Transcriptomics of Anterior Shoulder Instability: Differences in Gene Expression in the Blood of Patients With and Without Significant Glenoid Bone Loss

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INTRODUCTION: Currently the measurement of serum or synovial biomarkers does not have a role in diagnosis or monitoring of injury severity in young patients with recurrent anterior shoulder instability. The purpose of this study was to compare gene expression differences in the peripheral blood and tissue of young patients with recurrent anterior shoulder instability with and without significant glenoid bone loss (GBL). Additionally, we sought to determine a peripheral blood transcriptomic biomarker for the reliable delineation of the severity of GBL in anterior shoulder instability patients.
METHODS: All consecutive patients with symptomatic unidirectional anterior shoulder instability undergoing arthroscopic and open shoulder stabilization at a single institution were prospectively enrolled. Blood specimens and shoulder anterior capsular specimens obtained at the time of surgery were compared between patients with significant GBL (≥10%) N=10 and without (<10% GBL) N=7. RNA was extracted and a customized 277-gene expression panel was utilized. Gene expression levels were quantified. Differential expression analysis was performed to identify genes expressed at different levels between patients with and without significant GBL. The expression levels of the subset of genes identified were used to generate a ridge regression model to predict the severity of GBL (<10% or ≥10%).
RESULTS: Seventeen patients were included with a mean age of 26 years (range, 20-41). Seven patients had <10% GBL with a mean 2.3% (range, 0-8) and 10 patients had ≥10% GBL with mean 16.4% (range, 10-25). Nine genes were identified as significantly differentially expressed in the peripheral blood, and five of these IFIT1, IFIT3, IFI44, PRKCB, OAS2 (P values of $1x10^{-5}$, $1x10^{-4}$, $1x10^{-4}$, $1x10^{-4}$, and $6x10^{-4}$) were confirmed using non-parametric tests. No genes in the shoulder capsular specimens were differentially expressed. We developed a model using the 5 genes to accurately predict the severity of GBL. The predictive model had an accuracy of 88% (95% CI of 64% to 99%), a sensitivity of 0.90, a specificity of 0.86, and an area under the receiver operating characteristic (AUROC) curve of 0.99 (95% CI of 95% to 100%).
DISCUSSION AND CONCLUSION: There are significant gene expression differences in the peripheral blood of anterior shoulder instability patients with and without significant (≥10%) GBL. The differential expression of 5 genes allowed development of an accurate predictive model and transcriptomic classifier to predict the severity of GBL. This novel peripheral blood transcriptomic biomarker may assist in tracking glenoid bone loss and injury severity and progression in young patients with recurrent anterior shoulder instability.