Evaluating the Efficacy of Lateral Heel Wedges for Osteoarthritis of the Knee

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Principal Investigator: Marc Tompkins, MD

Significance

Given the prevalence of osteoarthritis of the knee and the general aging trends of the population it is important to develop effective non-operative interventions to reduce pain and improve function in the adult population with osteoarthritis (OA) of the knee. A large body of experimental evidence documents the potential for cartilage regeneration in the osteoarthritic joint under conditions of mechanical unloading of the involved joint. An easily applied, off-the-shelf shoe insert material that, when configured properly, will unload the medial compartment of the knee has been developed. The purpose of this investigation is to document the acceptability and effectiveness (with patient reported measures) of this insert compared to a control insert which does not unload the medial compartment of the knee in a group of patients with significant OA of the medial compartment of the knee in order to develop pilot data to document the effect size, acceptability of the inserts, compliance, feasibility, and power for a future clinical trial. Following communication with NIAMS officials we plan to submit an R34 proposal for this purpose. Multiple clinical trials measuring the impact of shoe inserts on knee OA symptoms report minimal benefit. These trials are conducted in a manner which used: 1. self-reported OA, 2. subjects not presenting for treatment and 3. Not in a stratified population of patients with moderate to severe medial compartment OA. Our study selects for patients with this moderate to severe medial compartment OA who pass the screening test of sufficient MCL laxity to allow correction of the weight bearing axis. Further the material used in these inserts is of a different stiffness which is molded to that of the human heel pad. This clinical trial will likely never be industry funded because of the inexpensive nature of the intervention.

Objectives and Hypothesis

Regularly wearing a 5 degree sloped insole over the course of one year will result in a wider joint space by x-ray in 60% of the subjects, a significant decrease in knee pain, decreased use of over the counter analgesics, and a clinically important 2 point improvement in the Womac pain and stiffness scale.

Methods

We will recruit 80 adults with Kellgren-Lawrence changes between grade 2-4 medial compartment osteoarthritis of the knee from the TRIA Orthopaedic Center in Minneapolis, MN. The subjects will be randomized to a 5 degrees lateral wedge shoe insert or a flat shoe insert of similar properties through a random table generator application which will be coordinated through the TRIA Orthopaedic Center.

Inclusion Criteria:

- Adult patients 30 years or older with symptomatic medial compartment knee osteoarthritis and Grade 2-4 Kellgren-Lawrence radiographic changes presenting for treatment of knee pain.
- Range of motion knee-flexion beyond 100 degrees and not lacking more than 15 degrees of extension.
- Subtalar and forefoot motion permitting foot/ankle eversion with weight bearing.
- Sufficient shoe toe box height to allow space for the insole and therefore comfort and compliance.
- Passive laxity of medial capsule and collateral ligament by knee extension test.

Exclusion Criteria:

- All other forms of knee arthritis other than osteoarthritis.
- Bilateral symptomatic osteoarthritis of the knee.
- Knee Instability- medial pseudo-opening of greater than grade 1 or detectable anterior-posterior instability.
- Less than Grade 2 Kellgren-Lawrence radiographic changes in the medial compartment of the knee.
- Kellgren-Lawrence radiographic changes that are greater than or equal to the medial compartment in either the patellofemoral or lateral compartment.
- Inadequate knee range of motion as demonstrated on exam.
- Balance problems requiring the use of a walker or wheel chair (ambulation with aid).
- Diabetes with peripheral neuropathy.
- History of knee arthroscopy on the index knee within the past three months of study enrollment.
- History of reconstructive (ligamentous etc.) knee surgery within one year of enrollment.
- Intra-articular steroid injection or visco supplementation on the index knee within 1 month of study enrollment.
- Stiff subtalar or forefoot joints as demonstrated on clinical exam.
- Inadequate shoe toe box depth to accommodate the shoe insoles.
- Charcot joint.
- Fixed contracture of the medial capsule and/or collateral ligament as demonstrated on clinical exam.

Rationale for Inclusion:

This group would otherwise be candidates for surgical intervention. Those with end stage osteoarthritic lesion would have biological potential for restoration of the cartilage. They would have range of motion that provided near normal gait and flexion enough to rise out of a chair. The insole fitting would accommodate the candidate's foot anatomy, any pathology and the geometry of their shoe.

