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ARVO Annual Meeting Abstract | June 2022

A polygenic risk score predicts functional progression in early primary open-angle glaucoma

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Investigative Ophthalmology & Visual Science June 2022, Vol.63, 4011 – A0353. doi:

Abstract

Purpose : Irreversible vision loss from primary open-angle glaucoma (POAG) can be prevented through timely diagnosis and treatment, although definitive diagnosis can be difficult in early-stage disease. As a consequence, large numbers of glaucoma suspects require regular monitoring, even though many low-risk suspects may never develop disease, and other high-risk suspects may have delayed or inadequate treatment. Given that POAG is one of the most heritable common diseases, unique opportunities exist to employ genetic instruments in risk-stratified screening, diagnosis and treatment of early glaucoma.

Methods : Here we assessed the impact of glaucoma polygenic risk on early glaucoma progression, using clinical and genetic data from a prospective longitudinal cohort study in individuals of predominantly European ancestry (PROGRESSA). A total of 1,605 eyes from 829 early manifest glaucoma cases or glaucoma suspects had sufficient data for visual field progression analyses using serial 24-2 Humphrey visual fields, with a glaucoma polygenic risk score (PRS) derived from genotyping array data on all 829 participants.

Results : Individuals in the top 5% glaucoma PRS risk group were at a higher risk of visual field progression compared to the remaining 95% after 5 years (HR 1.5, 95%CI 1.13–1.97, P=.005). Conversely, those in the bottom 20% PRS risk group were at a lower risk of visual field progression compared to an intermediate risk group over 3 years (HR 0.52, 95% CI

0.28–0.96, P=.038).

Conclusions : High polygenic risk was associated with more rapid visual field progression in early manifest glaucoma cases and glaucoma suspects. A PRS may serve as a valuable adjunct to identify individuals who stand to benefit the most from more frequent surveillance, and earlier or more intensive treatment.

This abstract was presented at the 2022 ARVO Annual Meeting, held in Denver, CO, May 1-4, 2022, and virtually.

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