway include imbalance, lower back discomfort and difficulty in posture maintenance (Hunt, Simic, Hinman *et al.*, 2011; Mündermann, Asay, Mündermann *et al.*, 2008). Changing the walking speed also has significant effects on KAM. As a rule of thumb, increasing the walking speed increases peak KAM, while decreasing the speed tends to reduce peak KAM values (van den Noort, Schaffers, Snijders *et al.*, 2013a). There, however, exists a trade-off between this reduction in peak KAM and the duration of load exposure to the knee joint (van den Noort, Schaffers, Snijders *et al.*, 2013a). The time integral of KAM, knee adduction angular impulse (KAAI), is found to be inversely related to the walking speed [41]. This study, therefore, focuses on the most widely probed gait modification method, that is changing the FPA.

A decrease in the FPA, commonly called toe-in gait (TI), is found to reduce the GRF lever arm by shifting the CoP laterally, just around heal-strike (van den Noort, Schaffers, Snijders *et al.*, 2013a). This lateral shifting reduces the lever arm of GRF and reduces the KAM. Validated results from several studies suggest that KB, LWI and gait modification methods are effective in KAM reduction individually (Cherian, Bhave, Kapadia *et al.*; De

Vita, Torry, Glover *et al.*, 1996; Dennis, Komistek, Nadaud *et al.*, 2006; Fantini Pagani, Potthast, & Brüggemann, 2010; Hinman, Bardin, Simic *et al.*, 2013; van den Noort, Schaffers, Snijders *et al.*, 2013b). As the next step, there is a growing research interest in the synergistic effect of these conservative treatment techniques when they are used in a combination (Khan, Khan, & Usman, 2017; Tokunaga, Nakai, Matsumoto *et al.*, 2016). One of such studies examined the combined effect of KB and LWI and found further reductions in KAM with their combined usage (Moyer, Birmingham, Dombroski *et al.*, 2013). Another study has shown that the combined effects of TI and LWI also lead to a better reduction in KAM (Tokunaga, Nakai, Matsumoto *et al.*, 2016). However, the combined effect of all three conservative treatment techniques (KB, LWI and TI) on KAM has not been tested yet.

Another hitherto unexplored effect of conservative treatment techniques is their effect on proprioception of the patients. Since wearing an orthosis or changing the foot's natural FPA dislocates the body's center of pressure, a potentially adverse effect of these techniques may be reducing the already compromised balance of the kOA patients [50, 51]. This potentially increased fall risk needs to be avoided, especially for the elderly, because of highly-reported fall-induced injuries (Alamgir, Muazzam, & Nasrullah, 2012; Kim, 2016; Ku, Abu Osman, & Wan Abas, 2014), hospitalization (Orces & Alamgir, 2014) and even fatalities (Gilbert, Todd, May *et al.*, 2009). Moreover, the fundamental aim of a conservative treatment technique is to facilitate the performance of the Activities of Daily Living (ADLs). Since maintaining balance and reducing fall risk is a major contributor in performing ADLs, the therapists should make sure that the prescribed conservative techniques are not impairing the proprioception of the patient.

Therefore, our primary objective is to test the immediate effects of the simultaneous use of KB, LWI and TI on KAM. Our secondary objective is to test immediate effects of the simultaneous use of KB, LWI and TI on fall risk in patients with medial kOA. It is hypothesized that TI would reduce the first peak KAM further when combined with KB and LWI while increasing the fall risk for knee osteoarthritis patients.

5.3 Material and Methods

5.3.1 Subjects

Twenty participants with bilateral symptomatic medial kOA were recruited from the Department of Sports Medicine, University of Malaya Medical Centre (UMMC). Medial compartment knee OA was confirmed through radiographic evidence and was graded according to the Kellgren-Lawrence scoring system. The patients' diagnosis was confirmed through clinical evidence at the UMMC. The experiment was conducted at the Body Performance Laboratory, University of Malaya.

5.3.2 Inclusion and Exclusion Criteria

Participants aged between 50-70 years, having a BMI of less than 30 kg/m^2 (non-obese) (Organization, 2000) were included in the study. The bilateral kOA participants were of Kellgren-Lawrence grades II and III. The participants were required to ascend and descend a 10-step flight of stairs and jog 5m safely. The participants were excluded on the basis of any neurological or musculoskeletal disorder, cardiovascular or respiratory disease, lower limb fracture/ surgery in the past 12 months or inability to adapt toe-in gait pattern.

5.3.3 Sample Size

The sample power calculations were based on KAM variables from previous studies (Moyer, Birmingham, Dombroski *et al.*, 2013; Tokunaga, Nakai, Matsumoto *et al.*, 2016) and considered an F-test statistical design for repeated measures (with-in effects), with a moderate effect size of 0.25 (Cohen, 1977), a power of 80%, and an alpha error of 5% suggesting at least 20 participants for this study.

5.3.4 Ethical Approval

Ethical approval was obtained from UMMC Medical Research Ethics Committee (MREC) (MECID.NO: 20161- 2070). All participants provided written informed consent for the study.

5.3.5 Interventions

5.3.5.1 Knee Brace

The study uses a 4-point leverage based knee brace (Donjoy OA Adjuster $^{\text{TM}}$ 3, USA), as depicted in Figure 5.1(a). The investigators used more symptomatic leg for knee brace application.

Figure 5.1: Interventions used as a conservative technique for knee osteoarthritis treatment. (a) knee brace (Donjoy OA AdjusterTM 3, USA), (b) laterally wedged insole (SalfordinsoleTM, UK), (c) toe-in foot position, where θ is the foot progression angle, which is lesser than 15° normal.

5.3.5.2 Lateral Wedged Insole

The lateral wedged insole (Salfordinsole $^{\text{TM,}}$ UK) was full-length, with 5° frontal plane inclination, see Figure 5.1(b).

5.3.5.3 Toe-in gait

The participants were introduced to walking with toe-in gait (TI: making A-shape with their feet) with the minimum toe-in angle of natural FPA minus 15° degree, see Figure 5.1(c). The toe-in angles were calculated by the degrees of which the foot vector (directed from the ankle joint center to the second metatarsal head) deviates from the progression axis of the walkway (Tokunaga, Nakai, Matsumoto *et al.*, 2016).

5.3.6 Data Collection

The study was a single visit study, starting with a briefing about the interventions and the study protocol. Before the start of the experiment, the participants filled out the WOMAC (Western Ontario and McMaster University Index of Osteoarthritis) questionnaire, version VA 3.1. It is a self-reported questionnaire containing 3 sections, one each for pain, stiffness and difficulty performing daily activities. Each of the 24 questions is represented by a score of 0 to 10, with a higher score indicating worse pain, stiffness or physical function. The participants were then provided with shoes (Supercloud, Adidas, UK) in order to minimize the influence of different shoes. Each participant was trained with the interventions especially for TI with adequate practice by the mutual discretion of the participant and the investigator. The data for motion analysis and fall risk assessment were then collected for the following six test conditions in a random order. Randomized orders were obtained through www.randomisation.com.

1. Natural condition (N)
2. With knee brace (KB)
3. With knee brace and toe-in gait combined (KB+TI)
4. With lateral wedged insole (LWI)
5. With lateral wedged insole and toe-in combined (LWI+TI)
6. With knee brace, lateral wedged insole and toe-in combined (KB+LWI+TI)

The participants were asked to continue walking with a particular test condition until the investigators obtained 5 legitimate trials (trials in which one foot is completely placed on one force plate). After each test condition, participants were asked to fill Wong-Baker FACES® Pain rating scale for the measurement of comfort level. The Wong-Baker pain rating scale is a pain scale showing a series of faces ranging from a happy face at 0, “No hurt” to a crying face at 10 “Hurts worst”. The patient must choose the face that best describes how they are feeling.

5.3.7 Procedure for Motion Analysis

The participants were asked to walk on the 5 m walk-way with a constant speed of 1.18 m/s obtained through pilot study (Khan, Khan, & Usman, 2017). Constant walking speed was maintained for all six conditions by calculating the time taken to cover the distance using s = vt; where s = 5m; t = time in seconds; and v = 1.18m/s. An investigator observed the time taken for each walk trial during experimental trials, the ones falling within a standard deviation of <0.05 m/s compared to the target speed that was to be considered for data processing. Data collection was performed via VICON Motion Capture System (100 Hz; Vicon, Oxford Metrics, Oxford, UK), consisting of five infrared-sensitive cameras. PlugIn Gait model (Oxford Metrics, Oxford, UK) of the driving software VICON Nexus was used to perform inverse dynamics analyses, obtaining joint moments calculated about an orthogonal axis system located in the distal segment of the joint.

The model requires the infrared markers to be attached to the participant’s skin or on the surface of the shoe that was directly above the bony prominence with the help of adhesive double-sided tape. Sixteen bony prominences defined by this model are anterior and posterior superior iliac spines, lateral thigh, lateral femoral epicondyle, lateral shank, calcaneus, lateral malleolus and second metatarsal head. For the test conditions involving knee brace, the marker was placed on the surface of the knee brace directly above the lateral epicondyle of the femur. Two embedded force plates (1000 Hz; Kistler, USA) in the walkway were used for the collection of GRF data. The data were smoothed with a third-order, 6Hz Butterworth low-pass filter. The Newington - Gage model was used to calculate the hip joint center (Davis, Ounpuu, Tyburski *et al.*, 1991). The knee and ankle joint centers were defined as the mid-points of the medial and lateral markers placed on the respective joints. The thigh segment was defined by the obtained hip joint center and the medial and lateral femoral epicondyles. The shank was defined by the obtained knee joint center and the medial and lateral malleoli. The foot was defined by the vector directed from the ankle joint center to the fifth metatarsal head. All KAM values were normalized to the percentage of the stance phase. Based on the previously- reported two-peak waveform of the KAM (van den Noort, Schaffers, Snijders *et al.*, 2013b), the first peak KAM was taken as the maximum value during the initial 50% of the stance phase, while the second peak was taken as the maximum value during the latter 50% of the stance phase.

