Reduced Mesopic and Photopic Foveal Contrast Sensitivity in Glaucoma

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Objective: To demonstrate differences in foveal constrast sensitivity (CS) between glaucomatous and nonglaucomatous eyes using a simple, rapid computerized test.

Methods: This study included consecutive patients with glaucoma (35 eyes) and age-matched control participants (23 eyes) with visual acuity of 20/30 or better. Patients with any other ocular disease, including cataract, were excluded. All participants underwent a comprehensive ocular examination, perimetry, and CS. Contrast sensitivity was examined by means of 2 computerized psychophysical tests. The transient method included the presentation of a target in a temporal, 2-alternative, forced-choice procedure, and the static method involved 4 forced-choice procedures. The targets were Gabor patches with spatial frequencies of 1.5 to 9.0 cycles per degree. The tests were conducted under photopic and mesopic conditions.

Results: Significantly lower foveal CS was found in glaucomatous eyes under photopic and mesopic conditions for all spatial frequencies ($P < .01$). The transient and static methods yielded similar results and were significantly correlated ($P < .001$). All transient photopic and mesopic CSs were significantly correlated with cup to disc ratio ($P < .05$). The static photopic spacial frequency of 6 cycles per degree was significantly correlated with the severity of the glaucomatous damage.

Conclusions: The results indicate that foveal CS is impaired in glaucoma despite good visual acuity, suggesting that central visual function damage occurs in glaucoma. The similarity between the 2 methods of testing implies that the static method, being the shorter and easier one, may be used in future research. Further research is necessary to establish a CS testing role in the screening and monitoring of glaucoma.

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SINCE THE FIRST REPORT BY Campbell and Green[1] of reduced contrast sensitivity (CS) in patients with open-angle glaucoma, CS has been studied extensively to determine its effectiveness as a test for diagnosing glaucoma. Various techniques have been adopted to measure CS; some reported a significant difference between glaucoma and normal eyes,[2-14] but others reported the lack of a significant difference between them.[15,16] Glovinsky et al[17] found that whole-field scotopic sensitivity is able to discriminate between patients with normal eyes and those with glaucoma or suspected glaucoma and thus may be useful in glaucoma screening. Their work was performed under scotopic conditions, and areas outside the fovea underwent testing. In addition, some work has been performed with scotopic CS in individuals with nonglaucomatous eyes,[18] and foveal scotopic CS was reported to decline with age.[19] These studies highlight the importance of scotopic sensitivity testing. However, little is known about foveal mesopic CS in glaucoma. Mesopic vision is the intermediate range between photopic and scotopic, in which both cones and rods function. Definition of the lighting conditions for mesopic vision varies from one study to another, with the lower boundaries of luminance in the range of 0.001 to 0.034 cd/m^2.[20]

Furthermore, in the present study, we compared 2 methods of CS testing, transient and static, under photopic and mesopic conditions. The static method, the shorter and easier one, was compared with the transient method to establish a new testing procedure that may be better accepted by the elderly population. New CS testing procedures are important for research because they can provide insight into the pathophysiologic mechanism of visual damage and may potentially become specific and sensitive tests for earlier diagnosis of glaucoma.

METHODS

PARTICIPANTS

This study included 27 patients with glaucoma (glaucoma group) and 23 individuals with healthy eyes (control group). The patients were

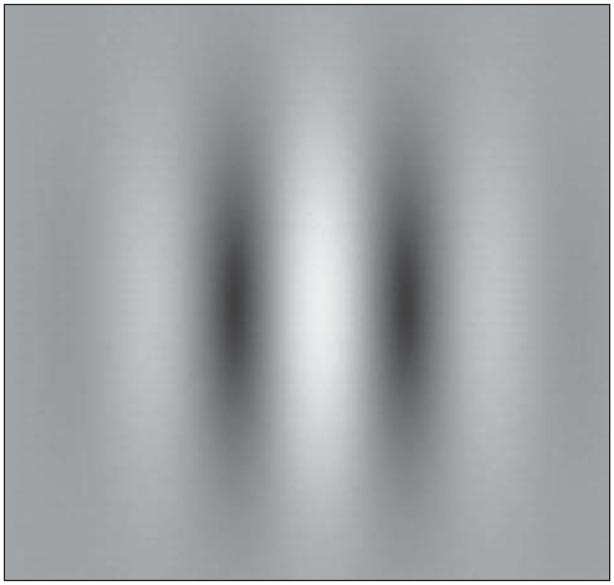

Figure 1. An example of the Gabor patch used in the study.

