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Assessing glaucoma deterioration using Spaeth/Richman contrast sensitivity test

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Abstract

Purpose: To assess changes in the central and peripheral contrast sensitivity in severe primary open-angle glaucoma (POAG) patients using a computer-based Spaeth/Richman contrast sensitivity test (SPARCS) over a period of 24 months.

Methods: Our pilot, observational study included 15 patients (30 eyes) with severe POAG. Visual acuity, intraocular pressure, number of anti-glaucoma drugs, visual fields, and SPARCS score were recorded at first visit and at 12 and 24 months.

Results: We observed changes in mean deviation (MD) from −19.37 ± 5.04 to −20.63 ± 4.07, mean pattern standard deviation (PSD) from 11.49 ± 2.61 to 11.35 ± 2.01, and mean SPARCS score from 54.97 ± 15.66 to 53.50 ± 16.42. We found no statistically significant difference between visual field parameters and SPARCS scores associated with the number or type of prescribed anti-glaucoma drugs. Spearman's correlation coefficient of SPARCS at baseline (SPARCS1) *versus* MD at baseline (MD1) was 0.274 ($p = 0.142$) and SPARCS1 *versus* PSD at baseline (PSD1) was −0.163 ($p = 0.389$). The correlation coefficient between SPARCS at 12 months (SPARCS2) *versus* MD (MD2) at the same time point was computed to be 0.391 ($p = 0.03$), whereas SPARCS2 *versus* PSD at 12 months was −0.212 ($p = 0.262$). Similarly, we found the coefficient to be 0.336 ($p = 0.069$) for SPARCS3 (SPARCS at 24 months) *versus* MD3 (MD at 24 months) and −0.242 ($p = 0.197$) for SPARCS3 *versus* PSD3 (PSD at 24 months). Correlation coefficients between SPARCS1/2, SPARCS1/3, MD1/2, MD1/3 PSD1/2, and PSD1/3 were 0.856, 0.865, 0.748, 0.722, 0.497, and 0.562, respectively ($p < 0.001$). MD changed by 9.46% ± 12.73%, PSD by 0.64% ± 14.03%, and average SPARCS by 3.31% ± 12.73% over 24 months.

Conclusion: The data from our study indicate the utilitarian application of SPARCS, an inexpensive and readily available tool for monitoring functional deterioration in cases with advanced glaucomatous damage, especially in resource-poor settings. Furthermore, it is a useful and reliable alternative to the imaging modalities where retinal nerve fiber layer measurement can be erroneous in advanced cases secondary to the floor effect.

Keywords: contrast sensitivity, glaucoma, Spaeth/Richman contrast sensitivity test

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Introduction

Contrast sensitivity (CS) is a sensitive and reliable indicator of glaucomatous damage.[1,2] Traditionally, standard automated perimetry (SAP) is performed to detect the visual field defects for diagnosing glaucoma and to monitor disease progression.[3] However, changes in CS of glaucomatous eyes have been detected before visible damage to the retinal nerve fiber layer (RNFL) or they manifest as field defects on SAP.[2,4,5] High variability and limited dynamic range of measurements make the monitoring of patients with severe glaucoma difficult. It has been proposed that assessment of spatial CS

might be a more efficient and inexpensive tool in monitoring the subtle functional deterioration of glaucoma than visual field testing.[6] In addition, CS assessment tests present a wide range of contrast levels and yield a more realistic measurement of functional changes than visual acuity assessment, SAP, or RNFL imaging. However, not much has been written about the characterization of CS tests for patients with severe glaucoma.

The Spaeth/Richman contrast sensitivity test (SPARCS) is an Internet-based CS test that features multiple answer choices and a bracketing technique to determine the contrast threshold.[6] SPARCS measures spatial CS in both central and peripheral vision, making it an excellent tool to assess glaucomatous damage.[7,8] SPARCS is advantageous over letter-based CS tests, such as the Pelli-Robson chart, the results of which may be influenced by literacy and chart fading.