5.3.8 Procedure for Fall Risk Assessment

The Biodex Balance System (BBS; Biodex Medical System Inc., Shirley, NY, USA) assesses a person's neuromuscular control over balance. In simpler terms, it measures the static standing balance and dynamic standing balance of a person. The machine consists of a circular platform and a display unit, see Figure 5.2. The subject stands on the circular platform which tilts up to 20º in each direction (360º range of motion). The platform tilts according to the level set through the display unit. There are 12 levels of platform tilt, with level 12 offering the most stable platform (with maximum resistance) and level 1 offering the most unstable platform (with minimum resistance).

For this study, the following set of platform settings was used in random order for all conditions:

(1) FR Static: No platform movement

(2) FR12: Each test trial starts from dynamic level 12 and keeps on decreasing to level 8

(3) FR8: Each test trial starts from dynamic level 8 and keeps on decreasing to level 2

The platform moves in anterior-posterior (AP) and medial-lateral (ML) axes simultaneously, giving three types of output measures: anterior/posterior stability index, medial/lateral stability index and overall stability index (OSI). These indices represent the standard deviations indicating the fluctuations around the reference point (a firm, horizontal platform). These indices are calculated by measuring the amount of time for which the platform has been deviated, along with the degree of angulation of this deviation from the reference point.

1. Medial/Lateral Stability Index (MLSI): represents foot displacements occurring in x-axis (ML: medial-lateral axis).

Figure 5.2: Biodex Balance System, Biodex Medical Systems, Inc. Courtesy: operation/ service manual

2. Anterior/Posterior Stability Index (APSI) represents foot displacements occurring in the y-axis (AP: anterior-posterior axis).
3. Overall Stability Index (OSI); is a composite of APSI and MLSI and represents body sway in both x and y-axes.

This study focused on OSI only because it is reported to be the most reliable parameter for assessing balance (Arnold & Schmitz, 1998). A higher score indicates lesser stability and greater postural variability in balancing the body on the platform (University, 1999). BBS has been proven to have a good inter-tester and intratester reliability (Cachupe, Shifflett, Kahanov *et al.*, 2001; Schmitz & Arnold, 1998).

The participants were asked to stand on the BBS facing the monitor, barefoot with eyes open and their hands on their hips. Trials were discarded if they supported themselves with handlebars. The distance between the heels was kept constant at 0.16m in order to avoid the adaptability effects on the stabilizing response due to different heel distances (McIlroy & Maki, 1997). They were asked to stand straight and sway without changing their foot positions, in order to keep the moving black dot at the centre of the crosshair displayed on the monitor. For each platform setting and each condition two trials were obtained, each of 30-seconds duration and separated by a 10-seconds rest period. For each participant, 18 data points were obtained (3 platform settings x 6 test conditions).

5.3.9 Variables of Interest

The parameters of interest were the first and the second peaks of KAM (fKAM and sKAM receptively), knee adduction angular impulse (KAAI) and fall risk. fKAM and sKAM values were identified as the two peaks in the KAM values (early stance and late stance) obtained from the motion analysis software VICON Polygon^{TM}. The cases in which sKAM was not very distinct, it was obtained as the KAM value at the time of second vertical GRF. fKAM, sKAM and KAAI values were normalized by dividing them by weight times height and taking them as a percentage (Moisio, Sumner, Shott *et al.*, 2003). KAAI was represented as the area under the KAM curve over stance phase and was obtained by the numerical integration of the curve.

5.3.10 Statistics

Shapiro-Wilk test was applied to the data to assess normality. Repeated measure ANOVA was used to find within- subject effects at α=5%. The Bonferroni corrections were applied during the posthoc pairwise comparisons to avoid false positives using IBM SPSS (SPSS Inc., USA).

5.4 Results

5.4.1 Demographics and WOMAC Scores

The mean ± SD for age, height and mass for the given sample were 61.5 ± 8.63 years, 1.63 ± 0.03 m, and 70.45 ± 8.80 kg respectively. The WOMAC pain (0-50), stiffness (0-20), physical function (0-170) and total scores (0-240) were found to be 13.5 ± 5.65, 7.25 ± 7.16, 61.75 ± 31.45, and 82.5± 39.85 respectively.

5.4.2 Foot Progression Angles

The mean ± SD for FPAs for the 6 test conditions were observed to be as N: 9.6º ± 3.7º, KB: 8.8º ± 3.5º, LWI: 9.4º ± 3.4º, KB +TI: -10.2º ± 4.8º, LWI +TI: -12.5º ± 4.9º, KB + LWI + TI: -10.4º ± 5.1º. These FPAs were kept the same for fall risk assessment.

5.4.3 Knee Adduction Moment

Figure 5.3 shows KAM profiles for the test conditions, normalized to 100% of the stance phase. Pairwise comparisons showed significant decrease in the fKAM from N

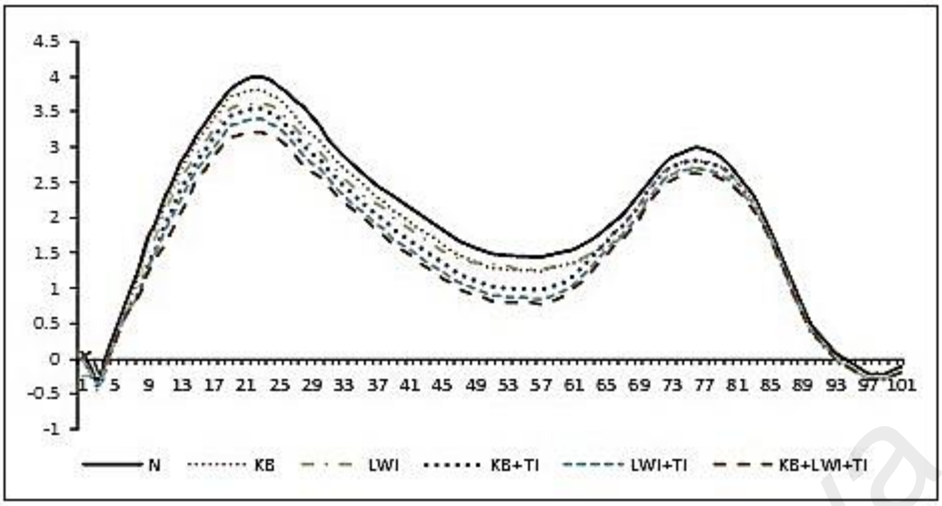


Figure 5.3: Knee adduction moment profiles of mean values for natural walk and different conservative treatment techniques for knee osteoarthritis normalized to 100% of the stance phase. Where N is Natural walk (without any intervention), KB is Knee Brace, LWI is Laterally Wedged Insole, KB+TI is Knee Brace along with Toe-In gait, LWI+TI is Laterally Wedged Insoles and Toe-In gait and KB+LWI+TI is Knee Brace along with Laterally Wedged Insole and Toe-In gait.

(4.00 N-m/%BW*Ht) when walking with KB+TI (3.56 N-m/%BW*Ht, *p* = 0.03), LWI+TI (3.41 N-m/%BW*Ht, *p* = 0.03) and KB+LWI+TI (3.21 N-m/%BW*Ht, *p* = 0.02), see Figure 5.4. An insignificant decrease was observed in the fKAM when the participants walked with KB (3.81 N-m/%BW*Ht, *p* = 0.23) and LWI (3.62 N-m/%BW*Ht, *p* = 0.12).

For sKAM, pairwise comparisons showed significant main effect among test conditions (*p* <0.001) as compared to N (2.90 N-m/%BW*Ht).For sKAM, pairwise comparisons showed significant main effect among test conditions (*p* <0.001) as compared to N (2.90 N-m/%BW*Ht). Significant reductions in the sKAM were observed for LWI (2.73 N-m-s/%BW*Ht, *p* = 0.01), KB (2.80 N-m-s/%BW*Ht, *p* =

For sKAM, pairwise comparisons showed significant main effect among test conditions (*p* <0.001) as compared to N (2.90 N-m/%BW*Ht). Significant reductions in the sKAM were observed for LWI (2.73 N-m-s/%BW*Ht, *p* = 0.01), KB (2.80 N-m- s/%BW*Ht, *p*

= 0.03), KB+TI (2.82 N-m-s/%BW*Ht, $p = 0.01$), LWI+TI (2.70 N-m-s/%BW*Ht, $p < 0.01$) and KB+LWI+TI (2.63 N-m-s/%BW*Ht, $p < 0.01$).

