Subjective and Objective Optic Nerve Assessment in African Americans and Whites

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Objective. To compare the ability of quantitative optic disc topography and subjective optic disc evaluation to discriminate early glaucomatous from normal eyes in African Americans and whites.

Methods. Monocular data from eyes of 88 African-American patients and 63 eyes of white patients with glaucoma were included in the analysis. Sixty-three eyes of African American normal subjects and 42 eyes of white normal subjects were used as a control group. Racial groups were defined by self-description. All subjects underwent topographic imaging, stereophotography, and standard perimetry. Glaucoma was defined by visual field defect alone. Stereophotos were graded in a masked fashion by three independent graders. The areas under the receiver operator curve (aROCs) were calculated for the overall stereophoto grade, each confocal scanning laser ophthalmoscope (CSLO) parameter, and previously described discriminant functions. After adjustment for disc area and age, the aROC associated with each parameter, discriminant function, and subjective stereophoto grade were compared between African Americans and whites.

Results. The aROC for masked stereophotographic disc evaluation and the best discriminatory CSLO parameter (cup-to-disc ratio, CDR) was similar in whites (0.869 stereophotographic, 0.858 CSLO CDR) and African Americans (0.865 stereophotographic, 0.850 CSLO CDR). No significant differences were found between the aROC with subjective stereophotographic assessment and the most discriminatory optic disc parameter in either racial group.

Conclusions. Previously described racial differences in optic disc structure have little impact on the relative ability of subjective or objective methods to discriminate between glaucomatous and nonglaucomatous optic discs; however, differences in normative values necessitate race-specific cutoffs, to optimize disease detection strategies. (*Invest Ophthalmol Vis Sci.* 2004;45:2272–2278) DOI:10.1167/iovs.03-0996

Although identifiable structural changes in the optic disc frequently precede reproducible functional deficits detectable with achromatic perimetry, subjective assessment of the optic disc is limited by poor agreement between observers and the wide range of variability among normal subjects. Confocal scanning laser ophthalmoscopy (CSLO) was developed to acquire quantitative topographic information on optic disc structure, to improve the ability to detect glaucoma and progressive glaucomatous damage, and it may provide a more reproducible assessment of the optic nerve head.[1] Two prior studies have found that the CSLO and subjective assessment of the optic disc are equivalent in their ability to discriminate glaucomatous from nonglaucomatous eyes.[2,3] The diagnostic ability of the CSLO, alone or in comparison with subjective disc examination,[2–10] has not been tested in African Americans to evaluate the role of quantitative optic disc analysis and subjective optic disc assessment in discriminating glaucomatous from nonglaucomatous eyes in this high-risk population.[11–13]

Several clinical and histologic studies have characterized racial differences in optic disc structure, including larger disc and cup area and lower rim/disc area ratio in African Americans than in whites.[14–17] These racial differences may have an effect on the discriminatory ability of both subjective and objective optic disc assessment.[18,19] In addition, we have demonstrated that structural characteristics of the optic disc defined by the CSLO that are independently associated with early glaucomatous field loss differ between African Americans and whites, even when adjustment is made for racial differences in disc area, and that most of these associations are stronger in whites than in African Americans.[20] The purpose of the present study was to compare the ability of quantitative optic disc topography with subjective optic disc evaluation in discriminating early glaucomatous from normal eyes in African Americans and whites and to determine the optimal discriminatory methods in each racial group in a clinical setting.

Methods

Patients with glaucoma and normal control subjects were recruited from the University of Alabama at Birmingham (UAB) Optic Nerve Imaging Center's glaucoma database consisting of patients with glaucoma and normal subjects who had undergone optic disc imaging and visual functional testing between 2000 and 2003 as part of a longitudinal glaucoma study. Patient lists for inclusion in this study were obtained from the UAB glaucoma service by chart review and were selected based on having a visual acuity of 20/40 or better in one eye and a spherical refraction within ±5.0 or cylinder correction within ±2.5, with a reliable glaucomatous visual field defect (defined later). Normal subjects were obtained primarily from referring ophthalmologists' and optometrists' offices and university employees. These normal subjects and patients were then interviewed and examined for inclusion in the longitudinal study. The specific inclusion and exclusion criteria used in this study are outlined later. Informed consent was obtained from all participants, and the University of Alabama at Birmingham Human Subjects Committee approved all methodology. All aspects of the protocol adhered to the tenets of the Declaration of Helsinki. Data from 88 African-American and 63 white patients with glaucoma in one or both eyes were included in the analysis. Sixty-three African-American and 42 white normal subjects were used as the control groups. Racial groups were defined by self-description.

