Title

Ganglion cell and retinal nerve fiber layer thickness predict the development of visual field damage in glaucoma suspects

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Retinal Nerve Fiber Layer Thickness Measurements With Scanning Laser Polarimetry Predict Glaucomatous Visual Field Loss

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• PURPOSE: To assess whether baseline retinal nerve fiber layer (RNFL) measurements obtained with a scanning laser polarimeter, the GDx Nerve Fiber Analyzer, (Laser Diagnostic Technologies Inc., San Diego, California) are predictive of development of repeatable glaucomatous visual field damage in glaucoma suspect eyes.
• DESIGN: Cohort study.
• METHODS: Participants were recruited from the UCSD longitudinal Diagnostic Innovations in Glaucoma Study (DIGS). One eye from each of 160 glaucoma suspects with normal standard automated perimetry (SAP) visual fields at baseline was studied. Study eyes were divided into convert and nonconvert groups based on the development of three consecutive glaucomatous visual fields during follow-up. SLP parameters, IOP, vertical cup disk ratio, stereophotograph assessment as glaucoma or normal, corneal thickness, and visual field indices were included in univariate and multivariate Cox proportional hazards models to determine which SLP RNFL and ocular parameters were predictive of visual field conversion.
• RESULTS: Sixteen (10%) eyes developed repeatable visual field damage (converts) and 144 (90%) did not (nonconverts). Mean (95%CI) follow-up time until visual field conversion for convert eyes was 2.7 (1.7, 3.6) years. Mean total follow-up of nonconvert eyes was 3.8 (3.5, 4.1) years. Four out of thirteen examined baseline SLP parameters and baseline SAP Mean Deviation (MD), SAP Pattern Standard Deviation (PSD), and glaucomatous stereophotograph assessment were significant univariate predictors of visual field conversion. In multivariate models adjusted for age, IOP and CCT, SLP parameters inferior ratio, ellipse modulation, and UCSD linear discriminant function (LDF) were significant predictors of visual field conversion. When SAP PSD and stereophotograph assessment were also included in the multivariate model inferior ratio and UCSD LDF remained independently predictive of visual field loss.
• CONCLUSIONS: Thinner baseline SLP RNFL measurements were independent predictors of visual field damage. In addition to thinner SLP RNFL measurements, higher baseline SAP PSD, and baseline glaucomatous stereophotograph assessment each contributed to an increased risk of the development of abnormal visual fields in glaucoma suspect patients. SLP RNFL measurements were independently predictive of future visual loss even when age, IOP, CCT, vertical cup disk ratio, and SAP PSD were included in the model. (Am J Ophthalmol 2004;138:592–601. © 2004 by Elsevier Inc. All rights reserved.)

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BY THE TIME GLAUCOMATOUS VISUAL FIELD LOSS IS detected by standard automated perimetry (SAP), there may be a loss of a significant percentage of retinal ganglion cells.[1,2] Using photography and computer-assisted optical imaging techniques, optic disk damage in glaucoma suspects has been observed before the development of visual field defects measured by standard achromatic perimetry.[2,3] Additionally, one study using photography to evaluate the optic disk and RNFL, indicated that RNFL damage precedes optic disk damage, suggesting that the condition of the RNFL might be a more sensitive indicator of glaucoma than optic disk topography.[4]

Scanning laser polarimetry (SLP) is an optical imaging technology developed to diagnose and monitor glaucoma by

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measuring RNFL thickness.[5,6] Scanning laser polarimetry has been shown to provide reproducible RNFL measurements in human eyes[7–10] and to differentiate glaucoma patients from normal-individuals with sensitivities and specificities between 72% to 78%, and 56% to 92%, respectively.[6,11–16] Some studies have shown that decreased RNFL thickness measurements are associated with increased age, as expected from histopathologic age-related RNFL loss,[5,17,18] and that RNFL thickness measurements decrease over time in normal-pressure glaucoma.[19] However, no information currently is available on the predictive value of SLP RNFL measurements for development of glaucomatous visual field loss.

The purpose of this study was to determine the predictive value of baseline SLP RNFL measurements in glaucoma-suspect eyes for development of repeatable SAP visual field loss.