5.4.4 Knee Adduction Angular Impulse

Post hoc analysis of repeated measure ANOVA showed significant differences among all test conditions when compared to N (1.39 N-m-s/%BW*Ht), see Figure 5.4. Significant reductions in KAAI were observed for LWI (1.31 N-m-s/%BW*Ht, $p = 0.04$), KB (1.30 N-m-s/%BW*Ht, $p = 0.03$), KB+TI (1.25 N-m-s/%BW*Ht, $p = 0.01$), LWI+TI (1.21 N-m-s/%BW*Ht, $p < 0.01$) and KB+LWI+TI (1.16 N-m-s/%BW*Ht, $p < 0.01$)

5.4.5 Risk of Fall Assessment

Table 5.1 shows the mean values of OSI at different test conditions. A significant increase in OSI was observed from N through pairwise comparison when the participants stood on the BBS with KB+LWI and KB+LWI+TI at FR8 platform setting. KB remained the only intervention that decreased OSI at FR8 setting, with a 7.14% reduction from N. The interventions found to be improving balance at FR12 were LWI and KB, which decreased the fall risk by 14.49% and 28.57% respectively.

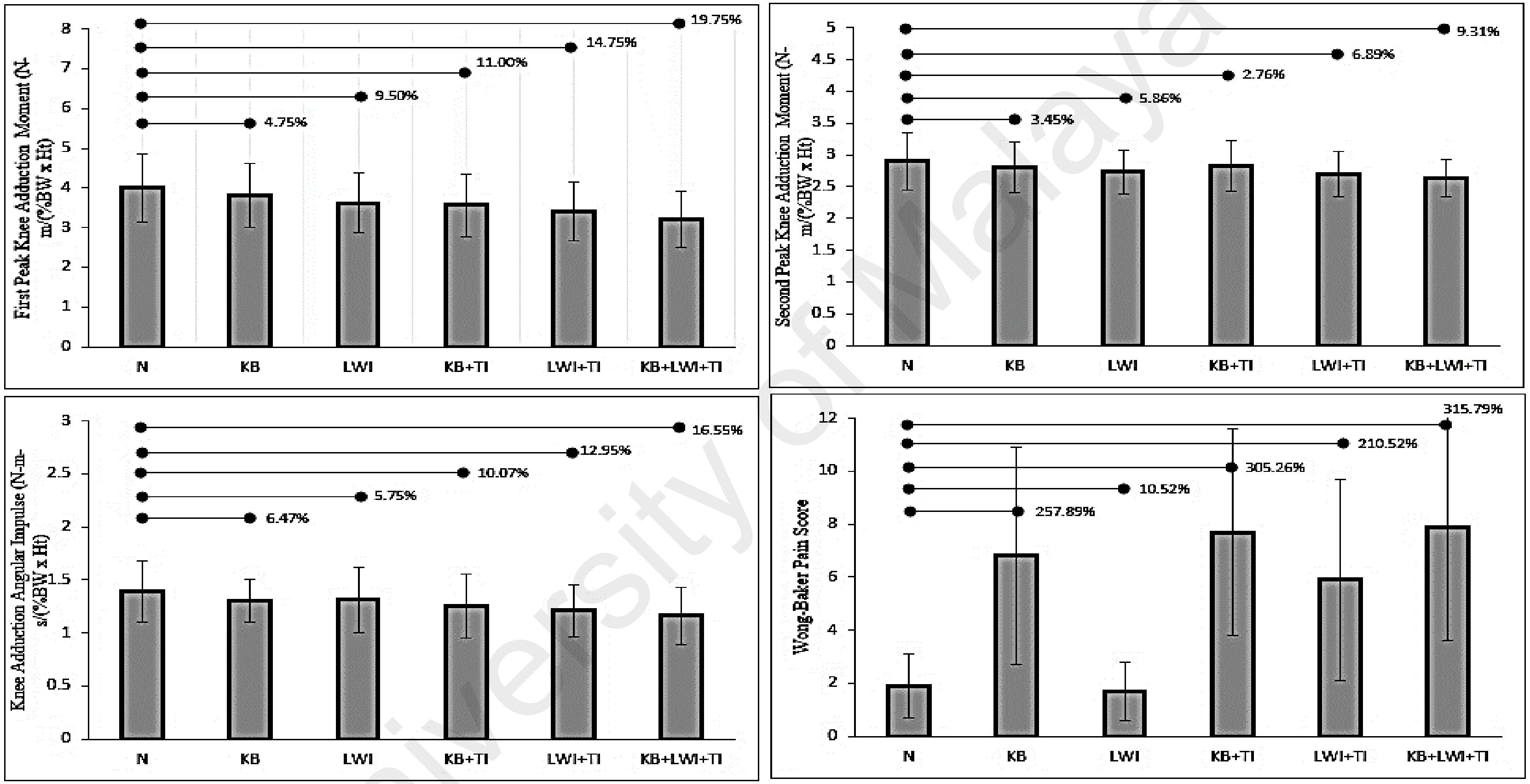


Figure 5.4: Bar charts representing first peak knee adduction moment, second peak knee adduction moment, knee adduction angular impulse and Wong-Baker FACES pain rating scale for N (natural walk), KB (knee brace), LWI (laterally wedged insole, KB+TI (knee brace along with toe-in gait), LWI+TI (laterally wedged insoles along with toe-in gait) and KB+LWI+TI (knee brace along with laterally wedged insole and toe-in gait). The horizontal lines and the accompanying numbers represent percentage difference from N.

No significant differences were observed among the tests condition at static platform setting.

Table 5.1: ANOVA results of Overall Stability Index values with natural walk and different conservative treatment techniques for knee osteoarthritis. The bold p-values denote statistical significance.

Test Condition	Mean Value	Mean Difference from N	Percentage Difference from N	*p*-value
Static				
N	0.30	--	--	--
KB	0.30	0.00	0	1.00
LWI	0.40	-0.10	↑33.33	0.96
KB+TI	0.40	-0.10	↑33.33	0.93
LWI+TI	0.40	-0.10	↑33.33	0.94
KB+LWI+TI	0.40	-0.10	↑33.33	0.97
FR12				
N	0.70	--	--	--
KB	0.50	0.2	↓28.57	0.58
LWI	0.60	0.1	↓14.29	0.82
KB+TI	0.90	-0.2	↑28.57	0.56
LWI+TI	0.80	-0.1	↑14.29	0.71
KB+LWI+TI	0.90	-0.2	↑28.57	0.84
FR8				
N	1.4	--	--	--
KB	1.3	0.1	↓7.14	0.99
LWI	1.6	-0.2	↑14.29	0.65
KB+TI	1.8	-0.4	↑28.57	**0.01**
LWI+TI	1.6	-0.2	↑14.29	0.78
KB+LWI+TI	1.9	-0.5	↑35.71	**<0.01**

Where N is Natural walk (without any intervention), KB is Knee Brace, LWI is Laterally Wedged Insole, KB+TI is Knee Brace along with Toe-in gait, LWI+TI is Laterally Wedged Insoles and Toe-in gait, KB+LWI+TI is Knee Brace along with Laterally Wedged Insole and Toe-in gait, Static is the static platform setting of the postural stability test, FR12 is the fall risk platform setting from dynamic levels 12 to 8 and FR8 is the fall risk platform setting from dynamic levels 8 to 2.

5.4.6 Level of Comfort

The comfort level of the participants was assessed using the Wong-Baker pain rating scale, the results are shown in Figure 5.4. Significant increases in the pain scores were observed from N (1.9) for KB (6.8, $p < 0.01$), KB+TI (7.7, $p < 0.01$), LWI+TI (5.9, $p = 0.01$) and KB+LWI+TI (7.9, $p < 0.01$). LWI showed no effect on the pain score (1.7, $p = 0.56$).

5.5 Discussion

The study evaluated the effects of toe-in gait modification in combination with laterally wedged insoles and knee brace on reducing the knee adduction moment during level-walking among knee osteoarthritis patients. The study also investigated the effects of these interventions on the fall risks and comfort level of these participants. The findings of these investigations, in summary, were consistent with the hypotheses. The results indicated that the toe-in gait reduced the first peak of the knee adduction moment. The maximum reduction in the first peak of the knee adduction moment was observed when toe-in gait modification was used in conjunction with laterally wedged insoles and a knee brace. A similar reduction in the knee adduction angular impulse was observed when all three interventions were used concurrently, indicating a synergistic effect of these interventions in knee joint load reduction. Also, fall risk was found to be increasing when toe-in was combined with knee brace alone and when combined with both the orthoses, when minimum resistance was offered by the platform (unstable platform).

Our results show that the laterally wedged insoles and toe-in gait when combined, lead to a maximum reduction of the first peak of the knee adduction moment. These findings are in agreement with previous studies focusing on the concurrent use of wedged insoles along with knee brace for a maximum reduction in the knee adduction moment (Jones, Nester, Richards *et al.*, 2013; Moyer, Birmingham, Dombroski *et al.*, 2013; Moyer, Ratneswaran, Beier *et al.*, 2014a). Also, recently, Tokunaga *et al* combined toe-in gait with wedged insoles suggesting a synergistic effect of both the interventions in reducing the first peak of the knee adduction moment (Tokunaga, Nakai, Matsumoto *et al.*, 2016). It was also found that the first and second peaks of the knee adduction moment were further reduced by the knee brace (20% and 12% respectively), alongside the application of laterally wedged insoles and toe-in gait.

