

Glaucoma Risk Alleles in the Ocular Hypertension Treatment Study

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PURPOSE: Primary open-angle glaucoma (POAG) is a major cause of blindness and visual disability. Several genetic risk factors for POAG and optic nerve features have been identified. We measured the relative risk for glaucoma that these factors contribute to participants in the Ocular Hypertension Treatment Study (OHTS) .

DESIGN: Comparative series.

PARTICIPANTS: One thousand fifty-seven of 1636 participants (65%) of the OHTS were enrolled in this genetics ancillary study.

METHODS: Samples of DNA were available from 1057 OHTS participants. Of these, 209 developed POAG (cases) and 848 did not develop glaucoma (controls) between 1994 and 2009. The frequencies of 13 risk alleles previously associated with POAG or with optic disc features in other cohorts were compared between POAG cases and controls in the OHTS cohort using analyses of variance. The 2 largest subgroups, non-Hispanic whites (n = 752; 70.7%) and blacks (n = 249, 23.7%) , also were analyzed separately. The probability of glaucoma developing over the course of the OHTS was compared between participants stratified for transmembrane and coiled-coil domains 1 (TMCO1) risk alleles using Kaplan-Meier and Cox proportional hazards analyses.

MAIN OUTCOME MEASURES: Association of POAG with known genetic factors.

RESULTS: No association was detected between the known POAG risk alleles when the OHTS cohort was examined as a whole. However, in the subgroup of non-Hispanic whites, allele frequencies at the TMCO1 locus were statistically different between cases and controls (P = 0.00028) . By 13 years, non-Hispanic white participants with TMCO1 risk alleles had a 12% higher cumulative frequency of glaucoma developing than participants with no TMCO1 risk alleles. Moreover, the Cox proportional hazard analysis demonstrated that

TMCO1 alleles increased relative risk comparable with that of some previously analyzed clinical measures (i.e., intraocular pressure) .

CONCLUSIONS: The size of the OHTS cohort and its composition of 2 large racial subgroups may limit its power to detect some glaucoma risk factors. However, TMCO1 genotype was found to increase the risk of glaucoma developing among non-Hispanic whites, the largest racial subgroup in the OHTS cohort, at a magnitude similar to clinical predictors of disease that long have been associated with glaucoma.

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