Rationale for exclusion:

This criterion removes those conditions that would have potential to add conflicting data to the study and/or produce discomfort for the subject.

Statistical analysis plan:

All analyses will be done using S.A.S. (version 9.2) and two-sided p-values of less than 0.05 will be considered statistically significant. Appropriate descriptive summary statistics (including means and s.d.) and graphs (including histograms, kernel smoothed density plots, error bar plots) will be utilized to summarize Womac pain, stiffness and function in each treatment group at baseline, 6 month visit and 12 month visit. We will consider a linear regression using the generalized estimating equation (gee) approach to estimate the Womac pain, stiffness and function differences between wedge insert and flat insert groups with intention-to-treat principle. We selected gee as the primary approach as it accounts for the potential correlations among repeated measures within subjects. In addition, it has been shown the gee is more efficient compared to the two sample t-test, the paired t-test, the analysis of covariance (including treatment and baseline response as covariates), and is asymptotically equivalent to the analysis of covariance ii (including treatment, baseline response and an interaction between treatment and baseline response as covariates) [40]. Missing data will be handled with multiple imputation using S.A.S. proc mi and mianalyze. Secondary outcomes will include clinical and functional outcomes with standardized knee radiographs, a validated University of Minnesota pain and acceptability scale, a medication log in terms of weekly hours of insert usage will be analyzed similarly and the Tegner Activity Scale to document any change in activity level in addition to the function addressed in the other outcomes instruments

Test Intervention:

The Insoles: A commercially available proprietary insole in the form of a slab 10.5 cm wide and 35.5 cm. long will be used. They are available in two geometries and materials. The control insole is blue in color with a thin felt cover to be next to the subject's skin. It is 3 mm level depth side to side and front to back. The material is a proprietary material known commercially as Poron® with a durometer of 25; the average durometer of the human foot is 25-35 depending upon the thickness of the plantar soft tissue and the presence of bone beneath.

The experimental insole is a slab is green in color and made of polyvinyl acetate with a felt layer opposite the patients skin. It has a 5 degree wedge and is 3 mm high on thin side and 10 mm high on the other side. This insole will be fitted with the pattern cut so the outer side of the foot would have the maximum depth of material (the highest side**).**

Study Procedures:

Patient related: We will recruit 80 subjects presenting for treatment of knee who have primary OA of the knee primarily involving the medial compartment and meet the inclusion criteria. The will be randomized via a random table generated computer program to the wedge inserts or the flat inserts. They will be screened for adequate knee laxity and subtalar motion before enrollment at each site.

Subjects, experimental and control, will complete the Womac based on their current function, have bilateral standing knee radiographs obtained in a standardized fashion and be fit with the inserts and instructed to return in 6 weeks to have new inserts fashioned. The patient contact will be performed by the clinical coordinator. At the 6-week visit, the patients randomized to the wedge insole will have the 5 degrees insoles fit after their 6-week adjustment period with the 2.5 degrees insoles while those in the control group will be fit with new inserts.

At 3, 6, 9 and 12 months, all patients will return for new inserts and to complete secondary radiographs (6 months only) and to turn in their shoe insert acceptability, use logs and medication logs. Patients will be supplied with as many inserts as they need to assure that the shoes they wear on a daily basis are included.

At 1 year, a convenience sample of 5 patients in the wedge (treatment) group and 5 patients in the control group who have had prior knee MRI's within 1 year of institution of the treatment shoe inserts will have knee MRI's repeated to check the quality of medial compartment articular cartilage.

Statistical Analysis

The data analysis will be done in a blinded fashion by our statistician. The Womac and Tegner data will be analyzed with standard statistical approaches and confounding variables of medication use and time of use of the shoe inserts will be analyzed with regression techniques. Knee medial compartment width will be measured by two blinded radiologists.

Subject Instructions: Subjects will be informed they are eligible to be part of a study testing various insoles of differing color, material and shape for their impact on arthritic knee pain and function. They will be instructed on insertion and removal of the insoles including printed material of such instructions. After a 6 week run in period utilizing the 2.5 degree lateral wedge test article in order to adjust to the altered weight bearing axis, the subjects will have a 5 degree wedge test article fashioned in the same manner. They will be instructed to return at 3 month intervals for fitting of new insoles and clinical evaluation. X-rays , medication logs, U of MN pain scale[1] , Tegner and Womac will be collected at enrollment, 6 weeks, 3 months, 6 months, 9 months and one year.