This synergistic effect is also seen in the knee adduction angular impulse, which was reduced maximally by 16.75% with the concurrent use of all three interventions. This may be due to the internal rotation of tibia caused by toe-in gait that shifted the knee joint's center closer to the frontal component of ground reaction vector, thus reducing lever arm and in turn reducing the first peak of the knee adduction moment. For late stance, toe-in reportedly causes the knee joint's center to move medially and increases the second peak of the knee adduction moment (Shull, Shultz, Silder *et al.*, 2013). But the concurrent application of wedged insole and knee brace limits the movement of the knee joint center by producing ankle eversion and knee Varus moment respectively. Therefore, both orthoses inhibit the increase of the second peak of the knee adduction moment by toe-in gait by limiting the motion of the knee joint's center.

The sample for our study consisted of patients with moderate knee osteoarthritis, who are reported to be more prone to impaired proprioception as compared to patients with mild knee osteoarthritis (Khalaj, Osman, Mokhtar *et al.*, 2014). Therefore, every treatment technique which is meant for moderate knee osteoarthritis patients must be safe enough in terms of its effects on balance. Based on our results, it can be stated that the combined usage of orthoses and gait modification method did not have adverse effects on static and dynamic balance parameters. In order to mimic highly unstable dynamic platforms, platform setting FR8 was applied, which makes the platform almost fully mobile with a maximum tilt of 20º. The combination of interventions was not found favorable in this setting. Up to 36% increase of fall risk occurred during high platform settings when toe-in posture was applied in concurrence with both the orthoses.

From the patient's perspective, the comfort level is equally important as balance and joint load. The simultaneous application of interventions was not received well by participants in terms of discomfort level especially with the brace due to its excessive weight, decreased knee range of motion and bulky nature. Simic *et al,* studied a range of foot progression angles, along with knee adduction moment and observed pain/discomfort at different lower limb segments (study knee, contralateral knee, ipsi-/

contralateral foot etc.) (Simic, Wrigley, Hinman *et al.*, 2013). They found a significant reduction in the knee adduction moment by toe-in gait, but did not find any significant change in the pain in the study knee joint. This study, on the other hand, did not record pain/ discomfort in segments but asked the participants to report pain/ discomfort as a whole. Furthermore, for recording pain, Simic *et al* used an 11-point numeric rating scale (NRS), which is a strictly number-based questionnaire. Moyer *et al* also found no significant change using NRS scale for a knee brace, wedged insole alone and with both knee brace and insole application (Moyer, Birmingham, Dombroski *et al.*, 2013). For this study, the Wong- Baker FACES pain rating scale was used, which uses the facial expression for the depiction of pain/ discomfort and records a more emotive and psychological representation of discomfort. Apart from this, previous studies used up to two interventions in concurrence, while this study applied three interventions. Future works should take into account the segmental and overall pain as a primary outcome with the usage of these three types of conservative treatment techniques.

5.6 Conclusions

The work suggests that toe-in gait decreases first peak knee adduction moment when combined either with a wedged insole or knee brace. The reduction in the knee adduction moment was maximum when all three interventions were used together indicating that there exists a synergistic effect of this combination. On the other hand, the simultaneous application of orthoses and toe-in gait leads to increased risk of fall and increased overall discomfort level.

CHAPTER 6: COMBINED EFFECTS OF KNEE BRACE, LATERALLY WEDGED INSOLES AND TOE-OUT GAIT ON KNEE ADDUCTION MOMENT, POSTURAL STABILITY AND RISK OF FALL FOR MODERATE MEDIAL KNEE OSTEOARTHRITIS PATIENTS

6.1 Introduction

The chapter addresses the toe-out aspect of objective 3 of this thesis, as stated in section 1.3. The study presented in this chapter tests the hypothesis that toe-in gait (TI) will further reduce first peak KAM and increase fall risk when combined with a knee brace (KB) and laterally wedged insoles (LWI) in medial knee osteoarthritis (kOA) patients. Previously, chapters 3 & 4, presented a comparison of orthoses and gait modifications in terms of physical function, knee joint load and balance, while Chapter 5 presented a synergistic effect of orthoses and TI on knee joint kinetics and balance. This chapter follows the same methodology as chapter 5, but with TO instead of TI. The chapter begins with a brief review of previous works dealing with knee joint load, altering the foot progression angles (toe-out gait modification), and their effects on knee joint kinetics and overall balance. It also states the hypothesis for the research. Further on, a methodology is presented defining sampling procedure, experimental setting, study protocol and statistical methods. Following this, is the presentation of results of the experiment. The chapter presents a discussion of the results and the conclusions drawn from the study.

6.2 Study Background

Knee osteoarthritis (kOA) is the most commonly occurring type of osteoarthritis in the world (Lawrence, Felson, Helmick *et al.*, 2008) largely because of its wearisome mobility and load-bearing characteristics during gait. It is an irreversible damage to the skeletal structures, including bone, cartilage and joint capsule (Felson, 2004). Pain and stiffness observed in this degenerative disease are mainly caused by the narrowing of the joint space (Arazpour, Bani, Maleki *et al.*, 2013). The considerably higher tendency of affecting the medial compartment of the knee joint in this disease as compared to the lateral compartment is the prime cause of an enormous share (~70%) of the knee joint born by the medial compartment (Jones, Nester, Richards *et al.,* 2013). Hence, quite understandably, the medial compartment of and osteoarthritic knee is the most commonly affected by the deteriorating effects. A resulting Varus alignment of the knee joint is not only a major risk factor in medial compartment kOA progression but it also further aggravates the aforementioned imbalance of load distribution between the medial and lateral compartments of the knee joint (Sharma, Song, Dunlop *et al.*, 2010). The knee adduction moment (KAM) when calculated through 3D motion analysis of kOA patients has proven this imbalanced load distribution across the joint (Andriacchi, 1994; Zhao, Banks, Mitchell *et al.*, 2007). Indeed, although limitations exist (Walter, D'Lima, Colwell *et al.*, 2010). Across these analysis, KAM has been accepted as a fairly reliable and accurate surrogate measure of the load exerted on the medial compartment of the knee joint (Bennell, Bowles, Wang *et al.*, 2011; Birmingham, Hunt, Jones *et al.*, 2007; Miyazaki, Wada, Kawahara *et al.*, 2002; Zhao, Banks, Mitchell *et al.*, 2007). Due to this reliability, the aim of most of the conservative treatment techniques for kOA is to reduce KAM during gait. KAM is the frontal plane component of ground reaction vector and is a product of ground reaction force (GRF) and its lever arm (Andriacchi, 1994; Hunt, Birmingham, Giffin *et al.*, 2006). In order to reduce KAM, one can reduce either GRF or its perpendicular distance to the knee joint center. Since GRF is a reaction force in response to the weight of a person, it cannot be reduced. The only plausible option hence is to reduce the lever arm. The aim, therefore, of conservative treatments for medial kOA is to reduce KAM by reducing its lever arm thus slowing down the progression of kOA. Generally, conservative treatments include the use of knee brace (KB), laterally wedged insole (LWI) and gait modification methods. The KB is designed to apply 3-point or 4-

point pressure system around knee joint to either push or pull the joint into a lesser-degree varus position during both stance and swing phases of gait (Arazpour, Bani, Maleki *et al.*, 2013). The LWI attempts to reduce KAM by laterally shifting the center of pressure (CoP) at the base of the foot and increasing the subtalar joint valgus moment. This lateral shifting of CoP and the counteractive moment lead to a decrease in GRF lever arm, decreasing KAM (Kakihana, Akai, Nakazawa *et al.*, 2007; Kakihana, Akai, Nakazawa *et al.*, 2005; Maly, Culham, & Costigan, 2002).

Currently, it is a matter of interest among physiotherapists and a subject of many scientific studies that an alteration in gait may result in a reduced joint load and a symptomatic relief among kOA patients (Shull, Shultz, Silder *et al.*, 2013; Simic, Bennell, Hunt *et al.*, 2011; Tokunaga, Nakai, Matsumoto *et al.*, 2016; van den Noort, Schaffers, Snijders *et al.*, 2013b). The gait alterations include medio-lateral trunk sway (Hunt, Birmingham, Bryant *et al.*, 2008; Mundermann, Asay, Mundermann *et al.*, 2008; Simic, Hunt, Bennell *et al.*, 2012), reducing the walking speed (Robbins & Maly, 2009; van den Noort, Schaffers, Snijders *et al.*, 2013a) and an alteration in the progression angle (FPA) (Chang, Hurwitz, Dunlop *et al.*, 2007; Guo, Axe, & Manal, 2007; Hurwitz, Ryals, Case *et al.*, 2002; Lin, Lai, Chou *et al.*, 2001; Lynn, Kajaks, & Costigan, 2008; Shull, Silder, Shultz *et al.*, 2013; Simic, Hinman, Wrigley *et al.*, 2011).

An increase in the FPA , commonly called toe-out gait (TO), is found to be reducing the GRF lever arm by shifting the CoP laterally, just around heal-off (Chang, Hurwitz, Dunlop *et al.*, 2007; van den Noort, Schaffers, Snijders *et al.*, 2013a).

Validated results from several studies suggest that KB, LWI and gait modification methods are effective in KAM reduction individually (Cherian, Bhave, Kapadia *et al.*; De Vita, Torry, Glover *et al.*, 1996; Dennis, Komistek, Nadaud *et al.*, 2006; Fantini Pagani, Potthast, & Brüggemann, 2010; Hinman, Bardin, Simic *et al.*, 2013; van den Noort, Schaffers, Snijders *et al.*, 2013b). As the next step, there is a growing research interest in the synergetic effect of these conservative treatment techniques when they are used in a combination (Khan, Khan, & Usman, 2017; Tokunaga, Nakai, Matsumoto *et al.*, 2016). One of such studies examined the combined effect of KB and LWI and found better results in reducing KAM with their combined usage (Moyer, Birmingham, Dombroski *et al.*, 2013). Another study has showed that the combined effects of TO and LWI lead to a better reduction in KAM (Tokunaga, Nakai, Matsumoto *et al.*, 2016). However, the combined effect of all three conservative treatment techniques (KB, LWI and TO) on KAM has not been tested yet.