Despite adequate intraocular pressure (IOP) control, glaucoma may continue to progress, and some patients eventually end up with severe, irreversible vision loss.[3,7,8] Delay in diagnosis, inadequate treatment, and difficulty in monitoring progressive damage prognostically impact the prospects of good visual outcomes in glaucoma patients. We designed this study to assess the change in CS, an important aspect affecting the quality of life of patients suffering from severe glaucoma using SPARCS. We hypothesize that CS changes occur before manifesting as visual field defects and hence may help in monitoring deterioration of the disease, especially in severe cases where a floor effect may exist due to RNFL loss, and RNFL no longer remains a reliable measure of progression. Therefore, a subtle deterioration may go unnoticed on RNFL imaging and SAP. With the availability of tools like SPARCS that can assess both central and peripheral CS, these can be employed for monitoring patients with severe glaucoma in whom currently available diagnostic methods have a limited utility.[3,8]

Materials and methods

Patient enrollment criteria

This prospective pilot study was conducted at Government Medical College and Hospital (Sector 32, Chandigarh, India) . The study complied with the tenets of the Declaration of Helsinki. The institutional ethics committee at Government Medical College and Hospital approved the study protocol (No. 2017/041), and an informed consent was obtained from all patients before enrollment. We enrolled consecutive patients of either sex with severe primary open-angle glaucoma (POAG) who presented to the Glaucoma Services at the hospital, which is a tertiary care center in North India. No a priori sample size calculation was done, and 30 eyes were included in the study for establishing a 'proof-of-concept'. The patients with severe/advanced POAG included in the study were enrolled (trial number CTRI/2017/05/008488).

The patient was diagnosed with POAG if he or she had evidence of optic nerve damage from either one or both of the following[9]: (1) optic disk or RNFL structural abnormalities and (2) reliable and reproducible visual field abnormality. The fundus examination and visual field and RNFL assessment were performed by a trained glaucoma specialist (P.I.). The visual field–based Hodapp, Anderson, and Parrish (HAP) grading system was used to define the severity of the disease. The criteria included a mean deviation (MD) worse than −12 dB on pattern deviation plot; >50% of points depressed less than the 5% level or >25 % of points depressed below the 1% level; any point within central 5^0 with sensitivity ≤0 dB; both hemifields containing points within 15^0 of fixation with sensitivity <15 dB.[10]

During the baseline visit, a carefully detailed history was taken in all cases, and the thorough ocular examination consisting of uncorrected and best-corrected visual acuity (BCVA), measurement of IOP using a calibrated Goldmann applanation tonometer (same tonometer used for all visits), slit-lamp examination of the anterior segment, and a fundus examination using a +90D lens was performed. The patients' current symptoms, past medical and surgical history, current systemic and ocular medications, and ocular comorbidities were documented. All the patients included in the study underwent visual acuity assessment on Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity charts. The observed values were converted to the LogMAR scale for statistical analysis. Patients with refractive error within ±6.00 diopter sphere and ±2.00 diopter astigmatism and with transparent lens or previous uncomplicated cataract surgery with implantation of a monofocal intraocular lens (IOL) done at least 6 months prior to enrollment were included.

Humphrey perimeter HVF 750 II (Zeiss Meditec Inc., Dublin, CA), using SITA-Fast (24-2 protocol; Stimulus size III), was used to test visual fields because of high patient load, and the element of fatigue was assessed using a longer test; SITA-Fast strategy was used instead of SITA-Standard. Both eyes of the patients were evaluated, and monocular CS testing was performed using SPARCS. All patients were familiar with the procedure of SAP, having performed at least three reliable visual field tests. A visual field test was deemed reliable only if the pupil diameter ranged between 3 and 3.5 mm at the time of testing, and fixation losses and false-positive rates were less than 20%. Patients with multiple etiologies associated with decreased CS or factors that could preclude the patient from providing reliable and valid data, patients with a history of incisional surgery in the past 6 months, patients with any cause of visual impairment [like cataract – nuclear sclerosis more than grade 2 using Lens Opacity Classification System (LOCS) III grading, diabetic mellitus, or neurological diseases], those with BCVA of less than 20/80, or patients who had undergone refractive surgeries were not included in the study. In addition, we did not include any patient with multifocal IOL as they may alter the CS.

