Synovial Fluid Biomarkers Can Be Used to Predict the Degree of Articular Cartilage Injury in the Knee

Matthew T. Kingery BA, Amit K. Manjunath BS, David Bloom BA, Elyse Berlinberg BA, Lena Kenny MSc, Eric J. Strauss MD
Department of Orthopedic Surgery, NYU Langone Health, New York, NY
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Normal biomechanics of the knee are disrupted by tears of the meniscus and anterior cruciate ligament (ACL)

These changes can lead to intra-articular inflammation and degenerative joint disease

Synovial fluid biomarkers have the potential to reflect this intra-articular environment and predict which patients are at risk for poor outcomes
The purpose of the current study is to evaluate the accuracy with which clinical information and synovial fluid biomarkers can predict the presence of high-grade cartilage degradation in patients undergoing knee arthroscopy.
Methods

• Inclusion criteria: Patients > 18 years indicated for primary knee arthroscopy

• Synovial fluid samples were collected at the time of surgery and prepared for analysis using a protease inhibitor and stored at -80 degrees C

• Synovial fluid samples were analyzed for 10 pro- and anti-inflammatory biomarker levels using a multiplex bead assay (Milliplex; Millipore, Billerica, MA)

• Biomarkers chosen as known players in joint pain, inflammation and cartilage degeneration
Methods

• Clinical and synovial fluid biomarker data was partitioned into training and test sets.

• A series of logistic regression models were built to predict the presence of high-grade cartilage degradation (ICRS 3 or 4) versus low-grade cartilage degradation (ICRS 1 or 2). The models were validated using repeated k-fold cross-validation.

• The prediction accuracy and quality of the models were compared using likelihood ratio tests.
Results

• 249 patients (mean age: 41.43 +/- 14.02 years) were included in this analysis

• Injuries included:
  – 37 patients (14.86%) had isolated ACL injuries
  – 118 (47.39%) patients had isolated meniscus injuries
  – 76 patients (30.52%) had combined ACL and meniscus injuries
  – 18 patients (7.23%) had focal chondral lesions

• Four logistic regression models were compared (full model, biomarker model, clinical model, stepwise model)

• Stepwise model (6 biomarker variables, age, BMI, and duration of injury) – predicts high-grade ICRS with 83.67% accuracy

• Based on likelihood ratio test and AIC, the model combining a select group of biomarkers in addition to clinical variables was confirmed to be superior to the other models
<table>
<thead>
<tr>
<th></th>
<th>Full Model</th>
<th>Biomarker Model</th>
<th>Clinical Model</th>
<th>Stepwise Model</th>
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<tr>
<td></td>
<td>$\beta$</td>
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<td>$\beta$</td>
<td>P Value</td>
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<td>AIC</td>
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<td>Prediction Accuracy</td>
<td>85.71%</td>
<td>71.43%</td>
<td>71.43%</td>
<td>83.67%</td>
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</tbody>
</table>
Conclusions

• The levels of 6 synovial fluid pro- and anti-inflammatory molecules in combination with clinical variables can be used to accurately distinguish between low-grade and high-grade cartilage degradation in the injured knee.

• This suggests that there are distinct inflammatory phenotypes among different degrees of cartilage damage following knee injury that may have prognostic benefit.

• By better understanding how the intra-articular microenvironment reacts to different stresses, it may be possible to identify distinct molecular targets for therapeutic intervention.
THANK YOU