recruited from the Glaucoma Clinic at the Goldschleger Eye Institute of Sheba Medical Center, and the controls were healthy individuals who accompanied their relatives for their eye examinations. Thirty-five eyes of the 27 patients (both eyes of 8 patients underwent testing) and 23 eyes of the 23 controls were tested. For all participants, the inclusion criteria included a best-corrected visual acuity of 20/30 or better. Glaucomatous eyes were defined by glaucomatous optic nerve damage and a repeatedly documented, characteristic, reliable visual field loss determined by the Humphrey visual field analyzer (Carl Zeiss Meditec, Dublin, California). The severity of glaucomatous damage was defined as severe (mean deviation [MD] worse than –10 dB), moderate (MD range, –10 to –5 dB), or mild (MD range, –5 to 0 dB). Visual field results were obtained within the past 3 months. In the case of numerous field results available, MD scores were calculated according to the average of the last 3 tests performed. None of the patients in the glaucoma group used pupillary constriction agents. Controls had normal eye examination results (including slitlamp biomicroscopy of the anterior segment and ophthalmoscopy of the macula and optic nerve), an intraocular pressure of less than 21 mm Hg, and normal visual fields. Exclusion criteria were eye diseases other than glaucoma in the glaucoma group, cataracts (patients with pseudophakia had undergone surgery at least 3 months earlier), and refractive errors greater than ±5.00 diopters (D) sphere and/or more than 2.00 D cylinder.

The Human Research Committee at the Sheba Medical Center approved the study. Informed written consent was obtained from all participants.

PROCEDURE

Participants underwent testing with natural pupils, and correction for intermediate distance (150 cm) was given to each participant, if necessary. If visual acuity of both eyes qualified for the study along with other criteria, both eyes underwent testing. For controls, the tested eye was the dominant eye. Patients and controls underwent monocular testing, with the untested eye covered with a translucent lens. The test was explained carefully to the participants, and a practice trial run preceded each testing. The initial method of testing, transient or static, was chosen randomly each time. In cases in which both eyes underwent testing, the initial eye tested was chosen at random.

VISUAL STIMULI AND EXPERIMENTAL TESTING

The stimuli consisted of a foveally viewed vertical Gabor signal (**Figure 1**), which is a grating limited in space by a Gaussian envelope (σ) that defines the size of the target. The number of cycles (λ) was kept constant ($\lambda = \sigma$) for all spatial frequencies (SFs), resulting in the decreasing size of the target with increasing SF. Stimuli were displayed as a gray-level modulation on a color monitor (Philips 107P; Royal Philips Electronics, Eindhoven, the Netherlands). Screen resolution was 1024×768 pixels covering a $9.2° \times 12.2°$ area. The mean display luminance in photopic testing was 20 cd/m^2 in an otherwise completely darkened room. For mesopic testing, the monitor was covered with neutral density filters that allowed luminance of only 0.03 cd/m^2. We applied gamma correction that enables linear presentation of the contrast. The stimuli were viewed from a distance of 150 cm.

TRANSIENT METHOD

The transient method used herein was similar to that of Polat and Sagi.[21,22] Briefly, the stimuli consisted of a single Gabor target at the fixation point with an SF ranging from 1.5 to 6.0 cycles per degree (cpd). The spatial luminance distribution of the target was described by the Gabor function, that is, a cosine grating multiplied by a Gaussian envelope.[23]

A temporal, 2-alternative, forced-choice procedure was used. Each trial consisted of 2 stimuli revealed sequentially, only 1 of which had a target. Each stimulus shown included 4 peripheral high-contrast crosses, marking the stimulus presentation to eliminate temporal uncertainty. Before each trial, a small fixation circle appeared at the center of the screen to ensure central fixation before initiating the trial sequence. The trial sequence consisted of a no-stimulus interval (500 milliseconds), a stimulus presentation (320 milliseconds), another no-stimulus interval (800 milliseconds), and a second stimulus presentation (320 milliseconds). The observers' task was to determine which of the stimuli contained the target. Given the participants' average age and excluding confounding factors such as finger errors, the participants performed an oral response, which was converted into a button press response by those conducting the experiment. Auditory feedback was given immediately for an incorrect response. Screen luminance was kept constant during the stimulus and the stimulus intervals. A 3:1 staircase method was used to determine the contrast threshold level at 79% correct.[24] The procedure was repeated for each SF (3.0 and 6.0 cpd for photopic conditions; 1.5 and 3.0 cpd for mesopic conditions) in randomized order to avoid bias of results or confounding effects of fatigue and adaptation time.

