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An Updated Simplified Severity Scale for Age-Related Macular Degeneration, Incorporating Reticular Pseudodrusen: Age-Related Eye Disease Study Report No. 42

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Abstract

Purpose

To update the Age-Related Eye Disease Study (AREDS) Simplified Severity Scale for risk of late age-related macular degeneration (AMD), including incorporation of reticular pseudodrusen (RPD), and to perform external validation on the AREDS2.

Design

Post hoc analysis of two clinical trial cohorts: AREDS and AREDS2.

Participants

Participants with no late AMD in either eye at baseline in AREDS (n=2719) and AREDS2 (n=1472).

Methods

Five-year rates of progression to late AMD were calculated according to levels 0-4 on the Simplified Severity Scale, following two updates: (i) non-central GA considered part of the outcome rather than a risk feature, and (ii) scale separation according to RPD status (determined by validated deep learning grading of color fundus photographs).

Main outcome measures:Five-year rate of progression to late AMD (defined as neovascular AMD or any GA).

Results

In the AREDS, following the first scale update, the five-year rates of progression to late AMD for levels 0-4 were 0.3%, 4.5%, 12.9%, 32.2%, and 55.6%, respectively. Following both updates, the proportion progressing to late AMD by five years was 8.4% in participants without RPD and 40.6% in those with RPD. As the final Simplified Severity Scale, the five-year progression rates for levels 0-4, respectively, were 0.3%, 4.3%, 11.6%, 26.7%, and 50.0%, for participants without RPD at baseline, and 2.8%, 8.0%, 29.0%, 58.7%, and 72.2%, for participants with RPD at baseline. In external validation on the AREDS2, for levels 2-4, the progression rates were similar, at 15.0%, 27.7%, and 45.7% (RPD absent) and 26.2%, 46.0%, and 73.0% (RPD present), respectively.

Conclusions

The AREDS AMD Simplified Severity Scale has been modernized with two important updates. The new scale for individuals without RPD has five-year progression rates of ~0.5%, 4%, 12%, ~25%, and 50%, such that the rates on the original scale remain accurate. The new scale for individuals with RPD has five-year progression rates of 3%, 8%, ~30%, ~60%, and ~70%, i.e., approximately double for most levels. This scale fits updated definitions of late AMD, has increased prognostic accuracy, appears

generalizable to similar populations, but remains simple for broad risk categorization.

Abbreviations:

AMD (age-related macular degeneration), AREDS (Age-Related Eye Disease Study), AUROC (area under the receiver operating characteristic), CFP (color fundus photograph), cRORA (complete retinal pigment epithelial and outer retinal atrophy), FAF (fundus autofluorescence), GA (geographic atrophy), iRORA (incomplete retinal pigment epithelial and outer retinal atrophy), OCT (optical coherence tomography), RPD (reticular pseudodrusen), SDD (subretinal drusenoid deposit)

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Conflicts of interest

No conflicting relationship exists for any author.

The AREDS Age-Related Macular Degeneration Severity Scale and associated five-year rates of progression to late disease have been modernized to include reticular pseudodrusen and to fit updated definitions of late age-related macular degeneration.

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