METHODS

• **SUBJECTS:** One randomly selected eye from each of 160 patients prospectively enrolled in the longitudinal Diagnostic Innovations in Glaucoma Study (DIGS) at the Hamilton Glaucoma Center of the University of California, San Diego, was included. Participants were glaucoma suspects defined by suspicious appearing optic disks by clinical examination, and/or elevated intraocular pressure according to a glaucoma expert (RNW). All patients had a normal (Glaucoma Hemifield Test and pattern standard deviation within normal limits) baseline SAP visual field test at the time of SLP testing with the GDx Nerve Fiber Analyzer (Laser Diagnostic Technologies, San Diego, California, USA). Additionally, participants could not have had repeatable glaucomatous SAP visual field loss before their baseline SLP examination.

All subjects underwent a complete ophthalmologic examination, including slit lamp biomicroscopy, intraocular pressure (IOP) measurement, dilated stereoscopic fundus examination, and visual field testing before imaging with scanning laser polarimetry. All eyes had open angles, best corrected visual acuity of 20/40 or better, sphere within ±5.0 diopters, and cylinder within ±3.0 diopters. Eyes with co-existing retinal disease, uveitis, or nonglaucomatous optic neuropathy were excluded. All included subjects were older than 40 years at baseline.

The study population was divided into two groups based on the development of the primary outcome measure, repeatable visual field loss. The first group was visual field convert patients who developed three consecutive glaucomatous SAP visual field results during follow-up. The second group was visual field nonconvert patients who did not develop 3 consecutive glaucomatous visual field results. A glaucomatous SAP visual field was defined as having a glaucoma hemifield test (GHT) outside normal limits and/or a pattern standard deviation (PSD) with $P \leq .05$. The glaucomatous visual field damage was repeated by the same criteria, a repeatable GHT or PSD outside normal limits, on the three visual field tests.

All patients had visual field testing within 1 year of their baseline SLP scan with the mean (±SD) time between these examinations of 0.50 ± 2.86 months. Participants did not have confirmed visual field loss for at least 1 year after enrollment.

Informed consent was obtained from each participant, and the University of California San Diego Human Research Protection Program approved all methodology. All methods adhered to the Declaration of Helsinki for research involving human subjects.

• **INSTRUMENTATION: SCANNING LASER POLARIMETRY:** The GDx Nerve Fiber Analyzer, a confocal scanning diode coupled with an integrated polarization modulator, was used to measure retardation of light that double-passed the birefringent fibers of the RNFL. Details of this instrument, which uses the fixed method of corneal compensation, and descriptions of parameters, have been provided elsewhere.[5,20,21]

Three scans (approximately 15-degree field of view) centered on the optic disk were obtained for each eye at baseline. Individual scans were included if assessed as good quality by one grader (K.M.) based on the Rotterdam GDx Course.[22] A mean image composed of two or three good-quality individual scans was created using SLP software. If only one good-quality scan existed for an eye on a specific date, the single image was used. Good-quality mean images required even illumination, clear focus, and good alignment with the absence of vessel doubling and motion artifacts. If good alignment of three images was not possible using the manual alignment feature of the software, mean images were made with the two images that aligned best. In addition, eyes were reviewed to detect a phase-shifted retardation pattern showing thicker RNFL in the nasal and temporal regions than in the superior and inferior regions (as is expected based on histology). This retardation pattern is observed among eyes in which the SLP fixed corneal birefringence compensation inadequately compensates anterior segment retardation.[23] No eyes exhibiting this retardation pattern were identified. The optic disk margin was outlined on the mean retardation (or single best) image. For patients with peripapillary atrophy, the disk margin contour line was enlarged to keep the SLP measurement ellipse outside of the area of peripapillary atrophy. Mean images with enough peripapillary atrophy to cause the contour line to be enlarged greater than 30% were excluded from the study. One eye was excluded because of the presence of a large zone parapillary atrophy. Corneal curvature (k) values and spherical equivalent values were entered in the SLP software for each mean (or single best) image.

The predictive value for visual field conversion was investigated for the following 12 parameters, automatically

TABLE 1. Baseline Demographic and Ocular Factors for Convert Eyes and Non-convert Eyes

