Development and validation of a novel mobility test for rod-cone dystrophies, from reality to virtual reality

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Highlights

•Traditional visual function tests don't fully capture patients' real-life visual deficits; performance-based outcomes are essential.
•This study validated a novel functional vision outcome, a mobility task, for tracking disease progression and treatment efficacy in rod-cone dystrophies, under both real and virtual conditions.
•This new outcome offers high reproducibility, sensitivity, construct validity, and content validity.
•This useful tool opens new possibilities for measuring disease progression and therapeutic benefit in rod-cone dystrophies.

PURPOSE:

To determine if AMD family history and genetic variants identify eyes at higher risk for progression to advanced AMD (AAMD), after controlling for baseline demographics, behavioral factors, and macular status.

DESIGN:

Prospective, longitudinal cohort study

METHODS:

Eyes with non-advanced AMD at baseline in AREDS were classified using the AREDS severity scale. Non-genetic and genetic predictors for progression to AAMD, geographic atrophy (GA) and neovascular disease (NV) were evaluated. Cox proportional hazards models using the eye as the unit of analysis were used to calculate hazard ratios (HR), accounting for correlated data. Discrimination between progressing and non-progressing eyes was assessed using C-statistics and Net Reclassification Improvement (NRI).

Dark adaptation thresholds were measured binocularly with Metrovision MonPackOne (MetroVision, Perenchies, France) after 5 and 20 minutes of dark adaptation.

RESULTS:

Among 4910 eyes, 863 progressed to AAMD over 12 years. Baseline AMD severity scale and status of the fellow eye were important predictors; genes provided additional discrimination. Family history of

AMD also independently predicted progression after accounting for genetic and other covariates: 1 family member vs. none (HR = 1.21, 95% CI: 1.02, 1.43; P = 0.03); ≥ 2 family members vs. none (HR= 1.55, 95% CI: 1.26, 1.90; P < 0.001). A composite risk score calculated using beta estimates of non-genetic and significant genetic factors predicted progression to AAMD (HR = 5.57, 90th vs. 10th percentile; AUC=0.92), providing superior fit versus other models with only ocular (NRI = 0.34, P < 0.001, AUC=0.87) or non-genetic variables (ΔAUC=0.05±0.005,P<0.001)����=0.05±0.005,<0.001). An online risk calculator is available.

CONCLUSION:

Genetic variants and family history provided additional discrimination for AAMD prediction, after accounting for ocular and other covariates.