Acute Ankle Sprain in a Mouse Model: Development of Knee Joint Degeneration

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INTRODUCTION

- The occurrences of joint injury accompanied by physical activity post-injury are known to increase the development of osteoarthritis (OA) as age progresses.
- Aging is one of the key factors that influences the arthritic condition and is expected to be the fourth leading cause of disability by the year 2020.
- Clinician's have questioned the influence of previous history of lower extremity injury on the development of knee OA.
- With ankle sprains being the most common musculoskeletal injury, and the known alterations in mechanical stability and neuromuscular control that occur after an ankle sprain, there may be alterations in knee function.
- Clinicians currently do not know if ankle injury may lead to changes at the knee.

PURPOSE

- To investigate the amount of knee degeneration that occurs after an acute ankle sprain across the lifespan.

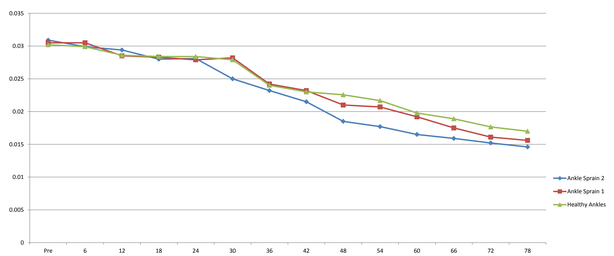
Figure 1: Cage set up including running wheel, magnetic sensor, and digital odometer.

Biodynamics Research Laboratory at UNC Charlotte

METHODS

- Thirty male mice (CBA/J), from Jackson Laboratory (JAX; Bar Harbor, ME) were randomly placed into one of three groups: the transected calcaneofibular ligament (CFL) group, the transected anterior talofibular ligament and CFL (ATFL/CFL) group, and a SHAM group.
- Mice were housed in a vivarium with 12-h light/dark cycles and standardized temperature (18-22°C) and relative humidity (20-40%). Water and standard chow were provided ad libitum. The UNC Charlotte Institutional Animal Care and Use Committee approved all study procedures as meeting the USDA and the Animal Welfare Act guidelines for the appropriate treatment of animal subjects.
- Under anesthesia and using proper sterilization techniques, all mice received a small curvilinear incision behind the lateral malleolus of the right hind foot. The respective ligaments were then transected for the CFL and ATFL/CFL groups but no ligaments were damaged or the SHAM group. Incisions were closed using surgical adhesive before post operative care was administered over 72-hours.
- Three days after surgery all mice were placed in individual cages with running wheels. Physical activity (i.e. distance run) was measured using a solid surface running wheel (127 mm, Ware Manufacturing, Phoenix, AZ), magnetic sensor, and digital odometer (Sigma Sport BC600, Olney, IL). Daily running wheel measurements were recorded beginning four days after surgery.
- Medial and lateral knee joint space (mm) in both hindlimbs were measured as a marker for the development of OA on all 30 mice every 6 weeks of their lifespan. Each mouse was anesthetized with isoflurane gas. The mouse was then shaved and ultrasound gel was applied to the medial and lateral aspect of both hindlimbs. Diagnostic ultrasound (SONOS 5500, Agilent Technologies, Andover MD) with a SONOS 15-6$_L$ ultrasound probe was utilized to image both hindlimbs (Figure 2). Once the medial and lateral joint lines were located, all joint space measures were made 1mm from the medial or lateral epicondyle. From this location, the distance from the medial or lateral condyle of the femur to the medial or lateral condyle of the tibia was measured to identify joint space for the respective hindlimb.

Figure 2. Right Medial Joint Space (in weeks across the lifespan)



RESULTS

- Right medial (p=0.003), right lateral (p=0.002), left medial (p=0.03), and left lateral (p=0.002) knee joint spaces decreased significantly across the lifespan.
- The mice in the ATFL/CFL group had significantly decreased right medial joint space (p=0.004) compared to the SHAM and CFL group (Table 1 and Figure 2). This difference indicated lesser joint space in the more severe ankle sprain group.

Table 1. Right Medial Knee Joint Space (mm)

	ATF/CFL group	SHAM Group
Baseline (6 weeks of age)	.38 ±.04	.38±.03
12 weeks	.37 ±.07	.38±.04
24 weeks*	.34 ±.06	.37±.05
48 weeks*	.29 ±.07	.35±.04

(*Significantly different $p < .05$)

CONCLUSIONS

- The mice with the more severe ankle sprain (ATFL/CFL) could have developed increased laxity and thus decreased stability in addition to impaired neuromuscular control.
- The mechanical and neuromuscular changes at the ankle may change the function at the knee.
- Biomechanical alterations of the ankle may lead to an increased force on the knee joint.
- This may lead to the increased joint stress and potential for knee OA development.

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