Therefore, our primary objective is to test the immediate effects of the simultaneous use of KB, LWI and TO gait on KAM. It is hypothesized that TO gait would reduce the second peak KAM further when combined with KB and LWI. Furthermore, as it is known that the people with kOA also experience a loss of proprioception (Knoop, Steultjens, Van der Leeden *et al.*, 2011; Sharma, Pai, Holtkamp *et al.*, 1997), our secondary objective is to test immediate effects of the simultaneous use of KB, LWI and TO gait on fall risk in patients with medial kOA. It is hypothesized that TO gait would increase fall risk significantly when combined with KB and LWI.

6.3 Material and methods

6.3.1 Subjects

Twenty participants with bilateral symptomatic medial kOA were recruited from the Department of Sports Medicine, University of Malaya Medical Centre (UMMC). Medial compartment knee OA was confirmed through radiographic evidence and was graded according to the Kellgren-Lawrence scoring system. The patients' diagnosis was confirmed through clinical evidence at the UMMC. The experiment was conducted at the Body Performance Laboratory, University of Malaya.

6.3.2 Inclusion and Exclusion Criteria

Participants aged between 50-70 years, having a BMI of less than 30 kg/m^2 (non-obese) (Organization, 2000) were included in the study. The bilateral kOA participants were of Kellgren-Lawrence grades II and III. The participants were required to ascend and descend a 10-step flight of stairs and jog 5m safely. The participants were excluded on the basis of any neurological or musculoskeletal disorder, cardiovascular or respiratory disease, lower limb fracture/ surgery in the past 12 months or inability to adapt toe-out gait pattern.

6.3.3 Sample Size

The sample power calculations were based on KAM variables from previous studies (Moyer, Birmingham, Dombroski *et al.*, 2013; Tokunaga, Nakai, Matsumoto *et al.*, 2016) and considered an F-test statistical design for repeated measures (with-in effects), with a moderate effect size of 0.25 (Cohen, 1977), a power of 80%, and an alpha error of 5% suggesting at least 20 participants for this study.

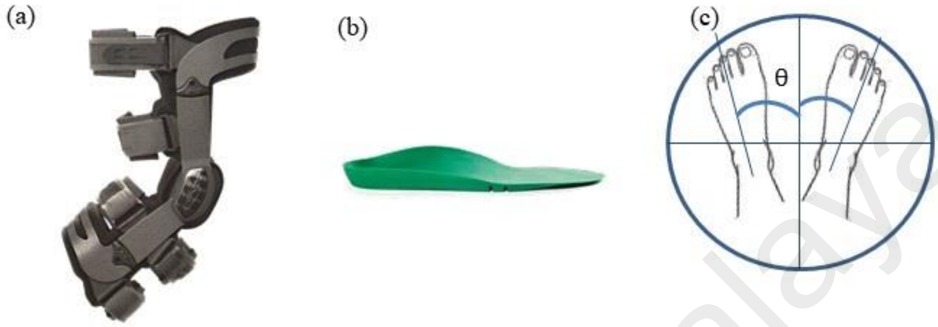
6.3.4 Ethical Approval

Ethical approval was obtained from UMMC Medical Research Ethics Committee (MREC) (MECID.NO: 20161- 2070). All participants provided written informed consent for the study.

6.3.5 Interventions

6.3.5.1 Knee Brace

The study uses a 4-point leverage based knee brace (Donjoy OA Adjuster TM 3, USA), as depicted in Figure 6.1(a). More symptomatic leg was selected for knee brace



application.

Figure 6.1: Interventions used as a conservative technique for knee osteoarthritis treatment. (a) knee brace (Donjoy OA AdjusterTM 3, USA), (b) laterally wedged insole (SalfordinsoleTM, UK), (c) toe-out foot position, where θ is the foot progression angle, which is greater than 15º normal.

6.3.5.2 Lateral Wedged Insole

The lateral wedged insole (Salfordinsole TM, UK) was full-length, with 5º frontal plane inclination, see Figure 6.1 (b).

6.3.5.3 Toe-out gait

The participants were introduced to walking with toe-out gait (TO: making V-shape with their feet) with the minimum toe-out angle of natural FPA plus 15º degree, see Figure 6.1 (c). The toe-out angles were calculated by the degrees of which the foot vector (directed from the ankle joint center to the second metatarsal head) deviates from the progression axis of the walkway (Tokunaga, Nakai, Matsumoto *et al.*, 2016).

6.3.6 Data Collection

The study was a single visit study, starting with a briefing about the interventions and the study protocol. Before the start of the experiment, the participants filled out the

WOMAC (Western Ontario and McMaster University Index of Osteoarthritis) questionnaire, version VA 3.1. It is a self-reported questionnaire containing 3 sections, one each for pain, stiffness and difficulty performing daily activities. Each of the 24 questions is represented by a score of 0 to 10, with a higher score indicating worse pain, stiffness or physical function. The participants were then provided with shoes (Supercloud, Adidas, UK) in order to minimize the influence of different shoes. Each participant was trained with the interventions especially for TI with adequate practice by the mutual discretion of the participant and the investigator. The data for motion analysis and fall risk assessment were then collected for the following six test conditions in a random order. Randomized orders were obtained through www.randomisation.com.

7. Natural condition (N)
8. With knee brace (KB)
9. With knee brace and toe-out gait combined (KB+TO)
10. With lateral wedged insole (LWI)
11. With lateral wedged insole and toe-out combined (LWI+TO)
12. With knee brace, lateral wedged insole and toe-out combined (KB+LWI+TO)

The participants were asked to continue walking with a particular test condition until 5 legitimate trials (trials in which one foot is completely placed on one force plate) were obtained. After each test condition, participants were asked to fill Wong-Baker FACES® Pain rating scale for the measurement of comfort level. The Wong-Baker pain rating scale is a pain scale showing a series of faces ranging from a happy face at 0, “No hurt” to a crying face at 10 “Hurts worst”. The patient must choose the face that best describes how they are feeling.

6.3.7 Procedure for Motion Analysis

The participants were asked to walk on the 5m walk-way with a constant speed of 1.18 m/s obtained through pilot study (Khan, Khan, & Usman, 2017). Constant walking speed was maintained for all six conditions by calculating the time taken to cover the distance using s = vt; where s = 5m; t = time in seconds; and v = 1.18m/s. An investigator observed the time taken for each walk trial during experimental trials, the ones falling within a standard deviation of <0.05 m/s compared to the target speed that was to be considered for data processing. Data collection was performed via VICON Motion Capture System (100 Hz; Vicon, Oxford Metrics, Oxford, UK), consisting of five infrared-sensitive cameras. PlugIn Gait model (Oxford Metrics, Oxford, UK) of the driving software VICON Nexus was used to perform inverse dynamics analyses, obtaining joint moments calculated about an orthogonal axis system located in the distal segment of the joint.

The model requires the infrared markers to be attached to the participant's skin or on the surface of the shoe that was directly above the bony prominence with the help of adhesive double-sided tape. Sixteen bony prominences defined by this model are anterior and posterior superior iliac spines, lateral thigh, lateral femoral epicondyle, lateral shank, calcaneus, lateral malleolus and second metatarsal head. For the test conditions involving knee brace, the marker was placed on the surface of the knee brace directly above the lateral epicondyle of the femur. Two embedded force plates (1000 Hz; Kistler, USA) in the walkway were used for the collection of GRF data. The data were smoothed with a third-order, 6Hz Butterworth low-pass filter. The Newington - Gage model was used to calculate the hip joint center (Davis, Ounpuu, Tyburski *et al.*, 1991). The knee and ankle joint centers were defined as the mid-points of the medial and lateral markers placed on the respective joints. The thigh segment was defined by the obtained hip joint center and the medial and lateral femoral epicondyles. The shank was defined by the obtained knee joint center and the medial and lateral malleoli. The foot was defined by the vector directed from the ankle joint center to the fifth metatarsal head. All KAM values were normalized to the percentage of the stance phase. Based on the previously- reported two-peak waveform of the KAM (van den Noort, Schaffers, Snijders *et al.*, 2013b), the first peak KAM was taken as the maximum value during the initial 50% of the stance phase, while the second peak was taken as the maximum value during the latter 50% of the stance phase.

6.3.8 Procedure for Fall Risk Assessment

The Biodex Balance System (BBS; Biodex Medical System Inc., Shirley, NY, USA) assesses a person's neuromuscular control over balance. In simpler terms, it measures the static standing balance and dynamic standing balance of a person. The machine consists of a circular platform and a display unit, see Figure 6.2. The subject stands on the circular platform which tilts up to 20º in each direction (360º range of motion). The platform tilts according to the level set through the display unit. There are 12 levels of platform tilt, with level 12 offering the most stable platform (with maximum resistance) and level 1 offering the most unstable platform (with minimum resistance).

