COLORADO MULTIPLE INSTITUTIONAL REVIEW BOARD
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**Protocol #:** 17-0611
**Project Title:** Comparison of braces for treatment of Sever's disease
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## I. Hypotheses and Specific Aims:

Primary Aim: To compare two types of braces: The X Brace (The X Brace, Grand Rapids, MI) and Cheetah Heel Cups (Tuli's®, Medi-Dyne, Colleyville, TX), in pain reduction for barefoot athletes (e.g. karate, gymnasts, dancers) diagnosed with Sever's disease (calcaneal apophysitis)

> Hypothesis 1 – The Cheetah Heel Cup will be significantly more effective than The X Brace in reducing pain for barefoot athletes diagnosed with Sever's disease, demonstrated by a mean score difference greater than the minimal detectable difference (7 points) on the OxAFQ-C in the physical domain.

## II. Background and Significance:

Sever's disease is an osteochondrosis of the calcaneal apophysis due to frequent repetitive foot impact and repeated traction from the Achilles tendon, which attaches to the apophysis.[1] Though there remains uncertainty about the exact pathomechanics of this ailment, it is generally considered an overuse injury affecting active skeletally-immature children aged 8-14 years.[2] Identified risk factors include high levels of athletic activity,[3] increased BMI,[4,5] and anthropometric differences compared to a normative peer group including increased weight, height, ankle range of motion, waist circumference, and foot posture index.[5] A recent, large cross-sectional study examining visits to primary care practices reported an incidence of 3.7 per 1,000 patients ages 6-17 with a median age of 10 years for girls and 12 years for boys.[6] One systematic review reports that Sever's accounts for 2%-16% of musculoskeletal complaints in children.[7] This condition, which presents as heel pain with physical activity, is one of the most common pathological entities among this age group and a serious concern for growing athletes.[6]

Sever's disease has real and tangible effects on quality of life.[2] Children with this condition report greater pain and discomfort, dissatisfaction with their symptoms, and less happiness than asymptomatic peers.[2] It is also suggested that children may postpone treatment as they have the "ability and the competitive motivation to endure the pain… for an extended period of time," which can delay healing and prolong pain. Even despite that the pain associated with Sever's is often so severe that the child will limp to relieve pressure on the affected heel during or after physical activity.[3,8,9]

It is widely accepted and scientifically confirmed that physical activity improves child health with positive effects on adiposity, musculoskeletal health and fitness, and cardiovascular health.[10] Beyond the health benefits of physical activity alone, participation in sports at this crucial age enhances psychological and social health outcomes.[11] Athletes with Sever's symptoms are limited

in their ability to participate in physical activity and athletics, and it is suggested that active intervention in the management of Sever's is most appropriate to improve quality of life and outcomes without substantial time lost from sport or physical activity.[2] Therefore, efficient and effective treatment is essential, especially for active and competitive athletes.

Standard treatment for Sever's disease is placement of heel cups in shoes and stretching or physical therapy. These interventions are effective in reducing Sever's patients' heel pain.[12-16] A retrospective study showed that with treatment with a heel cup or other foot orthoses, symptoms improved within 2 months.[8] However, there remains a distinct lack of randomized control trials evaluating treatments for Sever's in the literature.[17] For the many young athletes with Sever's who participate in barefoot sports such as gymnastics, dance, or tae kwan do, the standard treatment is inadequate. They cannot use the recommended heel cups, which are placed in an athletic shoe. Currently, two braces are commonly used for barefoot athletes with Sever's: Cheetah Heel Cups and The X Brace. Neither of these braces are currently FDA approved as they are not considered medical devices and are marketed as an insert. Health care providers often recommend barefoot athletes purchase these braces, but no published studies evaluating their effectiveness exist in the established literature. This study will compare these two braces in an investigator-blinded, randomized control trial in order to contribute to the understanding of standard treatment for barefoot athletes with Sever's disease and improve patient outcomes by affecting clinical practice. In light of the paucity of information on and the importance of optimizing patient outcomes to improve quality of life and maintain an active lifestyle for young barefoot athletes, this prospective, randomized treatment study will compare the effectiveness of two braces in decreasing pain severity in barefoot athletes diagnosed with Sever's disease.

## III. Preliminary Studies/Progress Report:

No preliminary studies have been conducted at this institution.