Photopic testing was performed first, followed by a short break (until the participants were prepared to start the second session) and a 1-minute dark adaptation,[18] after which mesopic testing began. Each complete testing session lasted approximately 15 minutes.

STATIC METHOD

The stimuli for the static method consisted of 1 Gabor target (SF, 3.0-9.0 cpd) shown in 1 of 4 white-bordered circles on the monitor. Higher SF stimuli were tested in the static method than in the transient method to improve discrimination levels. A task involving 4 spatial forced choices was used. The Gabor target appeared at 1 of 4 possible locations (denoted by a visible white circle) on the monitor: up, down, left, or right. The target remained on the monitor until the participant reported to the experimenter the location in which the target appeared. An auditory feedback was given after a wrong response. After each

Table. Clinical and Demographic Data[a]

	Group	
	Glaucoma	Control
No. of participants (eyes)	27 (35)	23 (23)
Sex, No. male/female	17/10	10/13
Age, mean (SD), y	64.4 (9.9)	62.6 (10.6)
Average visual acuity	20/25+	20/20–

[a]There were no significant differences between the groups.

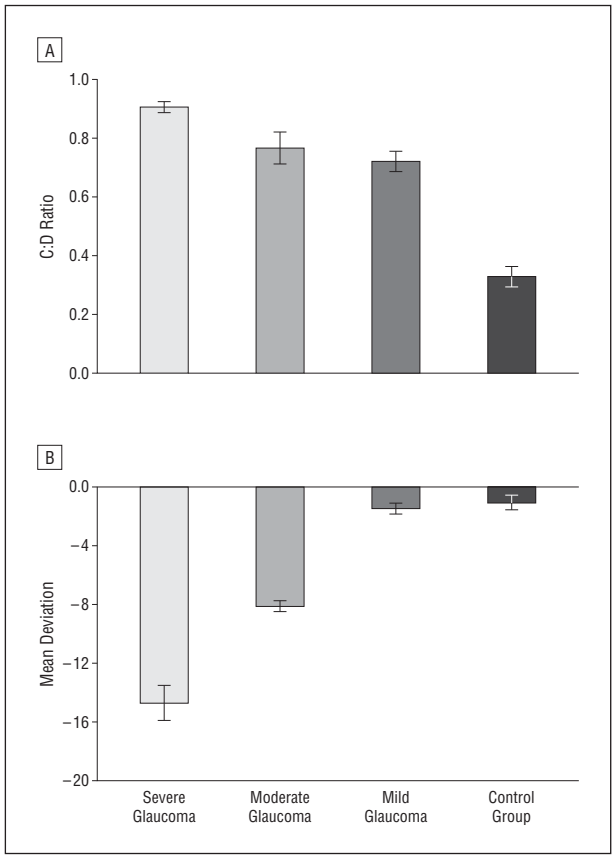

Figure 2. Cup to disc (C:D) ratio (A) and mean deviation (B) characteristics of patients with glaucoma. Patients with glaucoma were divided into the following 3 categories according to glaucomatous damage severity: severe, moderate, and mild. The results of the control group are also presented for comparison. The C:D ratio of patients with glaucoma is significantly higher than that of the controls ($P<.001$). The mean deviation of patients with severe and moderate damage was significantly different from that of the controls ($P<.001$).

trial, the target appeared randomly in 1 of the 4 locations. A 2:1 staircase method was used to determine the contrast threshold level at 70.7% correctness.[25] This procedure was repeated for each SF (6.0 and 9.0 cpd for photopic; 3.0 and 6.0 cpd for mesopic) in a randomized order to avoid bias of results or the confounding effects of fatigue and adaptation time. Photopic testing was performed first, followed by a short break. Our early results show that 1 minute of dark adaptation enables the beginning of testing under the foveal mesopic condition.[18] Each complete testing session lasted approximately 6 minutes.

The static method was used for the following 2 reasons:

1. It takes less time and is performed with greater ease than the transient method. Given that most patients with glaucoma are elderly, the short-term memory required in the transient method may prove demanding. The time taken to perform transient photopic and mesopic testing is approximately 15 minutes compared with 6 minutes in the static method. Fatigue and loss of concentration are major factors known to influence the results in testing such variables as visual field.[26]

2. To compare the effectiveness and reliability of the static results with those of previous studies reporting static CS.