	Convert Eyes (n = 16)	Non-convert Eyes (n = 144)	*P* Value
Age at baseline (yrs.)*	66.3 (61.1, 71.5)	62.5 (60.8, 64.2)	.17
	median = 68.1	median = 62.5	
Follow-up (years)*	2.7 (1.7, 3.6)	3.8 (3.5, 4.1)	.004
	median = 2.7	median = 3.5	
Gender (%Female)**	44%	60%	.20
Ethnicity (% Caucasian)**	88%	92%	.34
Baseline IOP (mm Hg)*	19.1 (16.3, 21.9)	22.0 (21.0, 22.9)	.06
	median = 18.0	median = 22.0	
IOP treatment at baseline**	56%	34%	.08
IOP treatment at baseline or during follow-up**	94%	58%	.005
Stereophoto assessment (% glaucomatous)**	88%	47%	.002
Stereophoto VCDR*	0.65 (0.54, 0.75)	0.56 (0.53, 0.60)	.13
	median = 0.68	median = 0.63	
SAP MD (dB)*	−1.46 (−2.12, −0.80)	−0.32 (−0.54, −0.10)	.001
	median = −1.41	median = −0.27	
SAP PSD (dB)*	2.02 (1.87, 2.17)	1.71 (1.66, 1.76)	.0002
	median = 2.11	median = 1.65	
Corneal thickness (μm)*	556.2 (538.3, 574.1)	567.0 (561.0, 572.9)	.26
	median = 549.3	median = 565.7	

*Mean (95% CI)-*P* value based on T-test (follow-up consisted of time to conversion for convert eyes and total follow-up time for non-convert eyes).

**Mean %-*P* value based on chi-square

calculated by SLP software (version 2.0.01): maximum modulation, ellipse modulation, inferior-nasal ratio, superior-nasal ratio, inferior ratio, superior ratio, inferior average, average thickness, ellipse average, superior average, inferior maximum, and superior maximum. In addition, the predictive value of a discriminant analysis model (UCSD linear discriminant function, UCSD LDF) proposed by Weinreb and associates[6] [LDF = −4.442655 − (0.156 × average thickness) + (0.935 × ellipse modulation) + (0.183 × ellipse average)] was examined. For this parameter, lower values indicate increased likelihood of glaucoma.

• **VISUAL FIELD TESTING:** Visual field testing was performed using either the 24-2 full-threshold or Swedish Interactive Thresholding Algorithm (SITA) test strategies with the Humphrey Visual Field Analyzer (Carl Zeiss Meditec, Dublin, California, USA). All visual field tests were reliable (≤30% false positives, false negatives, fixation losses). Baseline SAP mean deviation (MD) and PSD were assessed as predictors for future visual field conversion. For converts, follow-up time was defined as the number of years from baseline SLP image to the first of the three consecutive abnormal visual fields that defined conversion. For nonconverts, follow-up time was defined as the number of years from baseline SLP image to last visual field test.

• **STEREOPHOTOGRAPHS:** Simultaneous stereophotographs were obtained using a Topcon camera (TRC-SS; Topcon Instrument Corporation of America, Paramus, New Jersey, USA) after maximal pupil dilation. All photographic evaluations were performed using a stereoscopic viewer (Asahi Pentax Stereo Viewer II; Asahi Optical Co., Tokyo, Japan) with a standard fluorescent light-box. At least two experienced graders, masked to patient identification and diagnosis, reviewed each photograph independently for classification as glaucomatous or normal. Classification as glaucomatous was based on the presence of neuroretinal rim thinning, glaucomatous excavation, RNFL defect or asymmetrical optic disks (asymmetry of vertical cup-disk ratio <0.2). Disagreements in grading were resolved by adjudication by a third grader. Two graders estimated the maximum optic cup-to-disk ratio within 45 degrees of vertical. The mean of these two estimates was included as the predictor variable vertical cup-to-disk ratio (VCDR). All included patients had stereophotograph assessment ("glaucoma" vs "normal") within 1 year of the baseline SLP test date.

TABLE 2. Univariate Hazard Ratios for Visual Field Conversion

Predictive Baseline Factors	Hazard Ratio (95% CI)	*P* Value
13 SLP Parameters		
Superior maximum per 10 μm thinner	0.89 (0.63, 1.27)	.53
Inferior maximum per 10 μm thinner	1.17 (0.81, 1.67)	.40
Ellipse average per 10 μm thinner	0.93 (0.52, 1.65)	.93
Average thickness per 10 μm thinner	0.73 (0.43, 1.22)	.23
Superior average per 10 μm thinner	0.94 (0.59, 1.49)	.79
Inferior average per 10 μm thinner	0.84 (0.55, 1.26)	.39
Superior ratio per .1 units lower	1.11 (1.01, 1.23)	.03
Inferior ratio per .1 units lower	1.18 (1.06, 1.30)	.002
Superior-nasal ratio per .1 units lower	1.10 (0.94, 1.29)	.23
Inferior-nasal ratio per .1 units lower	1.16 (1.00, 1.35)	.06
Ellipse modulation per .1 units lower	1.12 (1.04, 1.21)	.004
Maximum modulation per .1 units lower	1.10 (0.99, 1.23)	.08
UCSD LDF per .1 units lower	1.11 (1.05, 1.05)	.0001
Baseline Demographic and Ocular Factors		
Age at baseline per 1 year older	1.04 (0.99, 1.09)	.14
IOP per 1 mmHg higher	0.90 (0.81, 0.99)	.03
SAP (full threshold) MD per 1 dB lower	1.95 (1.33, 2.86)	.0001
SAP (full threshold) PSD per 0.1 dB higher	1.38 (1.18, 1.62)	<.0001
Stereophotograph assessment glaucoma (y/n)	8.10 (1.84, 35.71)	.006
Stereophoto VCDR per .1 units higher	1.28 (0.97, 1.71)	.09
Corneal thickness per 40 μm thinner	1.41 (0.80, 2.51)	.24