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All subjects had a complete ophthalmologic examination including slit lamp biomicroscopy, intraocular pressure (IOP) measurement, stereoscopic fundus examination, simultaneous stereoscopic photographs of the optic discs in both eyes, bilateral standard (white-on-white) full-threshold visual field testing (Humphrey Field Analyzer II; Carl Zeiss Meditec, Dublin, CA) and bilateral CSLO imaging.

Patients with glaucoma enrolled in this study were defined by visual field characteristics alone. Glaucomatous visual field loss was defined as a pattern standard deviation outside the 95% normal limits or a glaucoma hemifield test outside of the 99% normal limits, which was confirmed on the enrollment examination. For subjects with both eyes eligible, the worse eye defined by a more negative mean defect was used for the analysis. Subjects with severe glaucoma (mean deviation [MD] > 15) were excluded. Patients with a best corrected visual acuity of worse than 20/40, visually significant cataracts (nuclear sclerotic cataracts with visual acuity worse than 20/40 or posterior subcapsular cataract), spherical refraction outside ± 5.0 or cylinder correction outside ± 2.5, comorbid neurologic or ophthalmic conditions, or use of medication known to affect visual sensitivity at the time of visual field testing were excluded.

Normal subjects were recruited into the study with a highest documented IOP of 22 mm Hg or less and normal visual field results defined as a pattern standard deviation within the 95% normal limits and a glaucoma hemifield test result within normal limits. Patients with a best corrected visual acuity of worse than 20/40, a family history of glaucoma, spherical refraction outside ± 5.0, or cylinder correction outside ± 2.5 were excluded. Patients using medications known to affect visual sensitivity at the time of visual field testing and those with ophthalmic surgery or neurosurgery or disease also were excluded.

Visual field testing was performed with the Humphrey 24-2 Swedish Interactive Thresholding Algorithm (SITA) testing strategy. SITA perimetry is an automated perimetric technique with a standard white-on-white stimulus on the Humphrey Field Analyzer II, which has been commercially available since 1997.[21] It differs from conventional full-threshold techniques in the method of threshold determination. In the SITA algorithm, visual field modeling and informational indexing are used to arrive at a threshold value more rapidly. In addition, SITA reduces testing time by test pacing, recomputing posttest thresholds, and using inferential calculation to determine reliability indices. Although most previous evaluations of CSLO have been performed using full-threshold standard perimetry, full-threshold SITA correlates well with standard perimetry,[22,23] has a lower inter- and intratest variability than standard full threshold perimetry,[24,25] and reduces testing time and subject fatigue.[21]

The CSLO (Heidelberg Retina Tomograph II, [HRT II]; Heidelberg Engineering, Heidelberg, Germany) provides topographic measurements of the optic nerve and peripapillary retina. The HRT II confocal scanning laser ophthalmoscope employs a diode laser (670 nm wavelength) to produce three-dimensional measurements of optic disc topography based on reflectance from the retinal and optic disc surface. The HRT II is a modified version of the original HRT designed specifically for imaging of the optic disc. Unlike its predecessor, the HRT II takes three consecutive scans per scanning session and averages them automatically. An image series is obtained from 32 to 64 transverse optical section images taken at consecutive 62-μm depth intervals over a scan depth of 1 to 4 mm. The scan depth and number of imaging planes are determined from a prescan of the optic disc to ensure that the entire optic disc is included in the image. Thus, the resultant three-dimensional topography image determined from the scan series may consist of $384 \times 384 \times 16$ voxel elements up to $384 \times 384 \times 64$ voxel elements.