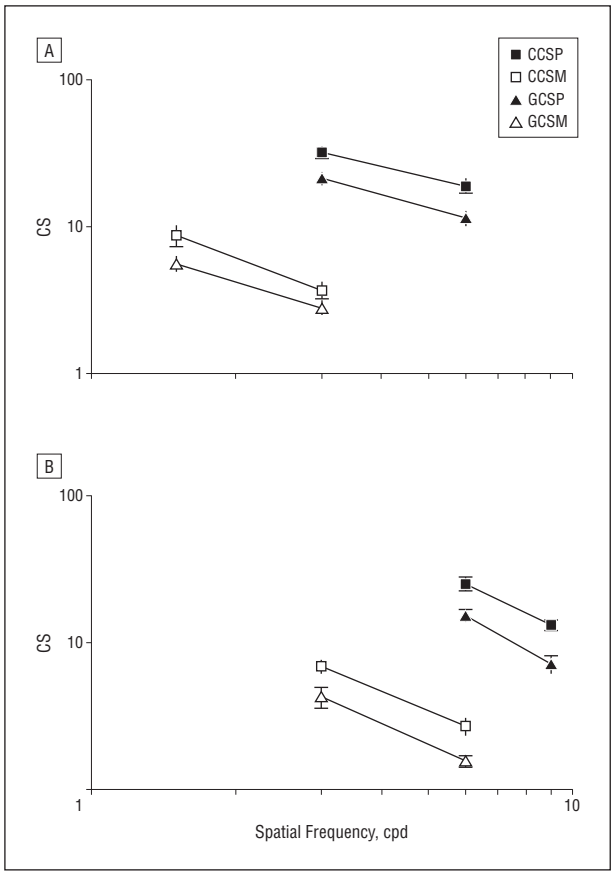

Figure 3. Transient (A) and static (B) contrast sensitivity (CS) using photopic and mesopic conditions for patients with glaucoma vs control participants. In both methods, the results showed significant differences between patients with glaucoma and controls ($P<.01$) at all spatial frequencies under photopic and mesopic conditions. Both axes are presented on a logarithmic scale. Error bars represent standard error. CCSM indicates control CS mesopic condition; CCSP, control CS photopic condition; cpd, cycles per degree; GCSM, glaucoma CS mesopic condition; and GCSP, glaucoma CS photopic condition.

Optical coherence tomography was performed on a subgroup of 4 patients who had undergone trabeculectomy in the past to exclude macular edema. The macular findings were normal for all patients with normal macular thickness.

STATISTICAL ANALYSIS

Statistical analysis was performed using the paired, 2-tailed *t* test for significance level testing, and the Pearson correlation was performed for correlation testing.

RESULTS

Fifty-eight eyes (50 participants) underwent testing. Patient demographics are summarized in the **Table**. The glaucoma group included 15 eyes with primary open-angle glaucoma, 6 with exfoliation glaucoma, 5 with chronic angle-closure glaucoma, 3 with normal-tension glaucoma, and 6 with suspected glaucoma. None of the