SPARCS test

SPARCS is a computer-based test and can be performed on any standard computer with an Internet access. The test is available at *https://www.sparcscontrastcenter.com*, where each patient is allotted a unique identification number. The standard testing protocol is followed, as per the instructions provided by the website on how to take the test.[7] Lighting conditions are standardized to minimize glare and maintain uniformity for all patients, which includes an LED light source of 22 W, color temperature of 6500 K, and luminous flux of 1900 lm. The patient is made comfortable and explained in detail about the test procedure, which is then followed by a demonstration test before the administration of the test. The patient's distance is fixed at 50 cm from the computer screen, and the testing screen occupies 30° of vision horizontally and 23.5° of vision vertically. The contrast threshold is determined using a staircase strategy with reversals. The patient is presented with vertical square-wave gratings having a spatial frequency of 0.4 cycles per degree that appear for 0.3 s in one of the five tested areas to determine the contrast threshold. Every correct response would step up the contrast level by four steps until the patient gives an inaccurate response, after which the contrast level would step down by two levels. Subsequently, the algorithm would advance or regress by one level at a time till the patient has given two incorrect responses for one particular level, which would determine the threshold for that patient in that specific area. The range of contrast tested is from 100% to 0.45% (Log CS, 0.00–2.35) and decreases by approximately 0.15 log units between levels. The central area and four peripheral areas each receive separate scores out of 20. A total SPARCS score is then calculated using the scores from each of the five areas, out of a maximum of 100. This total SPARCS score was used in this study for comparison with the visual field parameters [MD and pattern standard deviation (PSD)].

Follow-up

The patients included in the study cohort were followed up every 2 months to ensure maintenance of target IOP, and the follow-up compliance was ensured by telephonic reminders. SPARCS and visual field index (VFI) were, however, recorded at 12 and 24 months using the standard testing procedures. The patients who required change in medication, incisional surgery, or laser procedure at any time point after baseline visit were excluded from the study, as this would have had a confounding effect on the outcomes of the CS. The treatment cannot be denied if it is required, and a subsequent reduction in IOP, after additional treatment, would influence the study of natural course of CS changes. The decision to remove these patients from the analyses was made deliberately to have a standardized cohort with minimal confounding factors.

Statistical analysis

The statistical analyses were performed using IBM SPSS version 22 (SPSS, Inc., Chicago, IL).[11] Appropriate tests were used to assess the statistical significance of categorical variables. The association between quantitative explanatory and outcome variables was determined by calculating the Spearman's rank correlation coefficient. All statistical tests were two-tailed, and a value of $p \leqslant 0.05$ was considered statistically significant.

Table 1. Demographic profile and study parameters of the enrolled subjects.

Number of eyes (patients)		30 (15)
Sex		8 males (53.33%)/7 females (46.67%)
Age ± SD (years)		56.73 ± 8.32 (44–82)
No. of eyes with pseudophakia		16 (53.3%)
No. of eyes with prior trabeculectomy		11 (36.7%)
Mean IOP (mmHg) ± SD		12.63 ± 2.12
Mean anti-glaucoma drugs		2.3 ± 0.90 (1–3)
Mean BCVA (LogMAR)		0.35 ± 0.45
Mean MD (dB) ± SD	MD1	−19.37 ± 5.04
	MD2	−19.63 ± 5.56
	MD3	−20.63 ± 4.07
Mean PSD (dB) ± SD	PSD1	11.49 ± 2.61
	PSD2	11.72 ± 2.54
	PSD3	11.35 ± 2.01
Mean SPARCS score ± SD	SPARCS1	54.97 ± 15.66
	SPARCS2	54.77 ± 16.64
	SPARCS3	53.50 ± 16.42

BCVA, best-corrected visual acuity; IOP, intraocular pressure; MD1, mean deviation at baseline; MD2, mean deviation at 12 months; MD3, mean deviation at 24 months; PSD1, pattern standard deviation at baseline; PSD2, pattern standard deviation at 12 months; PSD3, pattern standard deviation at 24 months; SPARCS, Spaeth/Richman contrast sensitivity test; SPARCS1, average SPARCS score at baseline; SPARCS2, average SPARCS score at 12 months; SPARCS3, average SPARCS score at 24 months.

Results

The data analyses at baseline included 40 eyes of 20 patients. However, after the initial enrollment, two patients underwent cataract surgery, two underwent trabeculectomy, and one was lost to follow-up during the study period. Therefore, the final analyses included data of 30 eyes of 15 patients. The demographic profile and study parameters are summarized in Table 1. We found no statistically significant difference between the baseline visual field parameters and SPARCS scores based on age, sex, number or type of anti-glaucoma drugs, initial visual acuity, IOP, or family history of glaucoma. The patients with a history of surgical procedures such as cataract surgery or trabeculectomy also had no statistically significant difference between the visual field parameters and SPARCS scores.