Image acquisition takes approximately 1.5 seconds per series. Three 15° images of one eye are obtained in sequence per imaging session automatically by the instrument. A mean topography image adjusted for alignment and rotation is created automatically with existing software and were used for all analyses. Correction for magnification was determined based on keratometry readings. Although pupil dilation is often not required, all eyes were imaged after full dilation. An experienced operator evaluated image quality and outlined the disc margin while viewing stereoscopic photographs of the optic disc. Images were excluded if the acquisition sensitivity was above 90, the image had a standard deviation greater than 40, there was poor centration of the disc, there was excessive movement during the acquisition movie, there were floaters over or adjacent to the disc, or there was poor clarity or framing. Images from 33 subjects were excluded from the data collection for inadequate images. Two additional subjects were eliminated due to a corrupted image file. Most ($n = 25$) of these subjects were excluded due to poor scan sensitivity and poor clarity, and the remaining excluded subjects had vitreous floaters adjacent to the disc or poor framing.

The HRT II includes a comprehensive software package that facilitates image acquisition, storage, retrieval, and quantitative analysis. Software-determined parameters are retinal nerve fiber layer [RNFL] thickness, RNFL cross-sectional area, rim area and volume, mean height contour, cup volume, cup shape, mean cup depth, maximum cup depth, cup area, optic disc area, and cup-to-disc area ratio. RNFL thickness, RNFL cross-sectional area, rim volume, rim area, cup volume, and cup area are measured relative to a standard reference plane. The position of the standard reference plane is 50 μm posterior to the mean height of the optic disc margin contour line in a temporal segment between 350° and 356°.

Simultaneous stereophotos were obtained from each subject after pupillary dilation. The photographs of each patient were graded on a 5-point likelihood scale similar to that previously described by Greaney et al.[2] Stereophotos where graded independently in a masked fashion by three experienced stereophoto graders (CAG, CMG, JDL) with glaucoma subspecialty training. This 5-point scale increases in value with the clinical impression of glaucoma (1, definitely normal; 2, probably normal; 3, unsure; 4, probably glaucomatous; 5, definitely glaucomatous) and is based on the observations of typical optic disc characteristics consistent with glaucomatous optic neuropathy including the presence of neuroretinal rim thinning, notching, or undermining, nerve fiber layer defects, and optic disc hemorrhages. An over all photograde score was developed by the summation of the three independent grades to produce a 12-point ordinal scale. To compare this grading scale with more commonly used forced-choice grading, the stereophotos were also graded in a dichotomous manner (glaucoma or normal) by two of the masked stereophoto graders (JDL, CMG). The third grader (CAG) adjudicated cases of disagreement.

Statistical Analysis

Among African Americans and whites, *t*-tests were used to compare glaucomatous eyes and normal eyes with respect to continuous variables including: age, IOP, MD, photograde score, CSLO parameters, and previously described CSLO linear discriminant functions developed by Mardin et al. (LDF Mardin),[26] Bathija et al. (LDF Bathija),[9] and Mikelberg et al. (LDF Mikelberg).[5] Similar comparisons were conducted for categorical variables using χ^2 tests.

To compare the relative ability of quantitative optic disc topography and subjective optic disc evaluation in discriminating glaucomatous from normal eyes in African Americans and whites, the area under the receiver operating characteristic curve (aROC) was calculated for the overall stereophoto grade, each of the individual CLSO parameters, and each of the previously described CSLO discriminant functions. The aROC provides an evaluation of the ability to discriminate between those who experience the outcome of interest and those who do not. A model containing stereophoto grade adjusted for age was compared with a model containing the most efficient CSLO optic disc structural parameter adjusted for age and disc area. Separate models were constructed for each racial group. Sensitivity was assessed for each model by fixing the specificity at 80%. Statistical comparisons within each racial group of the aROC for subjective assessment of stereophotos and the aROC for the best performing CSLO parameter were performed using previously described methods of comparison that take into account the correlation between the areas that is induced by the paired nature of the data.[27]

TABLE 1. Demographic Data

	Glaucoma			Control		
	African Americans	Whites	*P*	African Americans	Whites	*P*
Eyes (*n*)	88	63		63	42	
Mean age (y)	57.68	58.18	0.827	46.30	43.86	0.42
Gender (% female)	73.86	49.21	0.049	87.30	76.19	0.02
Mean IOP	19.02	19.937	0.700	16.524	16.119	0.53
Mean MD	−4.968	−4.742	0.724	−0.782	0.22	0.21
Mean PSD	4.84	5.51	0.207	1.66	1.50	0.12

RESULTS

Demographic characteristics of the normal control and glaucoma groups are shown in Table 1. There were no significant differences in age, highest measured intraocular pressure, or MD in the visual field between African Americans and whites among the normal control subjects or the patients with glaucoma. Female gender was less common in the white group. In addition, normal subjects were significantly younger than patients, and thus age was adjusted for the analysis.