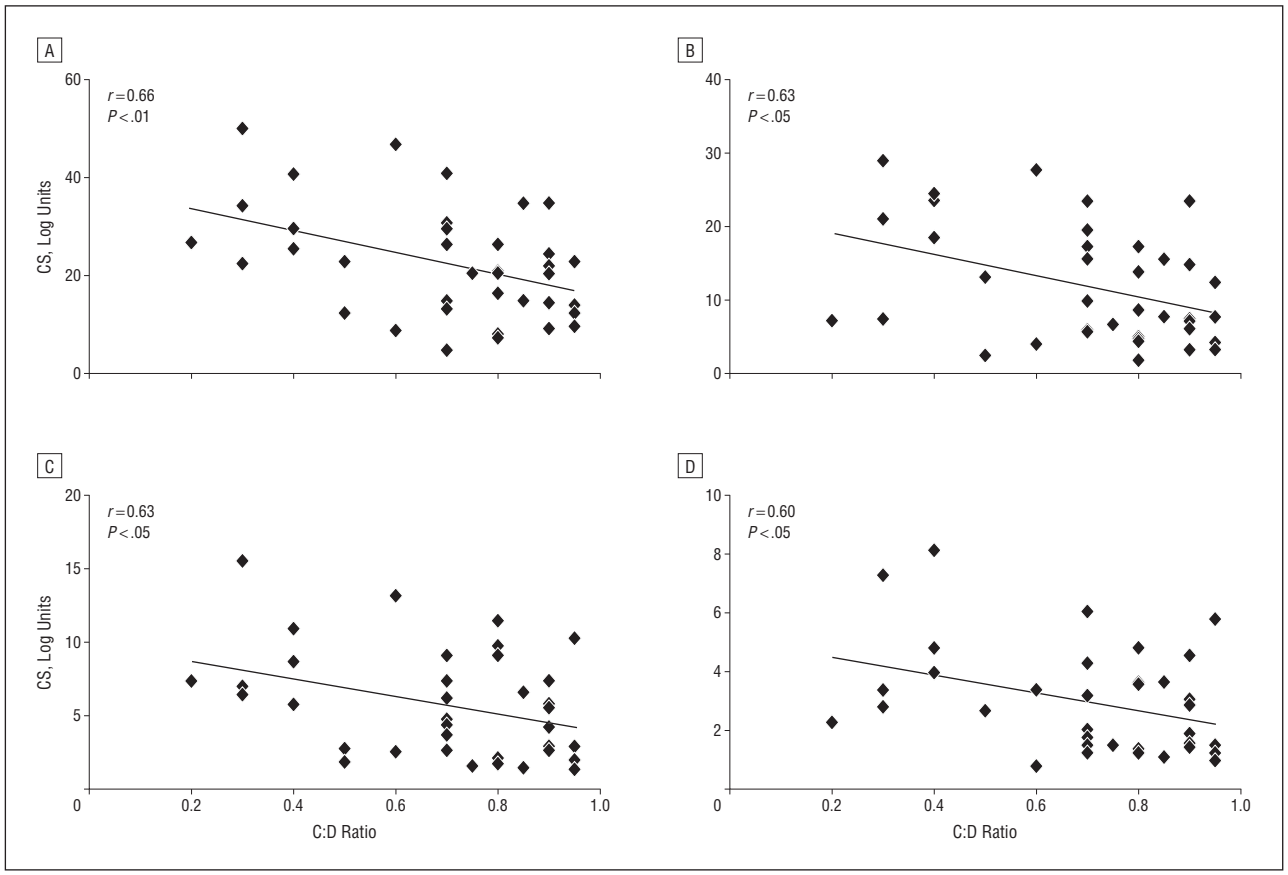

Figure 4. Correlation between cup to disc ratio (C:D) and transient contrast sensitivity (CS). A, Photopic condition, 3.0 cycles per degree (cpd). B, Photopic condition, 6.0 cpd. C, Mesopic condition, 1.5 cpd. D, Mesopic condition, 3 cpd. Significant correlations were found at all spatial frequencies. The solid lines represent the linear regression.

patients had an acute elevation of intraocular pressure. There was no significant difference in visual acuity between the groups. To scrutinize the relationships between CS and the visual field damage, the glaucoma group was divided into 3 categories according to the severity of their visual field damage (**Figure 2**). The differences between each glaucoma category and the control group and between glaucoma categories were significant ($P<.05$), apart from that between the moderate and mild groups. Not all patients could complete the transient and static methods in all SFs; thus, the number of participants differs between the 2 methods.

TRANSIENT METHOD

The results for the transient method showed significant differences between the glaucoma and control groups ($P<.01$) at all SFs under photopic and mesopic conditions (**Figure 3**A).

STATIC METHOD

The results for the static method showed significant differences between the glaucoma and control groups ($P<.01$) at all SFs under both conditions (Figure 3B). The static method yielded higher CSs than the transient method (38.8% higher for the common photopic SF of 6.0 cpd and 33.4% for the common mesopic SF of 3.0 cpd), but the trend of the results is similar. High correlations were found between the 2 methods under both conditions (photopic testing, $r=0.82$ [$P<.001$]; mesopic testing, $r=0.82$ [$P<.001$]).

CORRELATION BETWEEN GLAUCOMATOUS DAMAGE AND CS

Correlation was performed by including all patients with glaucoma and the controls (**Figures 4**, **5**, and **6**). In addition, we compared foveal CS between categories of different glaucomatous damage (**Figure 7**).