For this study, the following set of platform settings was used in random order for all conditions:

(1) FR Static: No platform movement

(2) FR12: Each test trial starts from dynamic level 12 and keeps on decreasing to level 8

(3) FR8: Each test trial starts from dynamic level 8 and keeps on decreasing to level 2.

The platform moves in anterior-posterior (AP) and medial-lateral (ML) axes simultaneously, giving three types of output measures: anterior/posterior stability index, medial/lateral stability index and overall stability index (OSI). These indices represent

the standard deviations indicating the fluctuations around the reference point (a firm, horizontal platform). These indices are calculated by measuring the amount of time for which the platform has been deviated, along with the degree of angulation of this deviation from the reference point.

1. Medial/Lateral Stability Index (MLSI): represents foot displacements occurring in x-axis (ML: medial-lateral axis).
2. Anterior/Posterior Stability Index (APSI) represents foot displacements occurring in the y-axis (AP: anterior-posterior axis).
3. Overall Stability Index (OSI); is a composite of APSI and MLSI and represents body sway in both x and y-axes.

Figure 6.2: Biodex Balance System, Biodex Medical Systems, Inc. Courtesy: operation/ service manual

This study focused on OSI only because it is reported to be the most reliable parameter for assessing balance (Arnold & Schmitz, 1998). A higher score indicates lesser stability and greater postural variability in balancing the body on the platform (University, 1999). BBS has been proven to have a good inter-tester and intratester reliability (Cachupe, Shifflett, Kahanov *et al.*, 2001; Schmitz & Arnold, 1998).

The participants were asked to stand on the BBS facing the monitor, barefoot with eyes open and their hands on their hips. Trials were discarded if they supported themselves with handlebars. The distance between the heels was kept constant at 0.16m in order to avoid the adaptability effects on the stabilizing response due to different heel distances (McIlroy & Maki, 1997). They were asked to stand straight and sway without changing their foot positions, in order to keep the moving black dot at the centre of the crosshair displayed on the monitor. For each platform setting and each condition two trials were obtained, each of 30-seconds duration and separated by a 10-seconds rest period. For each participant, 18 data points were obtained (3 platform settings x 6 test conditions).

6.3.9 Variables of Interest

The parameters of interest were the first and the second peaks of KAM (fKAM and sKAM receptively), knee adduction angular impulse (KAAI) and fall risk. fKAM and sKAM values were identified as the two peaks in the KAM values (early stance and late stance) obtained from the motion analysis software VICON Polygon™. The cases in which sKAM was not very distinct, it was obtained as the KAM value at the time of second vertical GRF. fKAM, sKAM and KAAI values were normalized by dividing them by weight times height and taking them as a percentage (Moisio, Sumner, Shott *et al.*, 2003). KAAI was represented as the area under the KAM curve over stance phase and was obtained by the numerical integration of the curve.

6.3.10 Statistics

Shapiro-Wilk test was applied to the data to assess normality. Repeated measure ANOVA was used to find within- subject effects at α=5%. The Bonferroni corrections were applied during the posthoc pairwise comparisons to avoid false positives using IBM SPSS (SPSS Inc., USA).

6.4 Results

6.4.1 Demographics and WOMAC Scores

The mean ± SD for age, height and mass for the given sample were 61.5 ± 8.63 years, 1.63 ± 0.03 m, and 70.45 ± 8.80 kg respectively. The WOMAC pain (0-50), stiffness (0-20), physical function (0-170) and total scores (0-240) were found to be 13.5 ± 5.65, 7.25 ± 7.16, 61.75 ± 31.45, and 82.5± 39.85 respectively.

6.4.2 Knee Adduction Moment

Figure 3 shows KAM profiles for the test conditions, normalized to 100% of the stance phase. Pairwise comparisons showed significant decrease in the fKAM from N (3.91 N-m/%BW*Ht) when walking with LWI (3.66 N-m/%BW*Ht, p = 0.03), LWI+TO (3.68 N-m/%BW*Ht, p = 0.04) and KB+LWI+TO (3.63 N-m/%BW*Ht, p = 0.01), see Figure 6.4. An insignificant decrease was observed in the fKAM when the participants walked with KB (3.82 N-m/%BW*Ht, p = 0.20) and KB+TO (3.85 N-m/%BW*Ht, p = 0.11).

For sKAM, pairwise comparisons showed significant main effect among test conditions (p <0.001) as compared to N (2.90 N-m/%BW*Ht). Significant reductions in the sKAM were observed for LWI (2.62 N-m/%BW*Ht, p = 0.01), KB+TO (2.67 N-m/%BW*Ht, p = 0.02), LWI+TO (2.51 N-m/%BW*Ht, p <0.01) and KB+LWI+TO (2.16 N-m/%BW*Ht, p <0.01), see Figure 6.4. KB (2.81 N-m/%BW*Ht, p = 0.29) remained the only test condition with an insignificant reduction in sKAM.

6.4.3 Knee Adduction Angular Impulse

Post hoc analysis of repeated measure ANOVA showed significant differences among all test conditions when compared to N (1.41 N-m-s/%BW*Ht), see Figure 6.4.

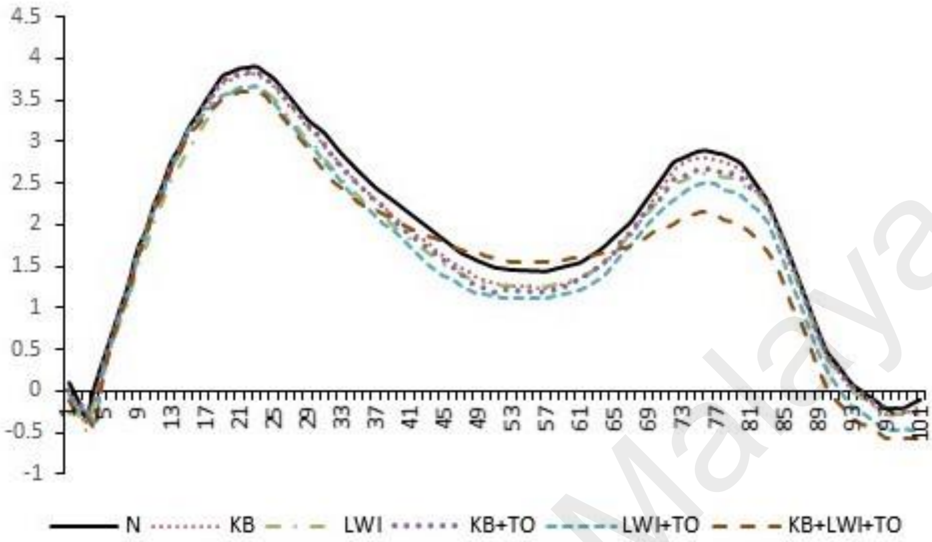


Figure 6.3: Knee adduction moment profiles of mean values for natural walk and different conservative treatment techniques for knee osteoarthritis normalized to 100% of the stance phase. Where N is Natural walk (without any intervention), KB is Knee Brace, LWI is Laterally Wedged Insole, KB+TO is Knee Brace along with Toe-Out gait, LWI+TO is Laterally Wedged Insoles and Toe-Out gait and KB+LWI+TO is Knee Brace along with Laterally Wedged Insole and Toe-Out gait

6.4.4 Risk of Fall Assessment

Table 6.1 shows the mean values of OSI at different test conditions. Significant reduction in the OSI were observed from N through pairwise comparison when the participants stood on the BBS with KB+LWI+TO at FR12 platform setting. Similar reduction in the risk of fall was observed for KB+LWI+TO at FR8. The only intervention found to be improving balance was KB at FR12 setting, which decreased the fall risk by 28.57%. No significant differences were observed among the tests condition at static platform setting.