• **OTHER OCULAR PARAMETERS:** Central corneal thickness measurements were obtained for all patients using ultrasound pachymetry (Pachette GDH 500; DGH Technology, Philadelphia, Pennsylvania, USA). The mean of three measurements was used in the analysis. Baseline IOP readings were obtained using Goldmann applanation tonometry (Haag-Streit, Köniz, Switzerland),

• **STATISTICAL ANALYSIS:** Cox proportional hazards models, using the PHREG procedure of the SAS statistical software (SAS Institute Inc, Cary, North Carolina, USA), were used to evaluate which factors were associated with development of repeatable glaucomatous visual field damage. These factors included baseline measurements of 13 SLP parameters (12 provided software and UCSD LDF) in addition to age and closest to SLP-baseline measurements of IOP, SAP MD, SAP PSD, corneal thickness, stereophotograph VCDR, and stereophotograph assessment (glaucoma vs normal). Both univariate and multivariate hazard ratios (95% CI) for developing repeatable glaucomatous visual field damage were calculated. For the multivariate models, hazard ratios were calculated after adjustment for age, baseline IOP, and CCT. These variables have been reported to be significantly associated with the risk of development of glaucomatous visual field loss among patients with ocular hypertension or glaucoma suspects.[24,25] Adjusted hazard ratios after inclusion of SAP PSD and stereophotograph assessment in the multivariate models are also provided.

The data met the proportional hazards assumption as tested by plotting Schoenfeld residuals against time. The Cox proportional hazards model assumes that the effect of each tested covariate on an individual's hazard function is the same at all points in time.[26,27] Statistical significance was defined as $P \leq .05$.

RESULTS

BASELINE DEMOGRAPHIC AND OCULAR DATA ARE PRESENTED in Table 1. Sixteen patients (10%) developed visual field loss during follow-up (converts), and 144 eyes did not (nonconverts). Baseline mean (95%CI) age of convert patients was 66.3 (61.1, 71.5) years compared with 62.5 (60.8, 64.2) years for nonconverts ($P = .17$). Mean follow-up before visual field conversion was 2.7 (1.7, 3.6) years for converts compared with 3.8 (3.5, 4.1) years total follow-up for nonconverts ($P = .004$). Ninety-four percent of convert eyes received IOP lowering treatment during the study compared with 58% of nonconvert eyes ($P = .005$). Baseline stereophotograph assessment was glaucomatous for 88% of convert eyes compared with 47% of nonconvert eyes ($P = .003$). Baseline mean SAP MD was −1.46 dB (−2.12, −0.80) for convert eyes and −0.32 dB

TABLE 3. Multivariate Hazard Ratios for Visual Field Conversion*

Predictive Baseline Factors	Hazard Ratio (95% CI)	*P* Value
13 SLP Parameters		
Superior maximum per 10 μm thinner	0.90 (0.64, 1.28)	.57
Inferior maximum per 10 μm thinner	1.18 (0.82, 1.69)	.38
Ellipse average per 10 μm thinner	1.00 (0.56, 1.77)	.99
Average thickness per 10 μm thinner	0.82 (0.48, 1.40)	.46
Superior average per 10 μm thinner	1.04 (0.65, 1.66)	.86
Inferior average per 10 μm thinner	1.25 (0.82, 1.90)	.30
Superior ratio per .1 units lower	1.09 (0.99, 1.21)	.09
Inferior ratio per .1 units lower	1.16 (1.04, 1.28)	.007
Superior-nasal ratio per .1 units lower	1.08 (0.91, 1.28)	.40
Inferior-nasal ratio per .1 units lower	1.17 (0.99, 1.38)	.07
Ellipse modulation per .1 units lower	1.10 (1.09, 1.19)	.02
Maximum modulation per .1 units lower	1.07 (0.95, 1.21)	.29
UCSD LDF per .1 units lower	1.09 (1.03, 1.15)	.004
Baseline Demographic and Ocular Factors		
Age at baseline per 1 year older	1.04 (0.99, 1.09)	.15
IOP per 1 mmHg higher	0.90 (0.81, 0.99)	.05
SAP (full threshold) MD per 1 dB lower	1.95 (1.30, 2.95)	.001
SAP (full threshold) PSD per 0.1 dB higher	1.34 (1.14, 1.58)	<.0001
Stereophotograph assessment glaucoma (y/n)	6.3 (1.41, 28.6)	.02
Stereophoto VCDR per .1 units higher	1.20 (0.89, 1.60)	.23
Corneal thickness per 40 μm thinner	1.17 (0.65, 2.11)	.61