Tailoring the Insole:

An exam will be performed ensuring the subjects foot and ankle range of motion.

The existing insoles will be removed from both shoes. This method provides maximum toe box height. It also makes a more uniform insole material bilaterally thereby providing consistency. In both groups the insole will be tailored to the subject's anatomy, pathology, and existing shoe geometry. The subjects will be fitted with the tailored insole that extends from the back of the heel to just beyond the metatarsal head, thereby maximizing room in the toe box. Multiple tailoring may be necessary to achieve comfort. The subjects are instructed on the ease of removing and placing the insole so they can move them shoe to shoe, day to day. The insoles will be replaced every 3 months. The Study Coordinator at the local site will have printed instructions to facilitate and perform the fitting of the test and control inserts based on patient randomization.

Our podiatry consultant will be involved with the training of the research coordinator for patient screening for adequate knee medial laxity and subtalar motion as well as proper fitting of the inserts. He will be the primary contact for questions during the trial related to insert fit. We will hold a one day meeting at TRIA Orthopaedic Center in Minneapolis for the site investigator to review study procedures emphasizing patient screening and consent, procedures for standardizing radiographs, and the technique for application of the shoe inserts and procedures for managing drop out of patients.

Procedures for standardization of subject screening and recruitment, application of test and control inserts; radiographic measure will be done at a one day meeting for the staff at TRIA Orthopaedic Center. The details of the administration of the U of MN pain scale, shoe insert use log, insert acceptability scale, medication log, Tegner and Womac will be reviewed.

With approval from NIAMS officials, we intend to follow this proposal with an R34 submission in order to plan the definitive clinical trial using the data from this proposal to develop a detailed Manual of Operations, calculate the subject numbers we will need to recruit, the estimated number of subjects we might lose to the one year follow-up requirement, the number of additional clinical sites needed to recruit the cohort within a 6 month period, and develop statistical approaches to manage confounding variables such as patient BMI, activity levels, and medical comorbidity.

Table 2:

	Initial visit (Randomization)	**6 week visit**	**3 month visit**	**6 month visit**	**9 month visit**	**12 month visit**
WOMAC, Tegner, and Pain scale	S	S	S	S	S	S
Standing AP bilateral	P	X	X	S	X	X
Lateral Affected knee	P	X	X	S	X	X
Medication log	X	S	S	S	S	S
Shoe insert log	X	S	S	S	S	S
Clinic visit	P	S	S	P	S	P
MRI						S

P = patient expense; S = study expense; X = not done

Benefits of this intervention and study design:

The subjects have end stage osteoarthritic lesions with potential for cartilage regeneration based upon the literature. Avoidance of surgery is advantageous to the patient. The material properties of the insoles are known. The durometer of the material is known which is relevant to the human plantar surface hardness. The material has an immediate memory to restore shape and depth which is a shorter interval than the human tissue on the plantar surface it is contacting. The fitting method provides the best opportunity for subject comfort and therefore compliance. The removal of the existing insoles removes a variable. The patient instruction during the fitting process; placement, removal and replacement educates them on the means of moving insoles from one shoe to the next. Insoles replacement every three months insures effectiveness of the material properties. The duration of the clinical trial is one year, a time sufficient to be compared to the time interval reported following high tibial osteotomy for cartilage to regenerate in similar lesion[22]

Strengths of the proposed intervention:

The method of tailoring the insoles for anatomical and pathological customization should minimize discomfort and increase compliance. The plain film standing x-ray with measured joint space is a clear marker for change. The final MRI is a valid means of measuring cartilage volume and nature. The measurement emphasizes anatomical and pathological variables, thereby removing subjectivity. The single subjective outcome measure will be the Womac. The cost of the insert to the patient would be far less than if a custom insert was constructed into the shoe or any other form of treatment, surgery or otherwise.

C) Research Timeline

	6 months	12 months
Specific Aim 1	Regulatory Paperwork Approval, Study Orientation for staff, and patient enrollment	Patient Follow-up, data analysis, project completion

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