Official Title: Foot progression angle modification: an exploratory six-week intervention in people with knee osteoarthritis.

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Study Protocol

Study Design

This parallel-group randomized clinical trial will consist of a 6-week gait modification intervention, delivered to two groups of older adults with medial compartment knee osteoarthritis (OA). The first group will receive a conventional delivery of gait modification (group name: SMOD), whereby they will practice the gait modification with a specific target (rotate foot 15° inward or outward relative to baseline). The second group will self-select the amount of modification they perform (group name: AMAC), guided by the instruction to "change foot rotation as much as is comfortable". Foot rotation (toe-in or toe-out walking) is measured during the stance phase of walking as the angle of the foot's long axis (heel to toe) relative to the direction of walking, and termed foot progression angle (FPA). In-lab and real-world gait analysis will be used to examine how the modification is learned, as well as the effect of the modification on biomechanical and clinical outcomes relevant to knee OA. In-lab assessment will be performed at baseline and a 7 week follow-up, while real-world assessment will be performed during the intervening weeks using wearable sensor technology (a custom sensorized shoe design). Both within-group and between-group comparisons will be made to identify differences in learning, difficulty, biomechanical, and clinical outcomes.

Primary Hypotheses

H1: Participants receiving the specific FPA target will exhibit improved learning outcomes (e.g. lower error in performance, higher proportion of steps with ≥7º of change from baseline FPA and lower variability) from week 1 to week 6, as measured during gait modification practice sessions, learning assessments, and during daily walking activity.

H2: Participants receiving the self-directed FPA modification will exhibit improved learning outcomes (higher proportion of steps with ≥7º of change from baseline FPA and lower variability) from week 1 to week 6, as measured during gait modification practice sessions, learning assessments, and during daily walking activity.

H3: We expect FPA variability will be larger in the self-directed group, but both groups will exhibit a similar proportion of steps with >7° of change from baseline FPA.

Secondary Hypotheses

H4: Those in the self-directed modification group will exhibit smaller average changes in FPA compared to those in the conventional gait modification group. However, those in the self-directed modification group will report lower ratings of difficulty in performing the modification, compared to the specific-target gait modification group.

H5: Both groups will exhibit improvements in biomechanical (e.g. knee adduction moment) and clinical outcomes (e.g. knee pain, physical function) at follow-up, compared to baseline.

H6: Biomechanical (e.g. knee adduction moment) and clinical outcome (e.g. knee pain, physical function) change scores from baseline to follow up will not differ between groups.

Participants

Adults with knee OA will be recruited and randomized into two treatment arms. All eligible

participants will: 1) be 50 years of age or greater, 2) exhibit signs of tibiofemoral OA (a score of ≥2 on the Kellgren and Lawrence (KL) grading scale [1]) predominantly in the medial compartment, 3) self-reported knee pain ≥ 3 / 10 on a numerical rating scale of pain (NRS; 0 = "no pain" and 10 = "worst pain imaginable") during most days of the previous month, 4) are comfortable walking intermittently for 30 minutes, and 5) fit into the available sizes of sensorized shoes (sizes spanning US women's 5 to men's 13).

Exclusion criteria include: 1) any knee surgery or intraarticular injections within the past 6 months, 2) a history of joint replacement surgery or high tibial osteotomy, 3) current or recent (within 6 weeks) corticosteroid injections, 4) use of a gait aid, 5) currently on a wait list for joint replacement surgery or high tibial osteotomy, 6) any inflammatory arthritic condition, 7) any other conditions that may affect normal gait or participation in an aerobic exercise program, and 8) cannot attend all required appointments at UBC. Additionally, potential participants will undergo an initial gait screening similar to a recent study [2] (details are outlined below), with the goal of identifying participants who are capable of reducing their KAM magnitude when FPA is modified. This gait screen will examine both natural walking FPA and changes in knee load while walking with increased toe-in and toe-out. Those who do not elicit a reduction in KAM impulse ≥ 5% when FPA is changed by 10° in either direction will be excluded from the study as they would be considered non-responders.

A total of 36 individuals will be recruited for this study, 18 in each group. Approximately 60% in each group will be female. The primary outcome measure of this study is the change in absolute FPA performance error (the difference between the performed and the targeted FPA), which is indicative of how 'accurate' the patient is when performing the modification. This outcome measure is only relevant to the SMOD group, who have a specific target for their modification; therefore, allowing an error value to be calculated. This outcome will be measured during immediate and delayed retention at week one compared to follow-up and will provide evidence of the extent to which motor learning has occurred. Previous FPA performance error during immediate retention testing after a six-week FPA modification resulted in a small effect (Cohens d = 0.35) [3]. We are also interested in exploring the clinical and biomechanical differences between the SMOD and AMAC gait modification groups; however, no study has previously compared these methods of gait modification. Therefore, we will be conservative and base our sample size calculation on the between-within interaction effect of a 2 x 4 (group = 2: SMOD vs AMAC; measure = 4: immediate and delayed retention tests at week 1 and follow up) repeated measures ANOVA with an effect size of f = 0.175 (f = d / 2). With power = 0.8 and alpha = 0.05, a total sample of 30 is required [4]. With a conservatively estimated attrition of 15%, we will recruit 36 participants total (18 per group).