*Multivariate model adjusts for age, IOP, and CCT.

(−0.54, −0.10) for nonconvert eyes ($P = .001$). Baseline mean SAP PSD was 2.02 (1.87, 2.17) for convert eyes and 1.71 (1.66, 1.76) for nonconvert eyes ($P < .0001$). The mean frequency of visual field testing for the converts and nonconverts was every 6 months and every 8 months, respectively. Gender, ethnicity, intraocular pressure (IOP), stereophotograph VCDR, and corneal thickness were not significantly different among converts and nonconverts at baseline.

Univariate hazard ratios for 13 SLP parameters (12 software provided plus UCSD LDF) and 7 baseline demographic and ocular factors are presented in Table 2. Thinner (i.e., the direction predicted by glaucoma) RNFL measurements in 4 out of 13 SLP parameters were significant univariate baseline predictors of future visual field conversion when $\alpha = 0.05$. IOP, SAP MD, SAP PSD and stereophotograph assessment were also significant univariate predictors of visual field conversion. Nine of 13 SLP parameters, stereophotograph vertical cup-to-disk ratio, and corneal thickness were not significant univariate baseline predictors, although some were borderline (all $P \geq .09$).

Because the ethnic makeup of the convert eyes and nonconvert eyes was very similar and for the most part Caucasian, ethnicity was not included as one of the candidate predictors of visual field conversion in this study.

Table 3 shows hazard ratios for each variable after adjustment for age, IOP and CCT. In multivariate analysis, the SLP parameters inferior ratio, ellipse modulation, and UCSD LDF were significant predictors of visual field conversion. When multivariate analysis was performed forcing the inclusion of SAP PSD along with age, IOP, and CCT, the only SLP parameter that retained statistical significance was inferior ratio (adjusted hazard ratio = 1.14 for 0.1 U lower; 95% CI: 1.02 to 1.27; $P = .021$). When stereophotograph assessment was included in the multivariate models in place of SAP, the SLP parameters inferior ratio (adjusted hazard ratio = 1.13/0.1 U lower; 95% CI: 1.01 to 1.25; $P = .032$) and UCSD LDF (Adjusted hazard ratio = 1.07/0.1 U lower; 95% CI: 1.004 to 1.13; $P = .035$) were significant predictors of future glaucomatous visual field loss.

For illustrative purposes, three SLP parameters that had significantly predictive power in the multivariate analyses were categorized into dichotomous variables. The 25% (or lowest quartile) value was chosen arbitrarily as a cut-off point for categorization. Kaplan-Meier survival curves are presented in Figure 1 for UCSD LDF, inferior ratio, and ellipse modulation. Twenty-five percent cut-offs for these variables were −0.78, 1.73, and 1.84, respectively.

Figure 1A shows the cumulative probability (Kaplan-Meier analysis) of developing visual field abnormality in