## IV. Research Methods

### A. Outcome Measures:

i. Primary Outcome: Oxford Ankle Foot Questionnaire for Children (OxAFQ-C) Scores
ii. Visual Analog Scale (VAS) Pain Score
iii. Subject-Reported Compliance with Brace Use
    1. Hours per week the brace was worn with barefoot sport activity
iv. Rest from Sport
    1. Amount of time per week taken off from barefoot sport due to pain (if applicable)
v. Acceptability of Brace
    1. Comfort (Comfortable: Y/N)
    2. Appearance (Acceptability: Y/N)
    3. Perceived Effect on Athletic Performance (Improvement: Y/N)
vi. Pain Medicine Usage
    1. Weekly dosage of pain medicine (if applicable)

### B. Explanatory Variables:

i. Demographic
    1. Name and Medical Record Number
    2. Date of Birth
    3. Age at time of visit

4. Gender
5. Ethnicity
6. Weight
7. Height
8. BMI
9. Athletic participation
10. Primary sport
11. Hours per week in a barefoot sport

ii. History

1. Previous diagnosis of Sever's or calcaneal apophysitis
    a. Brace previously used

Figure 1. Cheetah Brace

Figure 2. The X Brace

C. Description of Population to be Enrolled:

Barefoot athletes who present to sports medicine clinic for foot, ankle, or heel pain.

i. Inclusion Criteria:

1. Aged 7-14 years
2. Participate in barefoot sports including: martial arts, dance, gymnastics, or acrobatics
3. A clinical diagnosis of Sever's or calcaneal apophysitis

ii. Exclusion Criteria:

1. History of foot/ankle surgery
2. History of rheumatologic diagnoses
3. Prisoners, pregnant females, individuals with limited decision-making capacity

D. Study Design and Research Methods

i. Human Subject Considerations

1. All patients will have an established relationship with a Children's Hospital Sports Medicine Physician.
2. All PHI will be stored within REDCap.

ii. Study Design: Randomized Treatment Study

iii. Methods:

1. Subjects will be recruited face-to-face by a study team member at time of initial visit, diagnostic clinical visit, or phone call initiated by Dr. Sweeney. Subjects recruited via phone call will be patients of study personnel. Patients and families interested in participating in the study will be contacted by a member of the study team to set up a research only consent visit. If they cannot come into clinic, the informed consent and assent will be sent to the family and a research assistant with call the family, either via phone or video call, to go over the consent and assent in real time and to answer any questions. After a signed consent or assent form is received by the research assistant, the assigned brace will be sent in the mail to the family and the associated questionnaires will be sent via email.
2. Subject will be screened for inclusion/exclusion (enrollment) criteria by study team member through chart review.
3. If subject meets enrollment criteria, they and a legal guardian will be consented face-to-face by a study team member.
    a. Consent will be sought from subjects ages 13-14.
    b. Assent will be sought from athletes younger than 13 years of age.
    c. Consent will be sought from parents of subjects ages 7-14.
4. Dr. Sweeney or designated staff will answer any questions after the patient and his or her parents have read and reviewed the informed consent and assent forms. It will be emphasized to the patients that their decision to participate in the study will in no way impact their treatment. Comprehension will be assessed by reviewing the consent forms with the patient and his or her parents thoroughly and asking the subjects questions requiring more than a simple yes/no answer.
    a. Patients and parents will sign the appropriate line on the informed consent/assent form.
    b. Consent procedures will take place in a private room or over a private call.
5. Subject will complete initial demographics survey, OxAFQ-C, and VAS.
6. Subject will be randomized into either the Cheetah Heel Cup or The X Brace treatment group. The randomization scheme will be independently created by the research assistant. The random assignment will be kept blind to the PI and statistician.
7. Subject will receive their assigned brace in the mail following their consent visit. Subjects will receive an activity and rest log in the mail with their brace. This is a weekly log and will help subjects track their weekly activity in their barefoot sport (in hours), amount of time spent in brace during barefoot sport (in hours), and any rest time taken from their barefoot sport (in hours). This log is optional, but encouraged, to fill out as it will not be submitted to the researchers. The intended purpose of the log is to aid in answering the monthly questionnaire on weekly activity, time in brace, and rest time.
8. At 1, 2, and 3 months, a study team member will email the subject's parent the OxAFQ-C, VAS and questionnaire on activity/brace usage. During this time, subjects will also answer questions pertaining to pain medicine use and any adverse outcomes from brace use. A reminder phone call will be made if the

questionnaires have not been completed within 5 days. Subjects will not be seen after the visit where consent was obtained, unless an adverse outcome arises requiring an assessment by Dr. Sweeney.