Optic disc parameters from the CSLO and subjective disc evaluation obtained from the control group are illustrated in Table 2. Several parameters differed significantly between racial groups ($P < 0.05$). Disc area, cup area, and cup-to-disc area ratio were larger in the African-American group, whereas global rim area and volume were similar between racial groups. In addition, a significantly deeper cup was found in the African-American group. Stereophoto grade was not significantly different between the African-American and white groups. In addition, there was no significant difference in reference height between racial groups.

CSLO parameters and subjective disc grades for normal and glaucomatous eyes are shown for the African American and white groups in Table 3. Most tested CSLO parameters were significantly different ($P < 0.05$) between glaucoma and normal subjects in whites and in African Americans. However, there was significant overlap between diagnostic groups for all parameters, similar to our previous report and to similar studies in whites. There were no significant differences ($P > 0.4787$) in reference plane height between African-American (mean 0.385 ± 0.130; SD) and white groups (mean 0.371 ± 0.160).

The aROC, along with the sensitivity of each parameter at 80% specificity, for the subjective disc grading score and each CSLO parameter are listed in Table 4 for white and African American groups (subjective disc grading was adjusted for age, and CSLO parameters were adjusted for age and disc area). Subjective disc grading and CSLO cup-to-disc ratio had the highest aROC values in both African-American and white groups. CSLO-measured cup-to-disc ratio and subjective disc grading score correlated significantly in both groups (African Americans: aROC = 0.72, $P < 0.0001$; whites: aROC = 0.74, $P < 0.0001$). The performance of subjective disc evaluation did not differ significantly across graders ($aROC_{CAG} = 0.889$, $aROC_{JDL} = 0.871$, $aROC_{JDL} = 0.845$) and there was moderately good correlation between stereophoto graders ($r_{CAGvsCMG} = 0.754$, $r_{CAGvsJDL} = 0.795$, $r_{CMGvsJDL} = 0.736$, $P < 0.0001$). The dichotomous classification strategy produced similar results ($sensitivity_{whites} = 81.2$, $specificity_{whites} = 69.8$, $sensitivity_{African\ Americans} = 75.8$, $specificity_{African\ Americans} = 80.2$).

The aROC, along with the sensitivity of each parameter at 80% specificity, for the CSLO discriminant functions are listed in Table 5. The aROCs for subjective disc grading, any of the CSLO parameters, or discriminant functions were similar be-

TABLE 2. Comparison of Optic Disc Parameters between Normal Whites Study Eyes

	African Americans	Whites	*P*-Value
Eyes (*n*)	63	42	
Photograde (3–15 point scale)	7.2063 (3.1682)	6.5952 (3.1627)	0.3350
Mean CSLO parameters (mean ± SD)			
Vertical cup-disk ratio	0.3337 (0.2277)	0.2785 (0.2355)	0.2327
Cup-disc area ratio	0.2486 (0.1514)	0.1897 (0.1326)	0.0427
Rim area (mm^2)	1.6200 (0.3480)	1.5430 (0.3536)	0.2745
Cup area (mm^2)	0.5851 (0.4406)	0.3778 (0.2962)	0.0088
Maximum contour elevation (mm)	−0.1180 (0.1232)	−0.1030 (0.0984)	0.4694
Rim volume (mm^3)	0.4596 (0.1691)	0.3890 (0.1785)	0.6685
Horizontal cup-disk ratio	0.4755 (0.2158)	0.3873 (0.2177)	0.0434
Cup shape measure	−0.1040 (0.0880)	−0.1910 (0.0606)	0.4353
Cup volume (mm^3)	0.1470 (0.1746)	0.0727 (0.0800)	0.0113
Mean cup depth (mm)	0.2286 (0.1009)	0.1750 (0.0835)	0.0053
CLM temporal inferior (mm)	0.2070 (0.0858)	0.1944 (0.0987)	0.5010
Mean RNFL thickness (mm)	0.2755 (0.0774)	0.2581 (0.0763)	0.2592
RNFL cross-sectional area (mm^2)	1.4430 (0.4427)	1.2610 (0.3963)	0.0303
CLM temporal superior (mm)	0.2367 (0.0834)	0.193 (0.0839)	0.009
Maximum cup depth (mm)	0.6260 (0.2073)	0.4875 (0.2146)	0.0013
Maximum contour depression (mm)	0.3221 (0.1598)	0.2661 (0.1531)	0.0745
Height variation contour (mm)	0.4398 (0.1113)	0.3660 (0.1077)	0.0689
Disc area (mm^2)	2.2051 (0.5010)	1.8036 (0.3763)	0.0013

