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Age-Dependent Variation in Cytokine Type and Concentration in Knee Synovial Fluid Following Meniscal Injury

Purpose: To investigate the age-dependent variation in cytokine types and concentrations in knee synovial fluid following meniscal injury.
Methods: Patients undergoing arthroscopic knee surgery for isolated meniscal injury were prospectively enrolled between July 2011 and April 2024. Synovial fluid was aspirated from the operative knee and concentrations of 10 biomarkers were measured. Those at least 9 years following surgery were invited to complete patient-reported outcome (PRO) surveys. Multivariable linear regression assessed pairwise relationships between age at surgery, log-normalized biomarker concentrations, and PROs, while adjusting for relevant covariates. Conditional process analysis was used to further explore age-biomarker relationships with symptom duration as a moderator and baseline Outerbridge grade as a mediator.
Results: Moderator analysis found age to be positively associated with IL-6, VEG-F, and IL-1Ra in chronic meniscal injuries. Mediator analysis found an indirect positive relationship between age and MIP-B, VEGF, and MMP-3, and an indirect negative relationship between age and TIMP-1 and TIMP-2. Pre-operative TIMP-1 was positively associated with 10-year KOOS-PS and elevated in treatment responders.
Conclusion: Age at surgery was associated with higher concentrations of pro-inflammatory biomarkers and lower concentrations of anti-inflammatory biomarkers in the synovial fluid prior to meniscal surgery. Anti-inflammatory markers were associated with improved long-term PROs. These findings suggest an age-related intensification of the pro-inflammatory response and inhibition of the anti-inflammatory response that may contribute to long-term functional decline in older patients after meniscus surgery.