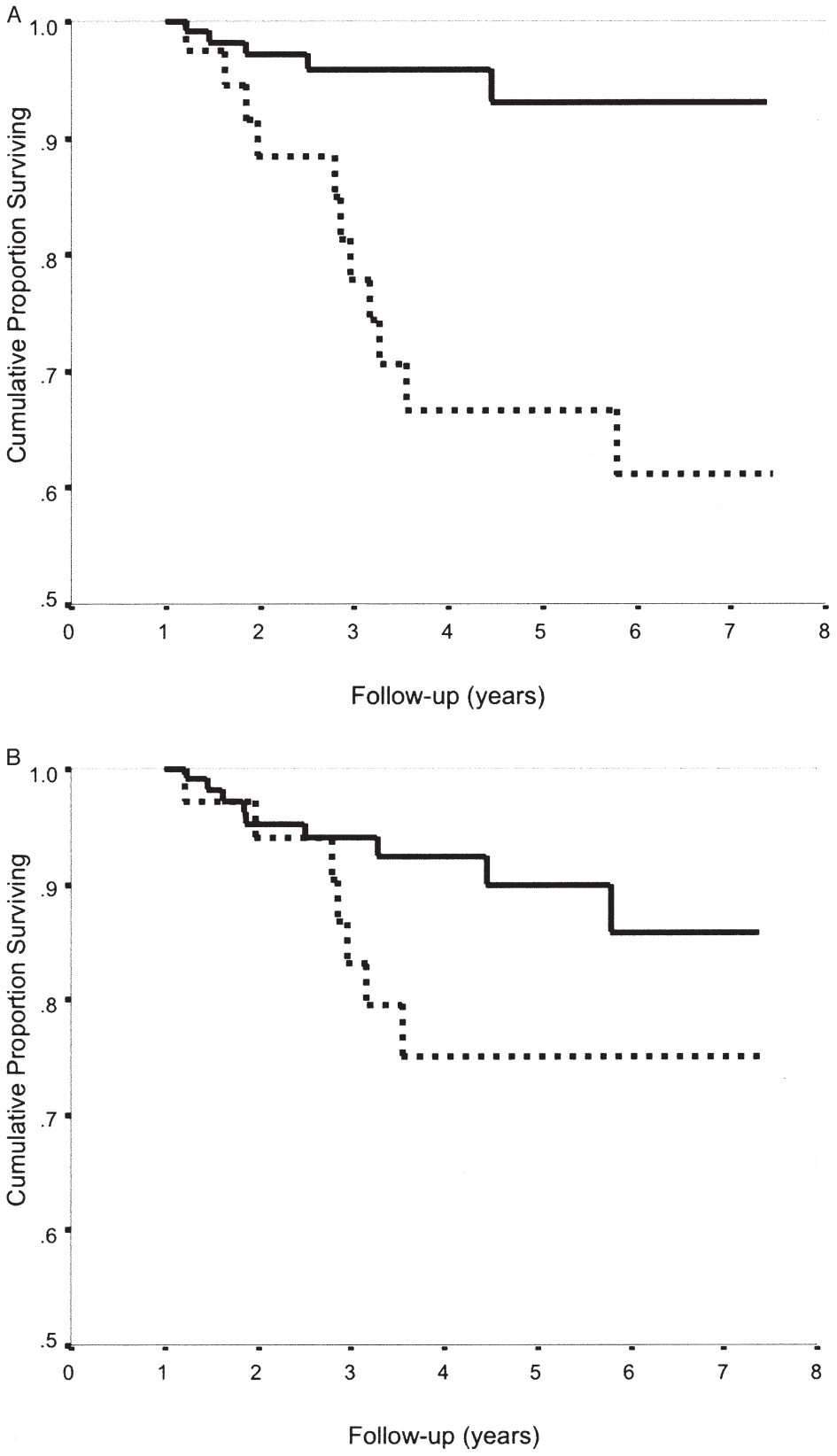

FIGURE 1. (A) Kaplan-Meier survival curves for the subjects with SLP UCSD LDF in the lowest quartile (1/4) (dashed line) compared with the subjects with UCSD LDF in the upper three quartiles (3/4) (continuous line). (B) Kaplan-Meier survival Curves for the subjects with SLP inferior ratio in the lowest quartile (1/4) (dashed line) compared with the subjects with inferior ratio in the upper three quartiles (3/4) (continuous line).