CLM, contour line margin.

TABLE 3. Comparison of Optic Disc Parameters between Glaucomatous and Normal Control Eyes for African Americans and Whites

	African Americans			Whites		
	Glaucoma	Controls	*P*	Glaucoma	Controls	*P*
Eyes (*n*)	88	63		63	42	
Photograde (3–15 point scale)	11.5300 (2.6955)	7.2063 (3.1682)	<0.0001	11.5560 (2.9555)	6.5952 (3.1627)	<0.0001
CSLO parameters (mean ± SD)						
Vertical cup-disk ratio	0.5271 (0.1987)	0.3337 (0.2277)	<0.0001	0.5528 (0.1891)	0.2785 (0.2355)	<0.0001
Cup-disc area ratio	0.4216 (0.1708)	0.2486 (0.1514)	<0.0001	0.3447 (0.1711)	0.1897 (0.1326)	<0.0001
Rim area (mm^2)	1.3671 (0.4438)	1.6200 (0.3480)	0.0002	1.3306 (0.4569)	1.5430 (0.3536)	0.0124
Cup area (mm^2)	1.0761 (0.6027)	0.5851 (0.4406)	<0.0001	0.8580 (0.4380)	0.3778 (0.2962)	<0.0001
Maximum contour elevation (mm)	−0.0030 (0.1021)	−0.1180 (0.1232)	<0.0001	−0.0350 (0.1265)	−0.1030 (0.0984)	<0.0001
Rim volume (mm^3)	0.3235 (0.1438)	0.4596 (0.1691)	<0.0001	0.3306 (0.2116)	0.3890 (0.1785)	0.0049
Horizontal cup-disk ratio	0.6101 (0.1841)	0.4755 (0.2158)	<0.0001	0.6115 (0.2070)	0.3873 (0.2177)	<0.0001
Cup shape measure	−0.0750 (0.0850)	−0.1040 (0.0880)	<0.0001	−0.1360 (0.0733)	−0.1910 (0.0606)	0.0001
Cup volume (mm^3)	0.3060 (0.2578)	0.1470 (0.1746)	<0.0001	0.2453 (0.2486)	0.0727 (0.0800)	<0.0001
Mean cup depth (mm)	0.2985 (0.1115)	0.2286 (0.1009)	<0.0001	0.2825 (0.1192)	0.1750 (0.0835)	<0.0001
CLM temporal inferior (mm)	0.1336 (0.0904)	0.2070 (0.0858)	<0.0001	0.1202 (0.1365)	0.1944 (0.0987)	0.0031
Mean RNFL thickness (mm)	0.1961 (0.0788)	0.2755 (0.0774)	<0.0001	0.2117 (0.0988)	0.2581 (0.0763)	0.0115
RNFL cros-sectional area (mm^2)	1.1548 (0.4302)	1.4430 (0.4427)	<0.0001	1.1056 (0.5355)	1.2610 (0.3963)	0.1109
CLM temporal superior (mm)	0.1441 (0.1080)	0.2367 (0.0834)	<0.0001	0.1200 (0.1401)	0.1930 (0.0839)	0.0113
Maximum cup depth (mm)	0.7012 (0.2067)	0.6260 (0.2073)	0.0292	0.7079 (0.2102)	0.4875 (0.2146)	<0.0001
Maximum contour depression (mm)	0.3486 (0.1433)	0.3221 (0.1598)	0.0235	0.3679 (0.1660)	0.2661 (0.1531)	0.0020
Height variation contour (mm)	0.3597 (0.1031)	0.4398 (0.1113)	0.0012	0.3650 (0.1492)	0.3660 (0.1077)	0.9085
Disc area (mm^2)	2.4432 (0.6346)	2.2051 (0.5010)	0.0144	2.1886 (0.4172)	1.8036 (0.3763)	0.0011