Procedures

Recruitment and screening

Volunteers will be recruited via print and social media, and via our database of previous participants who have indicated interest in participating in future studies. Interested volunteers will be screened via phone, email, or our lab website by the study coordinator to assess inclusion and exclusion criteria. Those deemed preliminarily eligible will be invited to attend a gait screening appointment. Eligible participants who pass the gait screen will be referred for a radiographic assessment of their knees to confirm the presence of structural signs of knee OA.

Standing, semi-flexed posteroanterior radiographs of both knees will be taken. A trained assessor will grade all radiographs based on the KL criteria. Those passing all screening requirements will be invited to enroll in the study.

Gait screening

The gait screen will be performed using motion capture to measure self-selected FPA, joint angles, and joint moments during over-ground walking. Fifty-two retroreflective markers will be placed on the skin over boney landmarks and 14-high speed cameras (sample rate = 100 Hz) will track the positions of these markers in three dimensions. Additionally, two floor-mounted force platforms (sample rate = 2000 Hz) will measure ground reaction forces during walking. Natural walking trials across the 10m instrumented walkway will be performed first (one length equals one walking trial), followed by toe-in and toe-out walking. The latter will be guided verbally such that several walking passes are completed at a range of FPA magnitudes (small toe-in/out, medium toe-in/out, and large toe-in/out). The specific amount of change in FPA is not relevant, as long as a range of FPA magnitudes are recorded over the collected walking trials. These data will be used to determine whether the participant is a responder to FPA modification, and which direction (toe-in or toe-out) elicits the greatest response. The threshold of a 5% reduction in the knee adduction moment impulse (area under the knee adduction moment – time curve) with a 10° change in FPA will be used to determine response. For recruitment purposes, those who respond to either toe-in or toe-out (≥5% reduction with a 10° change in FPA) will be provided this FPA modification. For those who elicit response to both, the modification (toe-in or toe-out) with the greatest reduction per 10° of change in FPA will be used in the intervention. This cutoff value is conservative, allowing for some regression in response while still maintaining overall reduced KAM impulse. A 5% threshold was chosen as the average reduction in KAM impulse after a 16 week toe-out modification program was 4.7% [5]. These methods of screening for response to FPA change and personalizing the direction of FPA change were shown to improve biomechanical outcomes relative to a non-personalized approach [6, 7].

Baseline and follow-up data collection

An identical baseline and follow-up gait assessment, separated by seven weeks, will be conducted in the laboratory, and using both optical-motion capture and the sensorized shoe system. These assessments will include questionnaires, a timed stair climb, and gait analysis.

A) Patient reported outcomes and physical function

Questionnaires will be administered which will include an 11-point numerical rating scale (NRS) depicting average knee pain over the previous week where 0 = “no pain”, 10 = “worst pain imaginable”, the Knee Injury and Osteoarthritis Outcome Score (KOOS) [8], and the Pain Catastrophizing Scale [9]. Medical history, anthropometrics (height, body mass etc.), age, and symptom duration will also be recorded by the assessor. The timed stair climb (a measure of physical function) will be performed on a 12-stair flight. Participants will be instructed to “climb as quickly, but safely as possible” [10]. Two repetitions will be performed, and the fastest time will be used.

B) Gait analysis

A total of 52 reflective markers (45 lower limbs; 7 upper limbs) will be affixed to the skin bilaterally over key anatomical landmarks as is standard in our laboratory [11]. Fourteen high-

speed cameras (sample rate = 100 Hz) will track the positions of these markers and two floor-embedded force platforms (sample rate = 2000 Hz) will measure ground reaction forces. Five passes along a 10m instrumented walkway will be performed barefoot and then shod. Walking speed at the baseline assessment will be measured using two timing gates placed at a known distance along the walkway. At follow-up, participants will first complete five walking passes at a self-selected speed and then be constrained to walk within ±5% of their baseline walking speed, due to the impact of walking speed on joint moments. After over-ground walking, a 5-minute treadmill walk will be performed while wearing a pair of sensorized shoes (details included below). This will provide a controlled measurement of FPA from the sensorized shoe for comparison with FPA measured at each practice session and during daily at-home walking.

A 1-minute dual-task assessment will be performed immediately after the 5-miniute treadmill walking trial, according to established methods [12]. Briefly, a single letter or category will be provided at the start of the 1-minute period. The instructions will be to continue walking naturally while simultaneously dictating as many words as possible (word-list generation) that start with the letter or belong to the category. The number of correct words dictated will be recorded.

