Baseline Risk Factors for the Development of Primary Open-angle Glaucoma in the Ocular Hypertension Treatment Study

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PURPOSE: Higher baseline pattern standard deviation (PSD) and larger vertical cup-to-disk ratio (VC/D) were factors in the predictive model for the development of primary open-angle glaucoma (POAG) in the Ocular Hypertension Treatment Study. Because early changes in PSD and VC/D may be indicative of early POAG damage, we repeated the prediction model excluding PSD and VC/D.

DESIGN: Reanalysis of baseline factors for the development of POAG.

METHODS: We compared the hazard ratios for baseline factors predictive of POAG in the multivariate Cox proportional hazards model that included PSD and VC/D and in the model that excluded them.

RESULTS: Hazard ratios for baseline factors predictive of POAG in Ocular Hypertension Treatment Study were not substantially affected by the inclusion or exclusion of PSD and VC/D in the proportional hazards model.

CONCLUSION: Whether PSD or VC/D was included in the Cox proportional hazards model, the same baseline factors were statistically significant and their hazard ratios were essentially similar. (Am J Ophthalmol 2004;138: 684–685. © 2004 by Elsevier Inc. All rights reserved.)

RECENTLY, WE REPORTED ON BASELINE FACTORS THAT were predictive for developing primary open-angle glaucoma (POAG) in the Ocular Hypertensive Treatment Study.[1] The predictive model included baseline pattern standard deviation (PSD) and vertical cup-to-disk ratio (VC/D) in addition to age, intraocular pressure, central corneal thickness, and diabetes. However, early changes in PSD and VC/D may be indicative of early POAG damage. An accepted paradigm in epidemiology is that risk factor models should not include covariates or factors that are involved in the definition of the outcome. Ocular Hypertension Treatment Study used the term "predictive" model and not "risk" model, because our goal was to identify baseline measures, including visual field indices and VC/D, that would be available to clinicians and be useful in the management of ocular hypertensive individuals. A true risk factor model includes factors in the causal pathway for disease and does not include factors that may be involved in the determination of the disease. Therefore, we repeated analyses excluding PSD and VC/D.

The study design, baseline population characteristics, and statistical analyses for Ocular Hypertension Treatment Study are described in detail elsewhere.[1–3] Briefly, 817 participants with untreated intraocular pressures of 24 to 32 mm Hg in at least one eye and 21 to 32 mm Hg in the fellow eye along with normal visual fields and optic nerves were randomized to the treatment group, and 819 participants were randomized to the observation group. The treatment goal was to reduce baseline intraocular pressure by 20% or more. The outcome for the study was a reproducible visual field and/or optic nerve abnormality consistent with glaucoma. There were 148 POAG endpoints first detected by June 1, 2002, that were confirmed with additional data by September 11, 2003. We calculated the hazard ratios for baseline factors predictive of POAG in the multivariate Cox proportional hazards model that included baseline PSD and VC/D and a model that excluded them. Agreement between the models was estimated by correlating the solution vector for each participant calculated from each model.

TABLE 1. Hazard Ratios for Baseline Factors Predictive of Primary Open-angle Glaucoma

Baseline Factor	Model Including PSD, VC/D	Model Excluding PSD, VC/D
Age (decade)	1.25 (1.04,1.49)	1.29 (1.09,1.53)
IOP (mm Hg)	1.11 (1.05,1.18)	1.10 (1.04,1.17)
CCT (per 40 μ decrease)	1.82 (1.51,2.19)	1.92 (1.60,2.30)
History of diabetes mellitus	0.35 (0.15,0.78)	0.38 (0.17,0.86)
PSD (per 0.2 dB)	1.25 (1.06,1.48)	Excluded
VC/D (per 0.1)	1.32 (1.20,1.45)	Excluded

CCT = central corneal thickness; IOP = intraocular pressure; PSD = pattern standard deviation; VC/D = vertical cup-to-disk ratio.

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Hazard ratios from the multivariate Cox proportional hazards models with and without PSD and VC/D were similar (Table 1). Age and central corneal thickness were slightly stronger in the risk factor model excluding PSD and VC/D compared with the predictive model including PSD and VC/D. The correlation coefficient between the solution vectors of each model calculated for each participant was 0.80.

The risk factor model that does not include PSD and VC/D may be more useful to clinicians who want to assess the risk of developing POAG in an ocular hypertensive individual. The inclusion of PSD and VC/D in the statistical model may overestimate the risk of POAG, because changes in these measures may be markers for early POAG damage. The statistical model that excludes PSD and VC/D calculates the risk of POAG from factors that affect susceptibility to disease, i.e., age. Whether PSD or VC/D is included in the proportional hazards model, the statistically significant factors in both models (age, intraocular pressure, central corneal thickness, and diabetes mellitus) were the same.

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