CLM, contour line margin.

tween racial groups. Figures 1 and 2 present plots of the ROC curves for subjective disc grading, along with the best performing CSLO parameter (cup-to-disc ratio) in each racial group for comparison.

DISCUSSION

This study demonstrated that, when controlled for disc area, the CSLO performs similarly to subjective expert evaluation of the optic disc in discriminating between glaucomatous and nonglaucomatous eyes in both African-American and white populations. In both racial groups, subjective disc evaluation had the highest aROC values overall, with CSLO defined cup-to-disc ratio with highest aROCs for the CSLO parameters. The discriminant function developed by Mardin et al.[26] had the highest aROC in both racial groups.

At a set specificity of 80%, the CSLO had a higher sensitivity than did subjective disc classification in whites. Conversely, in

TABLE 4. Comparison of Sensitivity at 80% Specificity and aROC for Subjective Photograde and CSLO Optic Disc Structural Parameters

	Whites		African Americans	
Diagnostic Measure	aROC	Sensitivity	aROC	Sensitivity
Photograde*	0.869	68.3	0.865	73.9
CLSO parameters†				
Cup-disc area ratio	0.858	74.6	0.850	71.6
Vertical cup-disk ratio	0.856	73.0	0.850	70.5
Rim area (mm^2)	0.850	73.0	0.848	72.7
Cup area (mm^2)	0.850	73.0	0.847	72.7
Maximum contour elevation (mm)	0.837	65.1	0.845	64.8
Rim volume (mm^3)	0.823	69.8	0.842	68.2
Horizontal cup-disk ratio	0.827	63.5	0.816	65.9
Cup shape measure	0.824	61.9	0.818	63.6
Cup volume (mm^3)	0.835	65.1	0.814	69.3
Mean cup depth (mm)	0.844	60.3	0.810	64.8
CLM temporal inferior (mm)	0.831	66.7	0.809	65.9
Mean RNFL thickness (mm)	0.795	63.5	0.809	65.9
RNFL cross-sectional area (mm^2)	0.794	63.5	0.811	65.9
CLM temporal superior (mm)	0.796	60.3	0.806	59.1
Maximum cup depth (mm)	0.841	61.9	0.786	59.1
Maximum contour depression (mm)	0.824	63.5	0.775	53.4
Height Variation contour (mm)	0.667	0.442	0.679	0.508

Parameters are listed from highest to lowest aROC value, and probabilities are given for comparison of aROC values between racial groups for each parameter. CLM, contour line margin.

* Adjusted for age.

† Adjusted for age and disc area.

TABLE 5. Comparison of Sensitivity at 80% Specificity and aROC for CSLO Discriminant Functions

	Whites		African Americans	
Parameter	**aROC**	**Sensitivity**	**aROC**	**Sensitivity**
LDF Mardin[26]	**0.813**	66.7	**0.854**	77.3
LDF Bathija[9]	0.792	65.1	0.810	70.5
LDF Mikelberg[5]	0.736	49.2	0.827	70.5

Parameters are listed from highest to lowest aROC in the whole group; highest aROC for the white and African-American groups are in bold; and probabilities are given for comparison of aROCs between racial groups. Data are adjusted for age.

the African-American group, subjective optic disc classification had a higher sensitivity than the best-performing parameter of the CSLO. Thus, whereas imaging in this study performed equally well in African Americans and whites based on overall aROC, race-specific cutoffs would still improve the statistical assessment of disease due to racial difference in parameters between the normal subject groups.