iv. Planned Duration of Study

1. Two-years from COMIRB approval date to allow for adequate enrollment

v. Duration of Participation of Each Subject

1. About 30 active minutes for consent and surveys
2. About 3 months for course of clinical care and resolution of symptoms

vi. Patient Incentives

1. Participants will receive a free brace after enrolling into the study. Upon successful completion of the study (once month 3 survey is completed), subjects will receive a $30 gift card in the mail.

E. Description, Risks and Justification of Procedures and Data Collection Tools:

i. Potential Risks to Subjects:

There are no anticipated risks in this study beyond those of standard care and daily living. There are no documented adverse outcomes associated with either brace that is known to the study team. Any adverse outcomes (skin irritation/rash) that arises during the study period will be documented during the monthly questionnaires sent out to subjects. Additionally, an unlikely and uncommon risk of this study is that PHI may be unintentionally disclosed to an outside party. We will put forth our best effort to keep the information about subjects secure, and we believe that the risk of accidental disclosure is minute. Identifying data will be protected as per REDCap protocol after subjects have been assigned a study number.

ii. Plan to Protect Subjects/Mitigate Risks:

Subjects will be instructed to call the research assistant if any adverse outcomes arise (skin irritiation/rash that causes discomfort or concern). The research assistant will document the adverse outcome in REDCap, and relay the message onto Dr. Sweeney who will contact the family to discuss the adverse event and if any of the following is needed: a new brace size, discontinued use of the brace/removal from study, a research visit to assess the adverse reaction. A REDCap database will be utilized for the organization and storage of patient information when necessary. Patients will be identified using individualized study numbers that will be stored securely in the REDCap database. Data containing spreadsheets will refer to patients only by the individualized study numbers, excluding all PHI.

iii. Participant Discontinuation Criteria:

1. Subject participation will be discontinued if:
    a. Subject no longer wishes to participate in the study
    b. Subject sustains an additional musculoskeletal injury or serious illness (hospitalization, injury to lower body requiring a visit to doctor).
    c. Subject fails to follow-up with clinical care.

d. Adverse reaction causing Dr. Sweeney to determine a discontinuation of the brace.

iv. Data Collection Tools:

1. Demographic and clinical data will be collected from the subjects' charts from EPIC and through subject input to REDCap questionnaires. REDCap will be used to store all study data electronically. REDCap is a secure, web application designed to support data capture for research studies. REDCap is hosted by the University of Colorado-Denver Development and Informatics Service Center (DISC).
2. The Oxford Ankle Foot Questionnaire for Children (OxAFQ-C) is used to measure subjective well-being for child patients (aged 5-16) affected by foot and ankle conditions using issues that are considered important to children. Typical clinical assessments fail to capture the child patient's perspective and may not accurately reflect how children function in their usual environments. The OxAFQ-C was therefore designed to supplement clinical assessments to evaluate the effectiveness of interventions for ankle/foot problems in children. It is a short (15-item) questionnaire and reported as valid and reliable in English[18] and Spanish and as responsive and longitudinally valid[19]. There are three domains to the OxAFQ-C: physical, school and play, and emotional well-being. Scores on the OxAFQ-C range from 0 to 100 with higher scores indicating better functioning and higher well-being.

v. Data Management:

1. Patients will be assigned patient study identifiers. These identifiers will be used for the identification of all study materials, and will only be linked to the patient's name, medical record number, or other PHI through REDCap. Non-identifiable data will be stored in Microsoft Excel, while PHI and any identifiable information will be stored with Redcap. Redcap is a secure, web application designed to support data capture for research studies, providing user-friendly web-based case report forms, real-time data entry validation (e.g. for data types and range checks), audit trails and a de-identified data export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). The system was developed by a multi-institutional consortium which includes University of Colorado-Denver and was initiated at Vanderbilt University. The database is hosted at the University of Colorado-Denver Development and Informatics Service Center (DISC), which will be used as a central location for data processing and management. REDCap data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team with planning assistance from the DISC. The iterative development and testing process results in a well-planned data collection strategy for individual studies. Both REDCap and REDCap Survey systems provide secure, web-based applications that are flexible enough to be used for a variety of types of research, provide an intuitive interface for users to enter data and have real time validation rules (with automated data type and range checks) at the time of entry. These systems offer easy data manipulation with audit trails and reporting for reporting, monitoring, and querying patient

records, and an automated export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus).

vi. Potential Scientific Problems:

The investigators recognize no other potential scientific problems at this time.