Cup to Disc Ratio and Foveal CS

All transient photopic and mesopic CSs were significantly correlated with cup to disc ratio ($P<.05$) (Figure 4). Static photopic SF values of 9.0 cpd, along with static mesopic SF values of 6.0 cpd, were also significantly correlated with cup to disc ratio ($P<.05$) (Figure 5).

Visual Field and Foveal CS

Mean deviation was found to be significantly correlated with a static photopic SF of 6.0 cpd ($r=0.65$ [$P<.05$]) (Figure 6). The other SFs were not significantly correlated with MD.

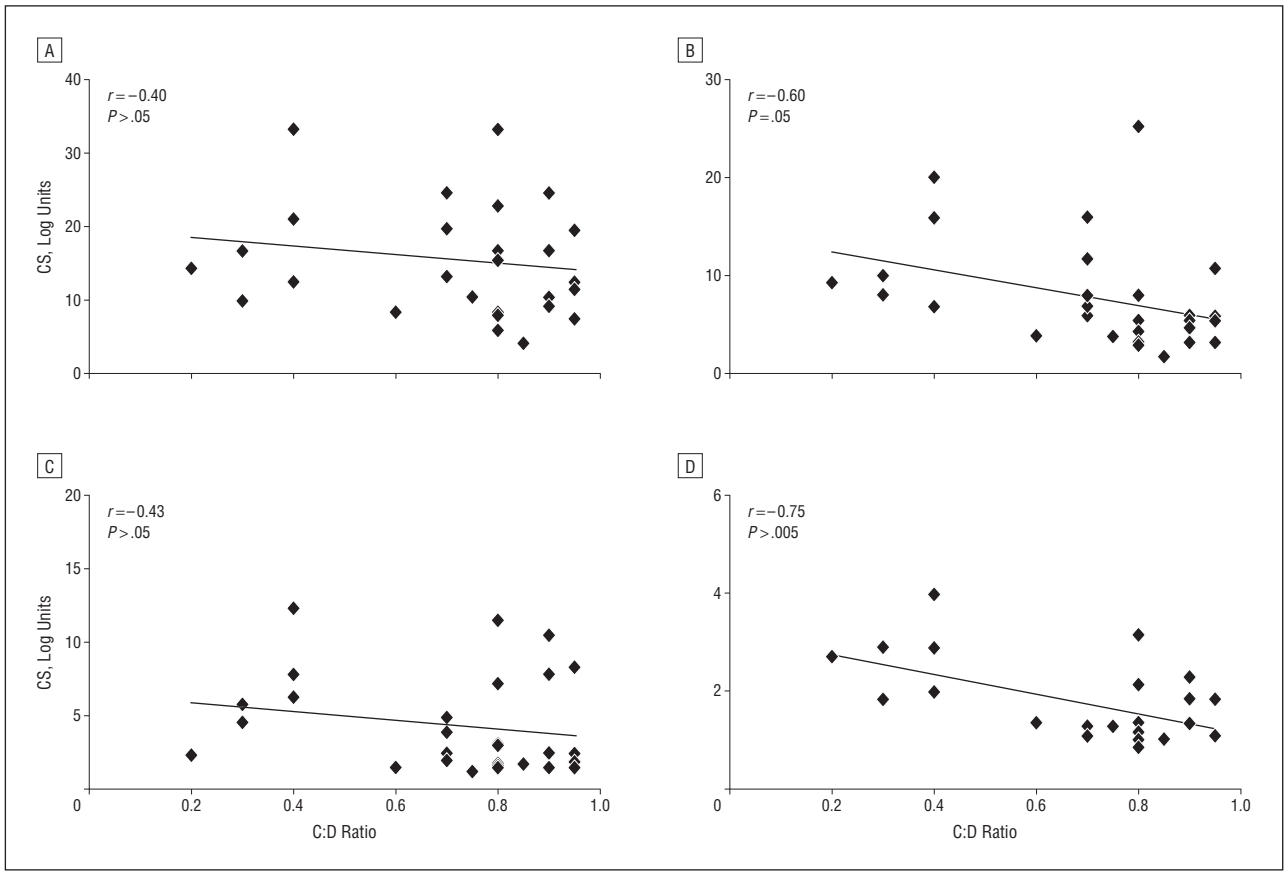

Figure 5. Correlation between cup to disc ratio (C:D) and static contrast sensitivity (CS). A, Photopic condition, 6.0 cycles per degree (cpd). B, Photopic condition, 9.0 cpd. C, Mesopic condition, 3.0 cpd. D, Mesopic condition, 6.0 cpd. Significant correlations were found in photopic 9.0-cpd and mesopic 6.0-cpd conditions only. The solid lines represent the linear regression.

