Abstract: 1403

Linking Imaging Biomarkers with Underlying Cytokine Expression and Treatment Response in Retinal Vascular Disease?The IMAGINE Study

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Purpose:
Macular edema in diabetes and retinal vein occlusion (RVO) is linked to a complex cytokine profile. The heterogeneity of anti-VEGF response requires a better initial assessment of responders to traditional anti-VEGF therapy versus more anti-inflammatory avenues. This study correlates aqueous cytokines in macular edema in diabetes (DME) and RVO to optical coherence tomography (OCT) and ultra-widefield fluorescein angiography (UWFA). To our knowledge, cytokines have not been assessed in conjunction with higher order outer retinal OCT changes and UWFA metrics.

Methods:
The IMAGINE study performs a post-hoc analysis of aqueous humor cytokine expression, higher order OCT analysis, quantitative UWFA from DAVE (DME) and WAVE (RVO). These were compared to higher order OCT and UWFA findings. Patients were grouped in Super, Early, Late and Nonresponders based on treatment response.

Results:
Twenty-four eyes from DAVE and 26 eyes from WAVE were included. In both groups, VEGF was significantly elevated at baseline. In DME eyes, Super responders had significantly higher VEGF, while Nonresponders had significantly higher LIF, IL-6 and MCP-1 levels. On OCT analysis in eyes with DME, VEGF correlated with central retinal thickness and macular intraretinal fluid index. Panmacular retinal volume correlated with IL-6 and decreased MCP-1, while central intraretinal fluid negatively correlated with PECAM-1. Several cytokines correlated with ellipsoid zone attenuation, including ANGPTL4, LIF. Contrastingly, in RVO eyes, IL-6 was not higher in Nonresponders. VEGF was correlated with intraretinal fluid volume, while angiogenin and TIMP-1 negatively correlated with intraretinal fluid. Additionally, ANG-1 and ANGPTL4 correlated with ellipsoid attenuation. In both cohorts, UWFA leakage correlated with VEGF and ANGPTL4, while IL-6 was specifically associated with leakage in DME. UWFA ischemia was associated with TIMP-1 in DME and ANGPTL4 and VEGF in RVO eyes. Microaneursym count was associated with MCP-4 and PECAM-1 in DME.

Conclusions:
Various cytokines outside of the traditional VEGF pathway correlate to higher order OCT and UWFA metrics. These inflammatory pathways may present future therapeutic targets for treatment. Integrating these can help build the anatomic-biologic bridge and define potential treatment responders and enhance precision-guided decision-making through the use of imaging biomarkers.