Prior studies using the CSLO have been performed in predominantly white study populations[2–10] and have not included and adequate number of African-American subjects to evaluate the role of quantitative optic disc analysis, the parameters that are most predictive of glaucoma, and optimum analysis strategies for detection of glaucoma in this at-risk population. Open-angle glaucoma is more common, more refractory to treatment, and more severe, with higher rates of blindness in the African-American population.[11–13]

Two prior studies have compared the diagnostic ability of the CSLO and subjective optic disc evaluation using a similar size sample, and both these studies used data obtained from predominantly white populations. Greaney et al.,[2] compared the aROC between the best-performing CLSO parameters with subjective optic disc simultaneous stereophoto evaluation, using a method similar to that used in our study in 63 normal and 63 glaucomatous eyes and also found no significant differences

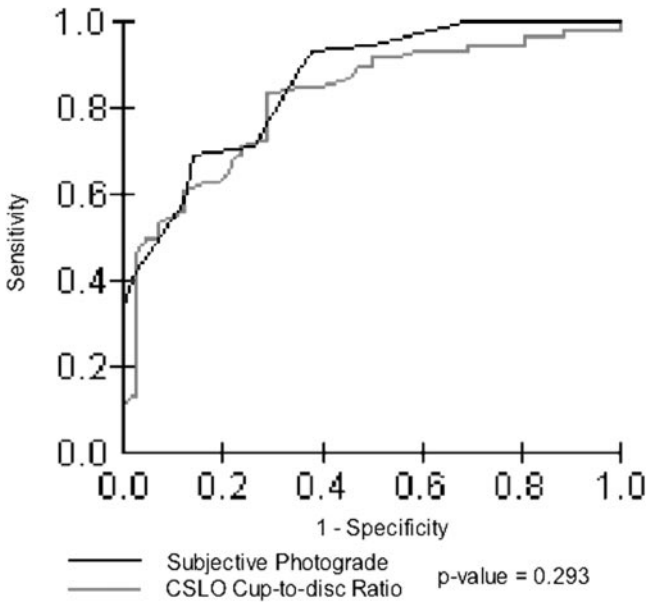

FIGURE 1. aROC curves for subjective disc grading, along with the best-performing CSLO parameter (cup-to-disc ratio) in the African-American group.

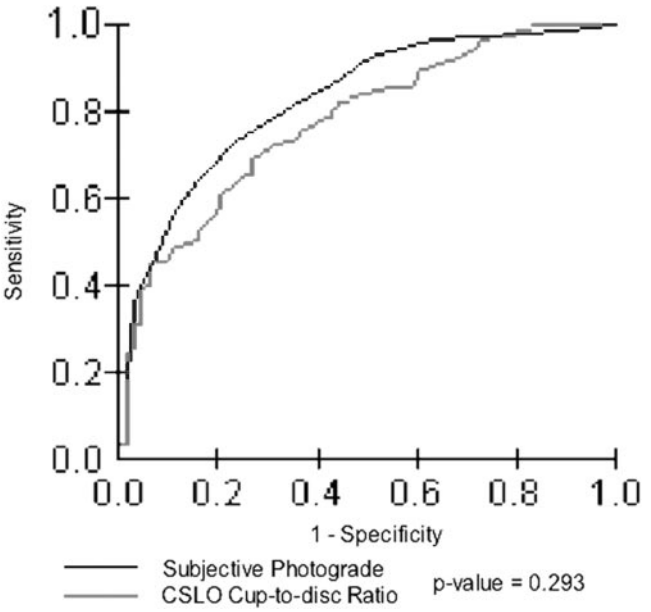

FIGURE 2. aROC curves for subjective disc grading, along with the best-performing CSLO parameter (cup-to-disc ratio) in the white group.

between the discriminatory ability of the CSLO and subjective techniques. This study also included optical coherence tomography and scanning laser polarimetry measurements of nerve fiber layer thickness found using a fixed compensation for anterior segment birefringence and no difference between these techniques.

Wollstein et al.[3] compared subjective optic disc evaluations of nonsimultaneous optic disc stereophoto pairs with the ability of the CSLO to discriminate glaucoma, using a linear regression technique based on rim-disc area ratio and found a higher sensitivity and specificity with the CSLO linear regression measure but no significant difference between objective and subjective measures. Neither of these studies contained an adequate number of African-American subjects to examine the effectiveness of these techniques in this at-risk population.