The Spearman's correlation coefficient (two-tailed) was 0.274 ($p = 0.142$) for SPARCS1 (SPARCS at baseline) *versus* MD1 (MD at baseline) and −0.163 ($p = 0.389$) for SPARCS1 versus PSD1 (PSD at baseline). The Spearman's correlation coefficient was 0.391 ($p = 0.033$) for SPARCS2 (SPARCS at 12 months) versus MD2 (MD at 12 months) and −0.212 ($p = 0.362$) for SPARCS2 versus PSD2 (PSD at 12 months). We computed the Spearman's correlation coefficient to be 0.336 ($p = 0.069$) for SPARCS3 (SPARCS at 24 months) *versus* MD3 (MD at 24 months) and −0.242 ($p = 0.197$) for SPARCS3 *versus* PSD3 (PSD at 24 months). The Spearman's correlation coefficient for mean SPARCS score was 0.473 ($p = 0.008$) and −0.240 ($p = 0.201$) for mean MD and PSD, respectively. The scatter plots for these data are shown in Figure 1. The correlation coefficients between SPARCS1 and 2, MD1 and MD2, and PSD1 and PSD2 were 0.856, 0.748, and 0.497, respectively ($p < 0.001$). The correlation coefficients between SPARCS1 and SPARCS3, MD1 and MD3, and PSD1 and PSD3 were 0.865, 0.722, and 0.562, respectively ($p < 0.001$).

While assessing the deterioration in disease, the MD changed by 9.46% ± 12.73% over 24 months, PSD changed by 0.64% ± 14.03%, and the average SPARCS score changed by 3.31% ± 12.73% from baseline. The maximum change in parameters was seen in the MD value, followed by the average SPARCS score, which showed a corresponding decline over time. Of the 30 eyes, only 6 eyes showed significant deterioration of MD on 24-2 visual fields at the end of 2-year follow-up, rate of change ranging from −0.5 dB/year to −1.2 dB/year. This deterioration was confirmed even on a 10-2 visual field test. The average SPARCS score was reduced in 11 eyes. All the patients who had deterioration of SPARCS scores also had deterioration of MD. In