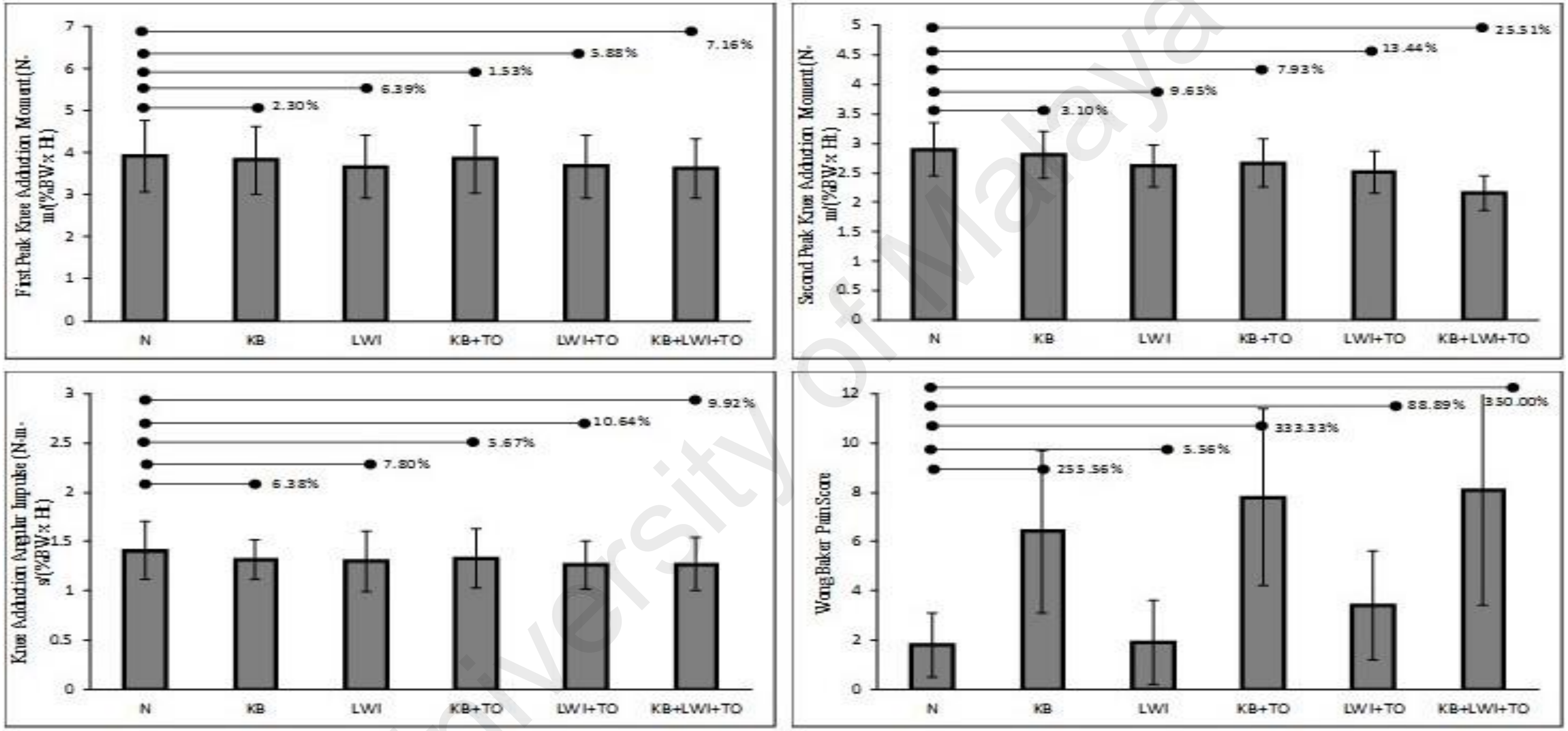


Figure 6.4: Bar charts representing first peak knee adduction moment, second peak knee adduction moment, knee adduction angular impulse and Wong-Baker pain scores for N (natural walk), KB (knee brace), LWI (laterally wedged insole, KB+TO (knee brace along with toe-out gait), LWI+TO (laterally wedged insoles along with toe-out gait) and KB+LWI+TO (knee brace along with laterally wedged insole and toe-out gait). The horizontal lines and the accompanying numbers represent percentage difference from N.

Table 6.1: ANOVA results of Overall Stability Index values with natural walk and different conservative treatment techniques for knee osteoarthritis. The bold p-values denote statistical significance.

Test Condition	Mean Value	Mean Difference from N	Percentage Difference from N	*p*-value
Static				
N	0.30	--	--	--
KB	0.30	0.00	0	0.92
LWI	0.40	-0.10	↑33.33	0.89
KB+TO	0.40	-0.10	↑33.33	0.82
LWI+TO	0.40	-0.10	↑33.33	0.81
KB+LWI+TO	0.40	-0.10	↑33.33	0.89
FR12				
N	0.70	--	--	--
KB	0.50	0.2	↓28.57	**0.05**
LWI	0.60	0.1	↓14.28	0.53
KB+TO	0.80	-0.1	↑14.28	0.66
LWI+TO	0.70	0.00	0	0.93
KB+LWI+TO	1.00	-0.3	↑42.85	**0.04**
FR8				
N	1.4	--	--	--
KB	1.3	0.1	7.14	0.79
LWI	1.6	-0.2	↑14.29	0.07
KB+TO	1.9	-0.5	↑35.71	**0.02**
LWI+TO	1.8	-0.4	↑28.57	**0.01**
KB+LWI+TO	2.1	-0.7	↑50.00	**<0.01**

Where N is Natural walk (without any intervention), KB is Knee Brace, LWI is Laterally Wedged Insole, KB+TO is Knee Brace along with Toe-Out gait, LWI+TO is Laterally Wedged Insoles and Toe-Out gait, KB+LWI+TO is Knee Brace along with Laterally Wedged Insole and Toe-Out gait, Static is the static platform setting of the postural stability test, FR12 is the fall risk platform setting from dynamic levels 12 to 8 and FR8 is the fall risk platform setting from dynamic levels 8 to 2.

6.4.5 Level of Comfort

The comfort level of the participants was assessed using Wong-Baker questionnaire, the results are shown in Figure 6.4. Significant reductions the in the pain score were observed from N (1.8) for KB (6.4, $p < 0.01$), KB+TO (7.8, $p < 0.01$), LWI+TO (3.4, $p = 0.01$) and KB+LWI+TO (8.1, $p < 0.01$). LWI showed no effect on the pain score (1.9, $p = 0.29$).

6.5 Discussion

The objective of this study was to test the combined effect of orthoses with toe-out gait on KAM and fall risk of medial knee osteoarthritis patients. The study also evaluated the participants' comfort level while using the interventions individually and when combined.

Walking with the brace alone, resulted in no significant change in peak KAM values. Previous studies have reported significant reductions in both peaks of KAM (Fantini Pagani, Potthast, & Brüggemann, 2010; Schmalz, Blumentritt, Drewitz *et al.*, 2006). The comparatively smaller and insignificant reductions in peak KAM values by KB might be due to the immediate testing of the intervention, without having any follow-up duration. The insoles, when used individually, reduced the first and the second peaks of KAM by 6% and 9.5% respectively. The reductions, however, are very small as compared to those previously reported (Butler, Marchesi, Royer *et al.*, 2007; Hinman, Bardin, Simic *et al.*, 2013; Kuroyanagi, Nagura, Matsumoto *et al.*, 2007), probably because of the effect of different walking speed. The study limited the participants' gait speed to 1.18 m/s, as per our pilot study, which was lower than the gait speed of previous studies.

The combination of LWI and TO provided similar results as of Tokunaga et al (Tokunaga, Nakai, Matsumoto *et al.*, 2016). Toeing-out reduced the KAM further during whole of the stance phase, when combined with brace and insole simultaneously. The present findings support the concept of combining orthoses with toe-out gait specially to reduce second peak of knee adduction moment. The study is novel in this nature as it provides insight of the combined effects of three conservative treatments. But the investigators are also aware of limited studies which combined KB and foot insole. Schmalz *et al* reported changes in KAM during walking with combined use of a wedged insole and rigid foot orthoses in healthy participants (Schmalz, Blumentritt, Drewitz *et al.*, 2006). Further extending their work, Hunter et al tested the combined behavior of valgus brace, customized foot orthoses and specialized shoes, in a randomized cross-over study (Hunter, Gross, McCree *et al.*, 2012). They found the combination of these treatment techniques to be further improving knee pain than the control treatment of neutral brace, neutral orthoses and motion control shoes.

The present results are consistent with the studies which suggest that the combined use of conservative treatments may reduce greater loads than if used individually for medial kOA patients. In our case, TO gait is very useful in reducing late stance KAM when combined with brace and laterally wedged insole. Although results are showing a significant reduction in early stance KAM also, which is contradictory to the previous studies showing no change or increase of fKAM with TO gait. The reduction in fKAM in this study was due to the use of LWI, not by TO. But it seems important that both KB and LWI limit the movement of CoP by toeing-out which in turn leads to no change in fKAM by TO. The largest change in combining orthoses and TO occurred at second peak of KAM (25.5%) which is 22.4% higher than KB-alone and 15.85% higher than LWI-alone. This reduction in sKAM might be considered disappointing given that three interventions were combined. Arguably, these smaller changes may also have profound effect on disease progression as walking is one of the most frequent activity of daily living (ADL) (Bennell, Bowles, Wang *et al.*, 2011; Maillefert, Hudry, Baron *et al.*, 2001).

Toeing-out shifts the CoP medially, shifting the line of action medial to the anterior-posterior axis of the shank. This shifting of the CoP and the line of action produces a torque about the talocrural joint and forces the knee joint center to move laterally. This effect is counteracted by the external rotation of tibia in the transverse plane, which decreases the perpendicular distance of the GRF vector (GRF lever arm) and the knee joint center. The reduced GRF magnitude and the GRF lever arm results in a decrease in early stance KAM. As for the late stance phase, toeing-out shifts the CoP externally, resulting a decrease in KAM (Chang, Hurwitz, Dunlop *et al.*, 2007; Rutherford, Hubley-Kozey, Deluzio *et al.*, 2008; Simic, Wrigley, Hinman *et al.*, 2013).

Postural stability is not affected by slight perturbations under normal conditions, despite the non-uniform load distribution across the body (Woollacott & Shumway-Cook, 2002). This can be changed however, by several external (injury to the head, vestibular apparatus and limbs) and internal factors (chronic vertigo, visual impairment etc). An alteration in the body posture, intended as a treatment option for any disorder, should be carefully devised such that it does not decrease the postural stability of the patient. Our results showed that the balance of kOA patients can be compromised when two or more than two conservative treatments combined with TO on unstable platforms. Number of application of conservative treatments had no effect on static conditions or with normal walking. The study tried to simulate a normal scenario of body movement with platform settings, like the static platform setting means the person is at a resting position, while FR12 refers to normal walk with slight variation in walking speed and FR8 refers to highly unstable platforms. This balance reduction was also reflected in the participants' comfort level questionnaires where the most uncomfortable situation for them was were walking with three interventions simultaneously. Although the major cause of discomfort in this study was the use of KB, but it also had synergistic effect when KB combined with TO.