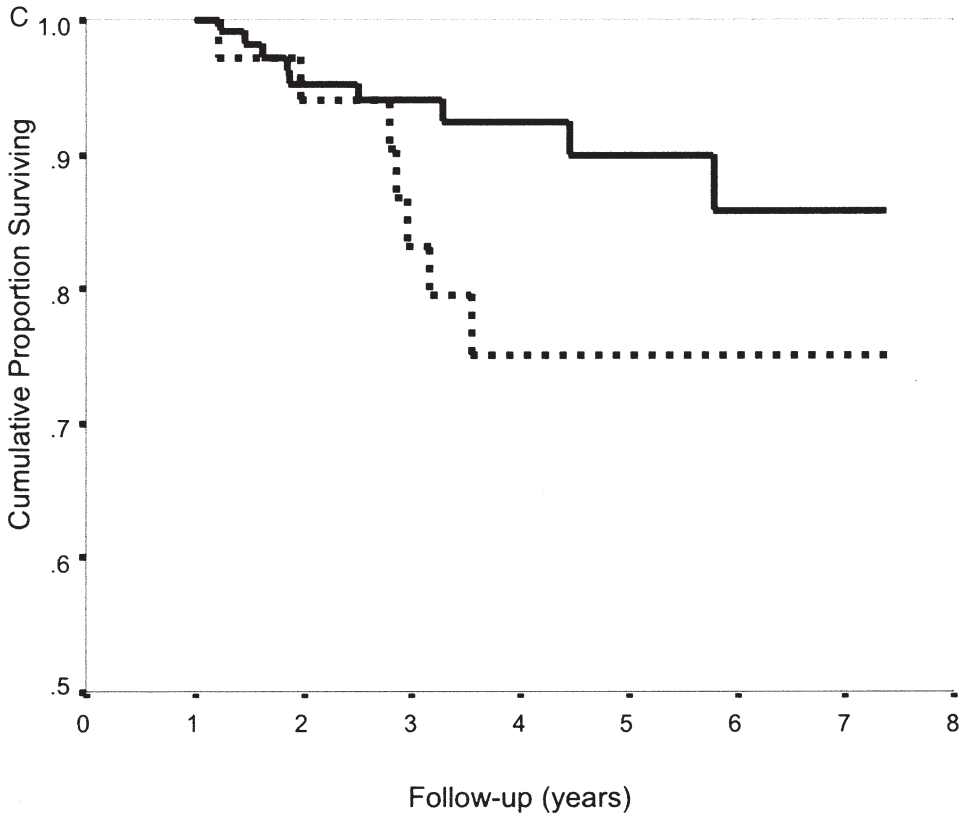

FIGURE 1. (*Continued*) (C) Kaplan Meier survival curves for the subjects with SLP ellipse modulation in the lowest quartile (1/4) (dashed line) compared with the subjects with ellipse modulation in the upper three quartiles (3/4) (continuous line). Cumulative proportion surviving = proportion without visual field conversion.

the group of patients with UCSD LDF in the lowest quartile (UCSD LDF < -0.78) compared with the group of patients with UCSD LDF in the upper three quartiles. Three-year (approximate mean follow-up time for all study participants) cumulative visual field conversion probabilities were 20% vs 3%, respectively. For the same follow-up time, visual field conversion probabilities for patients with an inferior ratio measurement in the lowest quartile (inferior ratio < 1.73) compared with the group of patients in the upper three quartiles were 23% vs 3% (Figure 1B), and conversion probabilities for patients with an ellipse modulation measurement in the lowest quartile (ellipse modulation < 1.84) compared with the group of patients in the upper three quartiles were 15% vs 5% (Figure 1C).

DISCUSSION

THIS STUDY FOUND THAT BASELINE MEASUREMENTS OF the RNFL thickness using SLP predicted the development of repeatable visual field loss in glaucoma-suspect eyes. Patients with thinner RNFL thickness at baseline, as indicated by the SLP parameters, had a greater chance of developing visual field abnormalities during the follow-up period. The SLP RNFL measurements provided additional independent information for predicting visual field loss, even after adjusting for other variables known to be associated with increased risk for conversion to glaucoma.

Several cross-sectional studies have suggested that patients with ocular hypertension (i.e., increased IOP with normal SAP results) have thinner RNFL thickness as assessed by the SLP, although a considerable amount of overlap exists with RNFL measurements obtained in healthy subjects.[28–31] However, other studies found no difference in SLP measurements between ocular hypertensive and healthy eyes.[32,33] In patients with SAP visual field loss restricted to one hemifield, Kook and associates[8] demonstrated that RNFL assessment with the SLP was able to detect a presumed loss of nerve fibers in the retinal area corresponding to the other hemifield. SLP abnormalities have also been demonstrated in the contralateral eye of patients with glaucoma and visual field loss restricted to one eye. However, few longitudinal studies evaluating RNFL measurements with SLP have been reported to date.[19,34] To our knowledge, this study is the first to longitudinally follow a cohort of glaucoma suspects and demonstrates that SLP RNFL measurements at baseline are predictive of development of glaucomatous visual field loss.