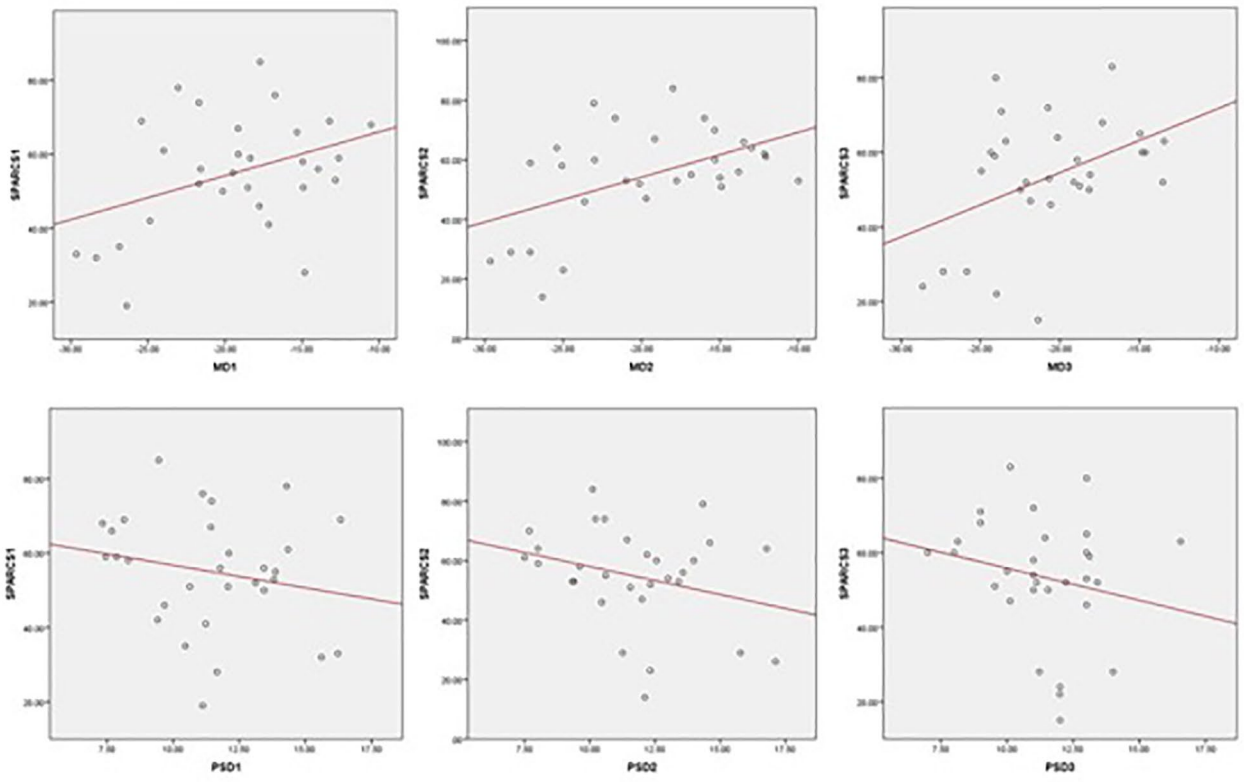

Figure 1. Scatter plots for SPARCS score and mean deviation/pattern standard deviation at 12 and 24 months.

four eyes, MD deterioration preceded change in CS, while in the remaining eyes CS changes preceded.

Although the MD remains the gold standard for evaluating the change in the disease profile, strong correlation seen between the MD and average SPARCS score over time makes SPARCS a potentially easily accessible and cheaper alternative for evaluating deterioration in susceptible subjects who need a closer watch on the structural and functional decline. This being a pilot study with a small number of subjects paves the way for further research to strengthen our findings using larger sample size and more longitudinal data.

Discussion

In most cases, glaucoma patients describe their visual compromise issues to be blurred vision and needing more light to perform any task, and these issues are reflected by associative worsening CS. However, most glaucoma specialists equate changes in the visual field printout, such as a nasal step or arcuate scotoma, while communicating with the patient, which the patients are unable to understand due to the lack of co-relation with the changes in vision and vision-related quality of life. Thus, glaucoma patients are unable to truly comprehend the critical need for compliance for glaucoma treatment as well as repetitive testing, as many cannot relate to the visual deficit that is explained to them. Thus, it is essential that glaucoma specialists include CS assessment as a standard testing technique during glaucoma assessment as well as during follow-up.

CS is one of the critical subsets of visual function, which helps to distinguish an object from the background. Currently, most of the well-established tests exclusively focus on central CS only. However, SPARCS is a novel test that measures the CS not only in the central area but also in peripheral areas (i.e., superotemporal, superonasal, inferotemporal, and inferonasal, respectively) and might stand more sensitive for glaucoma, as it characteristically affects the peripheral vision. The software conducts the test in a random order followed by a multiple answer choice, thereby reducing the chances of guesswork. As the test does not incorporate Latin letters, which might

be memorized by the patients, it also increases its precision and accounts for better test–retest reliability.

Gupta and colleagues have shown the test–retest repeatability of the SPARCS test in the healthy population by repeating the test three times in each eye, where a definite agreement was found between the SPARCS scores obtained at various visits. The authors reported that the factors affecting the CS in the healthy population were lens opacity and old age. Richman and colleagues, while studying the role of SPARCS in glaucoma patients, found that a score of <70 had a sensitivity of 79.7% and specificity of 92.8% in the identification of the disease.[7] SPARCS has previously been shown to be a sensitive and reliable indicator of glaucomatous damage.[6,12] Glaucomatous damage has been shown to reduce CS relative to normal aging across the spatial frequency range for both the steady- and pulsed-pedestal tasks, indicating a reduction in sensitivity that is not selective for magnocellular or parvocellular pathways.[7] This suggests that CS reduction in glaucoma precedes visual acuity and visual field changes.[7] In addition, it has been found that CS progressively decreases as the severity of glaucoma increases. Moreover, CS has been found to be more closely related than color perception or reading ability to disease severity. With the capability of understanding the mechanisms by which this selective vulnerability in glaucoma affects different RGC types, the potential for rescuing retinal ganglion cells (RGCs) if the damage is detected early enough before significant structural and functional alterations can occur offers an exciting alternative to glaucoma researchers to look beyond the visual fields for answers to glaucoma pathogenesis. Our study is a novel attempt to build on these findings and explores the potential of SPARCS in monitoring the disease deterioration by assessing the change in CS over 24 months in patients with severe POAG.