Although the current study demonstrated that the best quantitative CSLO parameters performed as well as qualitative expert assessment in discriminating early to moderate glaucoma, consensus-masked expert evaluation may not reflect how the optic disc is accessed in clinical practice. More commonly the optic disc is qualitatively assessed in the clinical setting by single observers, often with less experience and, perhaps more important, less time for assessment. Thus, the estimates of ability of qualitative assessments to discriminate correctly the glaucomatous and normal optic discs may be greater than that used in routine clinical practice, but a direct comparison of these techniques has not been made.

The racial differences in optic disc parameters seen in this study correspond to findings from prior case–control and population-based studies and histologic research studies, which have found a larger disc and cup area, yet a similar overall rim area in African Americans, yielding an overall larger cup-to-disc area ratio.[14–17] The present study demonstrated a similar pattern with a significantly larger disc area, cup area, and cup-to-disc area ratio and similar measurements in overall rim area.

These differences in optic disc structure may have an effect on the ability of CSLO techniques to detect glaucoma. Broadway et al.[19] demonstrated that the discriminating ability of the CSLO varies depending on the phenotype of optic disc damage present. In addition, Iester et al.[18] demonstrated that optic disc area has an effect on the diagnostic precision of the CSLO. This

is an important consideration, in that one of the differences in optic disc structure between African Americans and whites is disc area.[15] In addition, our previous research has demonstrated racial differences in the CLSO parameters that are independently associated with early glaucomatous field loss in a similarly defined population even when adjusted for racial differences in optic disc area.[20]

Given these previously described racial differences in optic disc structural associations with early functional damage, it remains important that we evaluate methods of disc analysis in African Americans, if these instruments are to be applied to this high-risk minority population, both for potential improvement of clinical management and for use as structural end points in clinical trials.

The sensitivity and specificity, although in the range of previously published results, were quite low when considering the CSLO as potential screening technique in the general population. A possible explanation for the lower aROC was that this study was limited to less severe disease, which would be more difficult to discriminate. In addition, our study obtained control subjects from those seeking eye care from referring practices or from employees who obtain eye care at our facility, which may better approximate the source population for the cases compared with those in other studies that have demonstrated much higher performance. The aROC for subjective disc evaluation was also lower than that reported by Greaney et al.,[2] indicating that this may indeed be an effect of the study population. If so, these results would be likely to reflect more accurately the performance of these techniques in the screening setting. Given these results, screening for early glaucoma based on the CSLO alone would not be fruitful in any but a very high-risk population. In addition, the recruitment of patients with glaucoma from a subspecialty clinic and including only high-quality images may further limit generalization of these results without additional confirmation.

There are several reasons to suspect that these results would overestimate the sensitivity and specificity of subjective and objective disc analysis when applied in the screening setting. First, any biases introduced by including subjects from a tertiary referral clinic would serve only to overestimate the performance of these techniques when used for screening. In addition, only subjects with good central vision and clear ocular media were included in the study, and highly trained technicians involved in a research protocol performed all imaging procedures.

It remains a problem that no technology exists or is likely to be developed that can adequately screen for a low-prevalence condition when the underlying structure (the optic disc and/or nerve fiber layer) on which the discrimination strategy is based has such a high variability in the normal population, which is the case with glaucoma. The more important issue is how well these instruments perform in the clinic settings in which they are used compared with existing methods—hence, the focus on more difficult early, more challenging, cases in this study.

In summary, in this study, we compared subjective and objective techniques of optic disc evaluation in both African Americans and whites and found no significant difference between the best diagnostic parameters using the CSLO when adjusted for disc area and subjective optic disc assessment in either population. In addition, subjective optic disc classification and the CSLO performed similarly across racial groups in the ability to discriminate between glaucomatous and nonglaucomatous eyes. Agreement between subjective and objective classification was moderate. Thus, although racial differences in CSLO parameters significantly associated with glaucomatous field loss may differ between African Americans and whites, these differences produced little impact on the relative ability of subjective and objective methods to discriminate between glaucomatous and nonglaucomatous optic discs in our study populations. However, differences in normative values necessitate race-specific cutoffs to optimize disease detection strategies.

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