The three SLP parameters, UCSD LDF, inferior ratio, and ellipse modulation, had the best predictive perfor-

mance among the SLP parameters evaluated. Lower values of these parameters indicate lower RNFL retardance that correlates with thinner RNFL. Patients showing values of these parameters in the lowest quartile range had approximately three to five times more chance of developing visual field loss during follow-up than patients with values in the upper three quartiles. The UCSD LDF is calculated from a linear discriminant function that takes into account three parameters from the standard SLP output (average thickness, ellipse average and ellipse modulation) and it has been shown to have the highest performance for discriminating glaucomatous from healthy subjects.[6,11,16] The other two parameters, inferior ratio and ellipse modulation, have also been demonstrated to have good diagnostic ability to separate glaucomatous from normal eyes.[11] In the current study, the absolute thickness parameters (e.g., superior average, inferior average), did not show good predictive power. This is in agreement with reports showing better diagnostic ability of the ratio parameters compared with absolute thickness parameters for diagnosing glaucoma when SLP with fixed corneal compensation is used.[35,36]

Other parameters also showed significant ability to predict development of visual field loss in the current study. Univariate analyses showed that glaucomatous stereophotograph assessment and higher value of SAP PSD at baseline were independently associated with an increased risk of developing visual field damage throughout the follow-up period. It may be expected that PSD would be a strong predictor, as it ispredictor used in the definition of visual field damage, and that eyes with higher baseline PSD but still within the normal range may be more likely to develop visual field damage. For this reason, SAP PSD was included in the multivariate analysis so that it could be determined whether structural parameters were independently predictive of future visual field loss. A recent report from the Ocular Hypertension Treatment Study found that age, IOP, vertical or horizontal cup-to-disk ratio, SAP PSD, and corneal thickness were significant predictors of development of primary open-angle glaucoma among patients with ocular hypertension.[24] After controlling for the effects of age, IOP, central corneal thickness, SAP PSD, and vertical cup-to-disk ratio, the SLP parameter inferior ratio was still a significant predictor of future visual field loss in this study (adjusted hazard ratio = 1.14 for 0.1 U lower, 95% CI: 1.01-1.28; $P = .03$). In previous investigations, it has been demonstrated that thinner corneas were significantly associated with an increased risk of visual field loss among patients with glaucomatous optic neuropathy or ocular hypertension.[37,38] In the current study, only a borderline association was found between thinner corneas and older age with increased risk of visual field loss during follow-up. However, because of the small number of converters, it is possible that the current study had an insufficient power to detect these associations.

Although baseline IOP was a significant predictor in univariate analysis, lower values of IOP at baseline were associated with increased risk of developing visual field loss. This may be explained by the fact that 36% of participants were receiving IOP-lowering medication at baseline and 61% received IOP-lowering treatment during the follow-up period. Convert eyes were more likely to receive treatment (94%) compared with the nonconvert eyes (57%) during the study period, probably because they were deemed at higher risk for glaucoma by the treating clinician.

This study used the GDx Nerve Fiber Analyzer with fixed corneal polarization compensation. There is a wide variation in both the axis and magnitude of corneal birefringence in normal and glaucomatous individuals[39–41]; therefore, some eyes in the current study may have been improperly compensated for corneal birefringence. A scanning laser polarimeter with variable compensation of anterior segment birefringence has been recently described.[23] Several investigators have demonstrated that using variable compensation increases the ability of scanning laser polarimetry to discriminate between glaucoma and healthy eyes.[23,35,36,42] Similarly, a stronger association between SLP RNFL measurements and SAP visual field results have been shown using variable corneal polarization compensation compared with fixed corneal compensation.[35,43,44] Because the increased variability caused by inappropriate corneal compensation would be expected to decrease the ability to detect an association between SLP measurements and visual field loss, the current findings may be more conservative than those resulting from a study using the currently available SLP with a variable corneal polarization compensator (GDx VCC). In addition, the use of fixed corneal compensation may explain why only SLP ratio parameters (including modulation parameters and UCSD LDF) had significant predictive power for visual field conversion in the current study. Recent studies have shown that SLP ratio parameters obtained using fixed and variable SLP are more similar than absolute thickness measurements obtained using the two types of compensation for anterior segment birefringence.[35,36]

In the current study, both full-threshold and SITA visual field tests were used to determine glaucomatous visual field conversion. There is evidence that the criteria for glaucomatous conversion (SAP PSD and GHT) are similar between SITA and full-threshold visual fields.[45–47] Baseline SAP visual field tests in the current study were done within 1 year of the baseline SLP scans. It is expected that this date difference will have a negligible effect on the results, because 90% of the baseline SAP tests were obtained within 2.5 months of the baseline SLP test date, and also because all patients required at least 1 year of follow-up without visual field conversion.

In conclusion, this study found that thinner SLP RNFL thickness measures were independently associated with the risk of future visual field loss among glaucoma suspect eyes. These findings may have significant implications for de-

tection of early glaucomatous structural damage in glaucoma suspect eyes.

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