

Predicting the Onset of Exudation in Treatment-Naïve Eyes with Nonexudative AMD

- **Nonexudative Macular Neovascularization (MNV) in AMD:**

- Nonexudative MNV can persist for months or years without exudation.
- Risk factors for progression to exudative AMD include the burden of drusen and pigmentary abnormalities.
- Indocyanine green angiography (ICGA) was historically used to identify nonexudative MNV, but swept-source OCT angiography is now comparable and more widely used.

- **Types of MNV:**

- **Type 1 MNV:** Arises from the choriocapillaris, grows through Bruch's membrane (BM), and proliferates between the retinal pigment epithelium (RPE) and BM. Often associated with a double-layer sign (DLS).
- **Type 2 MNV:** Grows through the RPE into the subretinal space and is often associated with exudation.
- **Type 3 MNV:** Arises within the retina from the retinal circulation and is also known as retinal angiomatous proliferation.

- **Predicting Exudation:**

- The onset of exudation in nonexudative MNV remains unpredictable despite advances in imaging techniques.
- Studies have explored various anatomic changes using OCT, such as MNV size and growth, vascular complexity, RPE elevation, choriocapillaris flow deficits, and choroidal thickness, but no reproducible near-term predictors have been identified.
- A recent study suggested that changes in outer retinal thickness might predict exudation, but this was later questioned due to methodological issues (inclusion of DLS/thickness between RPE and BM).

- **Preemptive Anti-VEGF Therapy:**

- Initiating anti-VEGF therapy before exudation has been debated.
- **The PRO-CON and PREVENT trials** found that prophylactic aflibercept or ranibizumab injections every 3 months did not prevent exudation or improve visual acuity outcomes.
- Concerns about lifelong treatment and unnecessary injections in patients who may never develop exudation limit the adoption of preemptive therapy.

- **Blood Flow Velocity as a Predictor:**

- Increased blood flow velocity within treated neovascular lesions has been associated with recurrent exudation.
- Techniques like variable interval scan time analysis (VISTA) and OCT angiography capillary velocimetry could potentially measure these velocities, though commercial availability is limited.

- **Immunologic Basis of Exudation:**

- Complement inhibition (e.g., pegcetacoplan and avacincaptad pegol) has shown an increased incidence of exudation in clinical trials.
- This may involve macrophage switching from M1 (prophagocytic) to M2 (proangiogenic) types, which produce angiogenic growth factors like VEGF.

- **Clinical Implications:**

- Vigilant monitoring of patients with nonexudative MNV is essential due to the potential for exudation.
- Early treatment of exudation improves visual outcomes, but reliable prediction strategies are still needed.
- Home monitoring strategies, such as patient education or home OCT devices, can help identify early signs of exudation in high-risk eyes.