F. Data Analysis Plan:

i. Sample Size: We will use a linear mixed model to test the null hypothesis that the difference in OxAFQ-C physical domain scores between the The X Brace and Cheetah Heel Cups does not depend on time (group*time interaction). Means for treatment group at each time point were estimated based on a related RCT by James et al. [13]. The common standard deviation for all OxAFQ-C physical domain scores was assumed to be 6 and the correlation between time consecutive points was conservatively assumed to be 0.6 based on this previous RCT. We intend to use a one-to-one block randomization scheme to ensure equal allocation of patients to each treatment group. Assuming a Type 1 error rate of 0.05, a sample size of 44 participants total, 22 in each group, will provide 0.9 power to reject the null hypothesis of no group*time interaction based on the Hotelling-Lawley test statistic with an alpha level of 0.05. Assuming there is no missing data, no time varying covariates, and the repeated measures are consistently collected (general linear mixed model reversibility criteria is met),the Hotelling-Lawley trace statistic is equivalent to the statistical test, the Wald statistic with Kenward-Roger degrees of freedom, described in the data analysis plan.[20] . With an expected 30% loss to follow up, we will inflate the sample size to account for attrition, for a total enrollment goal of 58. The clinic treats 10 barefoot athletes with a clinical diagnosis of Sever's Disease who meet the eligibility criteria for this study each month. We expect a consent rate of approximately 50%. At an effective enrollment rate of 5 patients per month, we will reach the enrollment goal of 58 participants within 12 months. All samples size calculations were performed with GLIMMPSE, an internet based open source software program capable of computing power and sample size for multi-level and longitudinal research designs[21]

ii. Table 1. Expected OxAFQ-C physical domain scores based on data from James et al[13]

| Treatment | 1 month | 2 months | 3 months |
|---|---|---|---|
| Cheetah Heel Cups | 67 (±6) | 83 (±6) | 85 (±6) |
| The X Brace | 64 (±6) | 82 (±6) | 78 (±6) |

iii. Analysis Plan: Demographic and clinical characteristics will be summarized and compared between the two treatment groups using chi-squared and two-sample t-tests for categorical and continuous data, respectively. Imbalance between groups will be adjusted for in subsequent statistical analyses. For hypothesis 1, Linear mixed model regression analyses will be used to compare group differences

(Cheetah Brace vs X brace) across the 1, 2 and 3 month visits. We will test the null hypothesis that the difference between groups does not depend on time (group*time interaction). The parameter estimate will be tested using the Wald statistic with Kenward-Roger degrees of freedom and an alpha level of 0.05. Intent-to-treat analyses will be performed for all the primary outcome variables. A per-protocol analysis will also be performed. For the secondary analysis, the other two domains of the OxAFQ-C questionnaire as well as VAS pain scores will be analyzed using separate linear mixed models that iwill also test the group*time interaction. Linear regression models will also be used to compare overall compliance. Logistic regression models will be used to test the null hypothesis of no difference between groups for each of the three brace acceptability metrics (comfort, appearance, and perceived effect on athletic performance).

## G. Summarize Knowledge to be Gained:

It is common practice to provide heel cups and stretching exercises for patients with Sever's. Because these heel cups cannot be used in barefoot athletes, alternative braces are used. Currently, there are two commonly used braces in barefoot athletes, Cheetah Heel Cups and the The X Brace. No previous study has looked at the effectiveness of these braces. This study would compare these braces in a blinded clinical trial to determine if these braces are effective and if one brace is more effective in decreasing severity of pain in barefoot athletes with Sever's. This study will contribute to the understanding of treatment for barefoot athletes with Sever's disease and will improve patient outcomes by affecting clinical practice. In order to improve quality of life and allow young athletes to remain active, this prospective, randomized treatment study will compare the effectiveness of two braces in decreasing pain severity in barefoot athletes diagnosed with Sever's disease.

## H. References:


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