Stair ascent and descent will be performed while wearing the sensorized shoes. This will take place at a building nearby the laboratory (5-minute walk) because of the availability of continuous linear sets of stairs for multiple flights. This allows the use of the sensorized shoe for measuring FPA during stair ascent and descent. These FPA data will be compared with transfer test data (details included below) examined at several points throughout the intervention. These same shoes will be provided to the participant to measure real-world FPA during at-home and community walking.

Sensorized shoes
A custom inertial sensor consisting of a 3-axis accelerometer (signal range: ±4g), gyroscope (±500°/s), and magnetometer (±1200μT), sampling data at 100 Hz will be embedded in the sole of the shoe. A previously published custom sensor fusion algorithm [13], programmed into a microcontroller, calculates the FPA in real time and stores it on a microSD card for later extraction. The sensorized shoe design and algorithm has been validated during treadmill [14] and over-ground walking [15] with excellent validity and reliability (absolute error = 1.7º and intraclass correlation coefficients > 0.9).

Randomization
Once deemed eligible and baseline data collection is complete, each participant will be randomized to either the SMOD or AMAC group. Randomization will be performed using an *a priori* block-stratified approach based on sex and KL grade. A predetermined randomization matrix will be computed [16] by a team member not involved in testing or the intervention. Group allocations will be stored in opaque envelopes, which will be opened in a sequential manner after baseline testing and before the first practice session. The group allocation will be communicated to the study trainer via email.

Gait modification intervention
Both groups will attend six practice sessions conducted weekly, which will last approximately 1 hour each. Walking practice will be conducted on a treadmill with a full-length mirror placed

directly in front of the treadmill. The SMOD group will be guided to increase their FPA by 15° in either the toe-in or toe-out direction (determined by the gait screen). A line of tape will be aligned on the mirror according to the target FPA, as we have done previously [5, 17]. This mirror-based method of providing a target for the FPA modification was shown to be similarly effective when compared to feedback delivered using an expensive real-time motion capture system, but with significantly greater clinical feasibility. The AMAC group will be instructed to increase their FPA by "as much as is comfortable". The mirror will be provided during practice sessions; however, no tapeline will be placed. The amount of time spent with the feedback (mirror) visible will be progressively reduced (faded feedback) across the six weekly practice sessions in order to reduce the reliance on feedback [18]. Before and immediately after the practice sessions, the participant will perform a warm-up and cool-down walk while wearing the sensorized shoes (10-minute outdoor standardized walking loop). This will provide a repeatable non-laboratory-based measure of FPA. Both groups will be encouraged to practice their gait modification at any opportunity during their daily at-home walking. Practice sessions will be led by a kinesiologist with experience delivering gait modification interventions.

Learning will be measured during 1) practice, 2) immediate and delayed retention tests, 3) dual-task tests, 4) transfer tests, and 5) during at-home/community walking. Each test (2-4) will last 1 min and be collected at each practice session. For the SMOD group, the absolute performance error (absolute error = |performed FPA – target FPA|), FPA variability, and the proportion of steps with >7° of change from baseline FPA will be measured using the sensorized shoe. For the AMAC group, FPA variability and the proportion of steps with >7° of change from baseline FPA will be measured. Retention tests will occur immediately before (starting at practice session 2) and after practice bouts. The participant will be asked to perform their gait modification as accurately as possible for 1 minute. Dual-task testing will be performed identically to the baseline assessment described above; however, the participant will be asked to simultaneously perform their gait modification. Lastly, transfer testing will be performed during stair ascent and descent in the same manner as the baseline assessment.

During each practice session, participants will be asked to rate their knee pain at the beginning, middle, and end of the session using an 11-point numerical rating scale (0 = "no pain" and 10 = "worst pain imaginable"). At the end of the sessions, they will be asked to rate the difficulty in achieving their FPA modification during that practice period using an 11-point numerical rating scale (0 = "not difficult" and 10 = "most difficult/unable to perform").

An instructional booklet will be provided which outlines details of how to care for and use the sensorized shoes while at home and in the community. Participants will track daily walking volume, walking times on each day, daily knee pain using an NRS (e.g. overall pain, pain during walking), non-walking exercise activities, and any adverse events related to their knees or walking. Additionally, an 11-point numerical rating scale will be used to report weekly confidence in how accurately the FPA modification was performed (0 = "no confidence at all/unable to perform" and 10 = "completely confident") and difficulty in performing the modification (0 = "not difficulty" and 10 = "most difficult/unable to perform"). A minimum of 10-minutes of daily walking will be requested to ensure enough data for the analysis.

Data processing and analysis

Marker-based motion capture data (as collected during the baseline and follow-up assessments) will be processed using commercially available software and using standard techniques our research group has established [5, 11, 19, 20]. Sensorized shoe data captured during the baseline and follow-up gait assessment, practice sessions, and at-home or community walking will be processed using custom MATLAB scripts. A trained research assistant, blinded to group allocation, will perform all data processing and analysis.

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