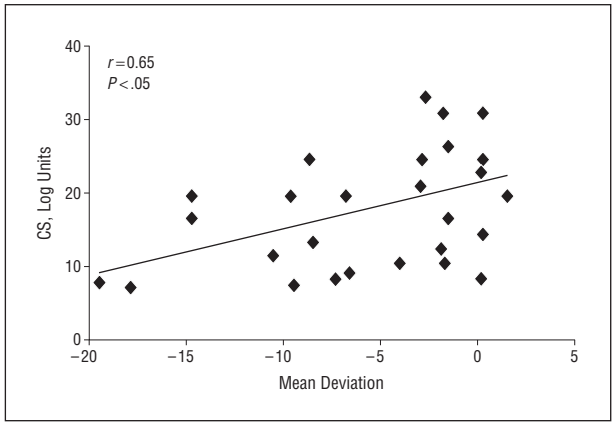

Figure 6. Correlation between Humphrey visual field mean deviation (MD) and static contrast sensitivity (CS) for photopic spatial frequency of 6.0 cycles per degree. The correlation was significant. The solid line represents the linear regression.

We used the common SF (6.0 cpd) that was used in both the static and transient methods to compare CS between different glaucoma categories and the controls. There was a trend of decreasing CS with increasing severity of glaucoma (Figure 7). Patients with severe glaucoma had significantly decreased CS compared with controls using the static or the transient photopic SF of 6.0 cpd ($P<.05$). All together, the results show that CS of at least 6.0 cpd is a good predictor of the severity of glaucoma.

Eight patients with glaucoma contributed both eyes to the data analysis. No patient contributed both eyes among the severe and moderate glaucoma groups. Three patients contributed both eyes in the mild glaucoma group. However, when we removed the results of the left eye of those patients, no significant difference was found between right eyes in the glaucoma and control groups. For example, at 6.0 cpd, we found that the difference between the right eyes in the glaucoma group and right eyes in the control group is highly significant ($P=.001$ and $P=.002$ for photopic and mesopic conditions, respectively), similar to what was found when both eyes were included. Moreover, we also compared CS results of both eyes vs 1 eye, and the difference was not significantly different ($P=.91$ and $P=.77$ for photopic and mesopic, respectively).

COMMENT

In this study, a significant decrease in both photopic and mesopic foveal CS in patients with glaucomatous eyes was found. Furthermore, the results showed that both the transient and static methods display the same trends and are equally accurate. The similarity in the results of the 2 methods of testing implies that the static method, which is shorter and easier, can be useful. In addition, the static and transient photopic methods were significantly correlated with severity of glaucomatous damage.

Our results are consistent with previous studies but add psychophysical evidence that foveal functions are affected in glaucoma, thus supporting various histopathological,[27,28] anatomical,[24,29] and other psychophysical studies.[6,30-32] Foveal involvement early in glaucoma has been a controversial issue.[33,34] The maintenance of good visual acuity until late in the disease and the absence of characteristic central visual field defects lead to the belief that the fovea remains unaffected in the early stages of the disease. However, the density of ganglion cells is 10-fold greater at the fovea than the density at 25° eccentricity and 100-fold greater than at the farther periphery,[19] an effect that enables substantial redundancy at the fovea[27] to overcome the early loss in the glaucomatous process, sparing normal foveal function. In automated perimetry, the central retina requires more ganglion cell loss to produce a criterion decrease in sensitivity than does the retina subtending the field at 10° to 30° from fixation.[35] One remaining ganglion cell per cone may suffice to detect a spot of light or high-contrast letters. Our study, using different modes of foveal CS testing, was able to detect significant differences between patients with glaucoma who have good visual acuity and controls.

We analyzed 2 methods herein. In a clinical setting, it is essential for a test to be accurate at diagnosing a disease, and it is advantageous for it to be fast and easy to use. The difference in conductance and timing between the tested methods makes the static method easier and faster. Results showed that both methods produce similar trends and are equally accurate, thus implying that the static method may be used safely in the future.