6.6 Conclusion

There is a synergistic effect of toe-out when combined with KB and LWI concurrently in second peak of knee adduction moment reduction but with greater degree of fall risk. Simultaneous use of conservative treatments also decreases comfort level. However, these results do lend support to future works investigating potential additive effects of combined interventions tailored to ensure patient comfort.

CHAPTER 7: DISCUSSION

This thesis worked on the premise of combining and comparing two different conservative treatment techniques (orthoses and gait modifications) for the treatment of mild to moderate medial knee osteoarthritis. This premise was built on the previous knowledge that there exist synergistic effects of combining different conservative treatment techniques. There are, however, no analyses reported that extensively investigate the biomechanical effects of toe-in and toe-out gait modifications along with knee brace and laterally wedged insoles. Before putting the two types of conservative treatment techniques (orthoses and gait modifications) in comparison to each other, the investigators probed the lesser known treatment technique first, that is the gait modification technique. Since there was a paucity of reported effects of changing the foot progression angles on standing dynamic balance, the need was felt to encompass this into our study protocol. Hence the first objective was to investigate the effects of varying degrees of foot progression angles on overall postural stability and fall risk. For this objective, it was hypothesized that changing the foot progression angles will affect the postural stability and risk of fall in both participant groups (healthy and osteoarthritic) for static and dynamic conditions. This hypothesis was found to hold true only for the highly unstable dynamic platform settings. Secondly, it was hypothesized that the different platform settings will affect the postural stability and risk of fall in both participant groups, which was also found to be true. In simpler words the experiment indicated that bringing small changes in foot progression angles does not produce considerable effects on balance. Also, if a knee osteoarthritic adult traverses a highly unstable terrain with toe-in or toe-out gait, then they are at a greater risk of fall than when a healthy adult walks the same terrain with toe-in or toe-out gait.

The study further probed the effects of conservative treatment techniques by comparing orthoses against toe-in and toe-out gait in terms of physical performance. The objectives were (1) evaluating the immediate effects of knee brace, laterally wedged insoles, toe-in gait and toe-out gait on standard physical performance tests in healthy knee osteoarthritic participants and (2) comparing the effects of these interventions with each other to find the most efficient treatment technique in terms of physical function. Through this experiment, wearing a knee brace was found to be the best technique if one wants to improve physical function. It was further learned that gait modification techniques are not favourable towards physical function in comparison to orthoses.

When investigating the combined effects of orthoses and gait modification methods, the investigators chose the knee joint load indicators (knee adduction moment and knee adduction angular impulse), balance parameters and pain as our outcome measures. Since one cannot combine toe-in and toe-out gait together, the study split the combinations in two categories: one, constituting the knee brace, laterally wedged insoles and toe-in gait and two, constituting the knee brace, laterally wedged insoles and toe-out gait. The hypothesis for the former combination was that the toe-in gait would reduce the first peak knee adduction moment further when combined with knee brace and laterally wedged insoles while increasing the fall risk for knee osteoarthritis patients. The experiments showed that the first peak knee adduction moment and knee adduction angular impulse was the lowest when toe-in gait was combined with knee brace and laterally wedged insoles. On the down side, this synergy of conservative techniques increased pain and the risk of fall at unstable platforms. The hypothesis for the other combination of techniques (involving toe-out gait) was that the toe-out gait would reduce the second peak knee adduction moment further when combined with knee brace and laterally wedged insoles while increasing the fall risk for knee osteoarthritis patients. The combination of knee brace, laterally wedged insoles and toe-out gait produced smallest values of second peak knee adduction moment and knee adduction angular impulse, indicating knee joint load relief through this combination. Pain and risk of fall were, however, increased by this combination.

From the experiments performed for this study, some generalizations can be drawn about the biomechanical effects of conservative treatment techniques. Firstly, it was found that toe-in and toe-out gait modifications, albeit being cost-free and easiest to perform, need to be investigated in more depth before being prescribed for the medial knee osteoarthritis patients. When used alone, toe-in gait or toe-out gait can have some hazardous effects on physical function and balancing strategies of the patient. As it is already known that the proprioception of a person with medial knee osteoarthritis is impaired (Khalaj, Osman, Mokhtar *et al.*, 2014), the toe-in or toe-out gait modifications need to be prescribed with a customized set of maximum and minimum foot progression angles. A healthcare professional would also be required to train the patient to walk with their prescribed foot progression angles. Furthermore, strategies can be developed to enhance the physical performance of the patients while walking with these gait modifications. It is possible that an adequate amount of practice with these gait modifications would improve their physical performance.

Secondly, on individual bases, knee braces have been found to stand out among the conservative treatment techniques in terms of physical performance and knee joint load reduction. But these effects are further enhanced when they are combined with laterally wedged insoles and toe-in or toe-out gait. This reduction is of utmost importance in the long run because it can delay the progression of knee osteoarthritis. This combined usage, however, should be modified through practice and further investigation as such to increase the comfort level of the patient and decrease their risk of fall.

CHAPTER 8: CONCLUSION

8.1 Limitations

A limitation of the study is that it analyzed the immediate effects of orthoses and gait modification techniques and did not have any follow-up sessions. Although, a brief training period was included in the experiments for each intervention, there might be some long-term effects if the treatment techniques are applied for prolonged periods.

Another limitation in balance analyses is that the participants were asked to keep their hands on their hips rather than hanging them by their sides. This might have acted as a balancing strategy and may have influenced the balance parameters. Secondly, the participants were asked to stand on the balance platform with a constant heel distance of 0.16 m, a distance which created slight discomfort to the osteoarthritis patients as their 'comfortable' heel distance is greater than 0.16m. These data collection protocols were set to ensure the uniformity and the repeatability of the test conditions.

8.2 Conclusions

By three-dimensional motion analysis, static and dynamic balance tests and performance-based physical function tests, the following key findings were observed:

The participants having moderate medial knee osteoarthritis have a poorer postural stability and increased risk of fall as compared to healthy participants. Changing platform settings had a profound effect on balance, and this effect was more pronounced for the participants with knee osteoarthritis than healthy participants. Changing toe angles produced similar effects on both the participant groups, with decreased stability and increased fall risk at extreme toe-in and extreme toe-out angles.

Physical performance was found to be affected by the immediate application of all the four conservative treatment techniques. Physical performance measures were improved the most by the valgus knee brace, indicating its effectiveness in improving physical function. On the other hand, toe-out gait modification was found to be considerably impairing physical function.

It was found that a synergistic effect of toe-in gait and toe-out gait when combined with knee brace and wedged insole concurrently produced reductions in the first and the second peaks of knee adduction moment respectively but with a greater risk of fall. Simultaneous use of conservative treatments decreased comfort level as well.

8.3 Future Directions

Future studies should develop balance enhancement strategies for osteoarthritis patients at higher foot progression angles and for highly unstable terrains. The results of this study lend support to future works investigating potential additive effects of combined interventions tailored to ensure patient comfort. Furthermore, future researches can repeat these experiments by investigating long-term synergistic effects of conservative treatment techniques.

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LIST OF PUBLICATINS AND PAPERS PRESENTED

Status	Title	Authors	Journal	Date of Submission/Acceptance
Journal Publications				
Published	Effects of different foot progression angles and platform settings on postural stability and fall risk in healthy and medial knee osteoarthritic adults	Saad Jawaid Khan, Soobia Saad Khan, Juliana Usman, Abdul Halim Mokhtar, Noor Azuan Abu Osman	Journal of Engineering in Medicine https://doi.org/10.1177/0954411917750409 (ISI Indexed)	Submission: January 24, 2017 Accepted: December 4, 2017
	Combined effects of knee brace, laterally wedged insoles and toe-in gait on knee adduction moment and risk of fall on moderate medial knee osteoarthritis patients	Saad Jawaid Khan, Soobia Saad Khan, Juliana Usman, Abdul Halim Mokhtar, Noor Azuan Abu Osman	Gait & Posture (ISI Indexed)	Submission: May 12, 2017 Accepted: January 23, 2018

Status	Title	Authors	Journal	Date of Submission/Acceptance
	Combined effects of knee brace, laterally wedged insoles and toe-out gait on knee adduction moment and risk of fall on moderate medial knee osteoarthritis patients	Saad Jawaid Khan, Soobia Saad Khan, Juliana Usman, Abdul Halim Mokhtar, Nahdatul Aishah Mohd Shariff, Noor Azuan Abu Osman	Prosthetics and Orthotics International (ISI Indexed)	First submitted: June 6, 2017 Accepted: July 15, 2018
Under Review	Orthoses Vs Gait Retraining: Immediate Response in Improving Physical Performance Measures in Healthy and Medial Knee Osteoarthritic Adults	Saad Jawaid Khan, Soobia Saad Khan, Juliana Usman, Abdul Halim Mokhtar, Noor Azuan Abu Osman	Sains Malaysiana (ISI Indexed)	December 12, 2016
Conference Publication	*A Pilot Study on Physical Performance Measures: What is Better for Knee Osteoarthritis Patients, Orthoses or Gait Modifications?	Saad Jawaid Khan, Soobia Saad Khan, Juliana Usman, Abdul Halim Mokhtar, Noor Azuan Abu Osman	3rd International Conference on Movement, Health & Exercise, 2016 in IFMBE Proceeding Series by Springer, Page 163 - 167 (ISI Indexed)	

**Received Young Investigator Award (Appendix D)*