Abstract ID# 22635
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Summary:
End-stage ankle OA synovial samples demonstrated a unique transcriptomic signature as compared to non-OA samples.

Data:
Introduction: Osteoarthritis (OA) of the ankle is a prevalent and debilitating condition that impacts millions of people and typically results from injury. However, current treatment strategies are focused on symptom management only and little is known about the cellular and gene level drivers of disease progression. Current literature has reported synovium specific findings in OA, but a clear understanding of its contribution to OA has not been established. The objective of the study was to use RNA-sequencing of synovium from OA and non-OA ankles to characterize the synovial transcriptome, and assess patient reported outcomes (PROs) of the cohort. We compared gene expression patterns in both OA and non-OA ankles to investigate alterations specific to ankle OA. Methods: Patients undergoing surgery for end stage ankle OA and patients undergoing arthroscopic surgery for non-OA conditions, were consented, samples harvested during surgery, and affected joint was scored using the Outerbridge scoring classification. PROs were collected from patients preoperatively and at 3, 6, and 12 months post operatively. PROMIS Physical Function (PF), Pain Interference (PI), Depression, Foot and Ankle SANE, Global Physical Health, and Global Mental Health, and Global Physical Health scores were collected. Bulk 150 bp, paired-end RNA seq was performed using the Illumina NovaSeq6000 platform, and alignments made to Human Reference genome (GRCh38/hg38) using Hisat2 (v2.0.5). Adjustment using a scaling normalization factor and P-values were corrected using the Benjamini Hochberg method prior to differential expression was determined using the edgeR (3.22.5) package for R. Differences in PRO outcomes between non-OA and end-stage OA patients were determined non-parametrically using Mann-Whitney U tests. Results: Synovial samples from 30 end stage ankle OA and 31 from non-OA were used for analysis. Clear clustering of OA and non-OA samples were observed on principal component analysis. Functional enrichment analyses displayed enrichment in genes and pathways related to the extracellular matrix (ECM) and its organization, and collagen formation and degradation in the OA samples. Preoperative Foot and Ankle SANE (p=2.75X10-5), PF (p=0.027), and PI (p=0.011) were significantly worse in the OA subjects compared to the non-OA subjects. The increases in foot and ankle SANE scores from pre-op to most recent follow-up were significant in both the OA (p=0.001) and non-OA (p=0.02) groups. Conclusion: Synovial samples from end-stage OA display a unique transcriptomic signature from non-OA. We identified an upregulation in genes and pathways related to gene expression and macromolecule processing in OA samples. Knowledge of specific cellular changes in OA tissues is crucial, as it identifies potential mechanisms of disease progression and targets for future disease modifying therapies. End-stage ankle OA patients demonstrated worse pre-operative PROs compared to the non-OA cohort, however no significant difference was observed at six months post-op. Further investigations of specific epigenetic signals associated with ankle OA may lead to therapeutic pathways mitigating OA following ankle injury.

Category: Ankle/Foot/Calf

Genetic and Epigenetic Signals in Ankle Osteoarthritis

Abstract ID# 22578
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Summary:
Patients with retained arthroscopic BMS for OLT reported satisfactory clinical outcomes at average 15-years follow-up. Patients with non-primary OLT may benefit less from the procedure due to inferior pain scores. Two in three patients report participating in sports at long-term follow-up. The present study shows that arthroscopic BMS remains a viable treatment option for OLT as clinical results a

Data:
Purpose: Long-term clinical outcomes of arthroscopic bone marrow stimulation (BMS) for the treatment of osteochondral lesions of the talus (OLT) are rarely reported in the literature, even though the procedure remains the most common treatment for OLT. Understanding of long-term clinical outcomes in patients with retained (i.e., non-failed) BMS can inform clinicians on the sustainability of BMS and may justify its continued practice. It was therefore the aim of this study to assess the patient-reported outcome measures (PROMs) of patients with a minimum follow-up of 10-years after arthroscopic BMS for OLT who did not undergo revision surgery. The secondary aim of this study was to assess the influence of baseline demographic and lesion characteristics on PROMs. Methods: All consecutive patients who underwent arthroscopic BMS with retained results (i.e., no revision surgery for OLT after index surgery) were cross-sectionally contacted and included. PROMs were collected using the online CASTOR portal. The primary outcome was the numeric rating scale (NRS) for pain during walking. Additionally, the NRS during rest, stair climbing, and running, as well as the foot and ankle outcome score (FAOS) were collected. Participation in sports at follow-up and desired level of sports were also collected. A two-sample T-test was used to compare the primary outcome in sub-groups for prognostic factors: primary vs. non-primary lesions (i.e., failed prior surgical treatment), lesion size (> 150mm2 vs. < 150mm2), presence of cystic lesion, and sex. P < 0.05 was considered significant. Results: At final follow-up of mean 15.1 ± 4.7 years 102 patients were included. Patients were a mean 34.4 ± 10.8 years old at index surgery. 85 (83%) patients presented at baseline with a primary OLT. The average pre-operative lesion area was 279 ± 189 mm2, and 75% of patients presented with a cystic lesion. The primary outcome, the NRS during walking was 1.8 ± 2.4 out of 10 at final follow-up. Patients with a non-primary OLT reported a significantly higher NRS for pain during walking compared to primary OLT patients (2.9 ± 2.8 vs. 1.5 ± 2.3 out of 10, P = 0.04). Contrastingly, no significant differences were observed in the primary outcome when considering lesion size (P = 0.12), cystic lesions (P = 0.68), or sex (P = 0.56). The NRS during rest, stair climbing, and running was 0.8 ± 1.8, 1.5 ± 2.5, and 2.2 ± 3.0 out of 10, respectively. The following FAOS sub-scales were reported; symptoms: 69.8 ± 19.6, pain: 82.8 ± 19.7, ADL: 99.2 ± 1.4, sport: 67.1 ± 28.3, QoL: 62.6 ± 27.5. At final follow-up, 66 (65%) patients participated in sports. Of these, 61% reported participating in sports at their desired level, while 33% reported other reasons for not reaching their desired level of sports, and 6% of patients reported being restricted in their desired level of sports due to their ankle complaints. Conclusion: Patients with retained arthroscopic BMS for OLT reported satisfactory clinical outcomes at an average 15-years follow-up. Patients with non-primary OLT may benefit less from the procedure due to inferior pain scores. Two in three patients report participating in sports at long-term follow-up. The present study shows that arthroscopic BMS remains a viable treatment option for OLT as clinical results are maintained over time in the majority of patients.

Category: Ankle/Foot/Calf

Satisfactory Patient Reported Outcomes at 15-Years Follow-Up Of Arthroscopic Bone Marrow Stimulation for Osteochondral Lesions of the Talus