When comparing the method used herein with others cited in the literature, we note 2 important points. First, the results of the static testing are consistent with those of previous studies[2,5,10,11,16] but seem to be advantageous because they are computerized and randomized and have limited target sizes that are detected by the fovea. Second, because patients with glaucoma report difficulties in night vision,[36] an added factor unique to this foveal CS testing is the use of mesopic CS, a test rarely used in assessing CS. Previous studies of mesopic or scotopic CS usually used 30 minutes of dark adaptation,[37] thus making the technique impractical as a clinical procedure. The added information of mesopic CS contributes an additional dimension in understanding the loss of CS in glaucoma.

Some studies reported specific SFs to be affected in glaucoma, pointing to the possibility that different stages of the disease affect different SFs.[4] In our study, a loss of sensitivity was found in all SFs. Similar results were obtained by Ansari et al,[9] who found significant losses of CS in the glaucoma group compared with the control group; they were unable to demonstrate a greater loss of sensitivity across a range of spatiotemporal frequencies (0.5, 2.0, and 8.0 cpd).

In this study, we found a significant correlation among cup to disc ratio, MD, and CS, suggesting that CS is affected by the severity of the disease and may be used as an aiding tool for assigning the progress of glaucoma.

A number of important points should be considered. We designed our study to eliminate optical and other nonneural factors that may affect CS. For this reason, the inclusion criteria were very strict. Lack of confounding effects by lens opacities were ensured by excluding patients with cataracts, with older patients being pseudophakic. In clinical practice, however, patients with glaucoma may have coexisting abnormalities, such as cataract or age-related macular degeneration, which individually affect CS. Hence, interpretation of CS results may be confounded by numerous factors that cannot be easily controlled. The results of CS for these eyes must therefore be interpreted with caution.

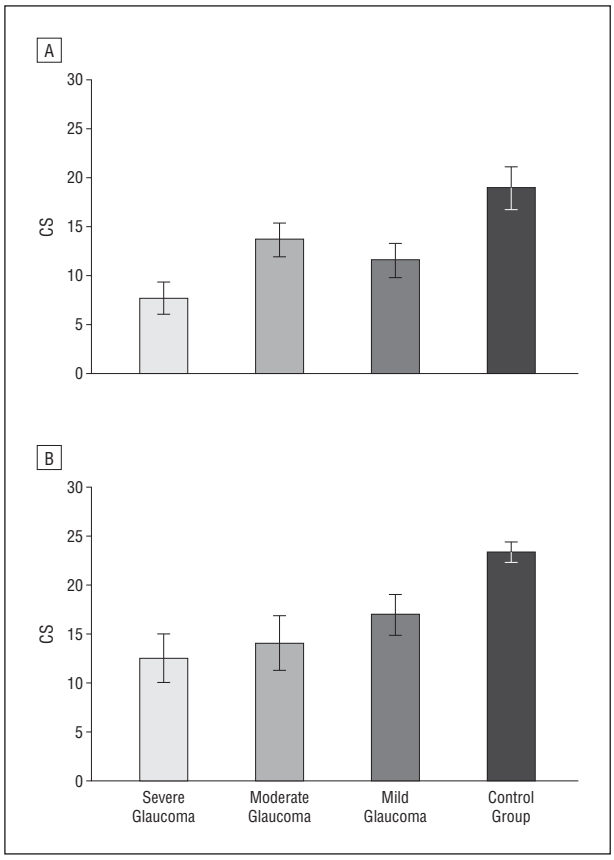

Figure 7. The difference of photopic contrast sensitivity (CS) for 6.0 cycles per degree (cpd) between the control group and different degrees of glaucomatous damage. Transient (A) and static (B) photopic CS for 6.0 cpd of the following 3 glaucoma groups: severe, moderate, and mild, compared with the control group. There is a trend of decreasing CS with increasing severity of glaucomatous damage. The CS of patients in all categories is significantly decreased compared with the control group ($P<.05$).

Further longitudinal prospective studies should subdivide the glaucoma group into different levels to evaluate the correlation between CS and glaucoma progression. Furthermore, it is still unknown whether CS declines linearly with the progression of glaucoma in a stepwise fashion or in an all-or-none manner. Our results found a significant correlation of CS and cup to disc ratio with both methods but a significant correlation with visual field MD with the static method only.

The CS test provides a comprehensive assessment of spatial vision. The CS testing methods used in this study detected damage in central vision despite good acuity. Regardless of the prognostic or diagnostic value of these tests, the results lend strong support to the conclusion that disruption of central visual function may occur in glaucoma. Further research is recommended to possibly establish the CS test's role in the screening and monitoring of glaucoma.

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