Cataract has been shown to affect CS and MD values significantly, but in our study population there was no visually significant cataract in any patient as per the LOCS grading. We suggest that for a patient with coexisting cataract and glaucoma, CS assessment be done after cataract surgery with monofocal IOL implantation. Similarly, SPARCS is reliable across a spectrum of refractive errors. In our study, the change in BCVA between the two visits was not statistically significant and did not affect the MD, PSD, or SPARCS values ($p > 0.05$). Pseudophakic status can alter CS, but in our patients, the history of cataract surgery was not a significant determination factor of final SPARCS, MD, or PSD value.

We know that while assessing the glaucoma progression, the critical parameters that need consideration are visual field MD, PSD, and VFI. Correlations between SPARCS and MD/PSD were nonlinear in our study. MD is the current gold standard to detect disease deterioration, but as the disease advances, MD becomes more unreliable.[3] PSD, on the contrary, is used to identify localized loss. It is based on the pattern deviation plot, and as the defects become more diffuse, PSD values return to normal (toward zero). PSD thus is not a useful parameter to monitor patients with advanced disease, and findings of our study indicate the same. In addition, in severe/advanced glaucoma patients, the standard SAP 24-2 SITA-Standard or SITA-Fast strategies are likely to miss defects that develop or progress between the 6° spacing of the test points. The outer field area may already be depressed, and therefore reliability of visual fields reduces with advancing glaucoma.

In our study, only SPARCS2 *versus* MD2 and mean SPARCS *versus* mean MD showed a statistically significant correlation. The SPARCS scores, however, correlated better with each other than MD and PSD, indicating the robustness of CS measurement in the assessment of glaucomatous damage. Previously, SPARCS has also been shown to correlate well with varying severity of glaucoma, including sensitivity across mild, moderate, and severe groups.[6,12] Waisbourd and colleagues in a prospective study found the factors that showed a significant correlation with progression of glaucoma to be worsening of MD scores, subjective worsening of quality of life, and also worsening of SPARCS scores, which pointed significantly toward glaucoma progression.[13] These findings indicate that SPARCS can become an adjunct to contemporary methods of assessment of glaucoma progression.

CS measurements have also been compared with the structural assessment of RNFL, but these often just limit themselves to central CS and hence are not able to effectively assess glaucomatous damage. Fatehi and colleagues used the CSV-1000 (Vector Vision, Grenville, OH) and macular spectral domain optical coherence tomography (SD-OCT) imaging with Cirrus and

Spectralis devices to evaluate the role of CS in outcome prediction of glaucomatous eyes.[14] They could demonstrate the role of central visual field indices and central full macular thickness measurements with CS, most markedly at 6 cpd. Still, they could not show a significant relationship with the severity of glaucoma. Their population, however, was considerably different and only included mild and moderate glaucoma patients.[8] Some prior studies have also reported a decrease in CS at 3, 6, and 12 cpd in glaucomatous eyes. Amanullah and colleagues compared CS with RNFL thickness in patients with glaucoma and noted that the CS in the left upper areas of vision for both eyes had the strongest correlation with the RNFL thickness of the inferior quadrant, that is, 7 o'clock sector for the left eye and 6 o'clock sector for the right eye.[15] Thus, the CS test might have a potential role as a predictive tool for structural damage.

VFI is more accurate than MD and PSD in determining the change in the disease over time.[16] However, this approach requires at least five initial visual field test results to be reliable. The mean number of fields in our population was 4 ± 1.2, and thus we did not include VFI comparisons with SPARCS in our results. A future study could, however, explore this relationship through the robustness of VFI in fields with >-20 dB MD, which still needs to be reliably evaluated.[17]

There is a significant increase in socioeconomic burden as well as a decline in the vision-related quality of life from glaucoma as the disease progression occurs.[18] Timely intervention (in the form of addition of medication or offering surgery) when the CS starts to decline may help in functional rehabilitation and improvement in vision-related quality of life for such patients. Currently, available imaging tools have been shown to be unreliable and inefficient while monitoring the change in advanced stages of the disease.[3,10] In a recent article, Jammal and coworkers evaluated CS in patients with advanced glaucomatous visual field damage using two clinical CS tests, Pelli–Robson test and the Freiburg Visual Acuity and Contrast Test (FrACT), and found moderate to advanced deficits in CS.[19] Thus, a baseline as well as follow-up CS tests may be included in the examination protocol for patients with advanced glaucoma. Our preliminary results of this study pave the way for further studies to compare SPARCS results with structural parameters like OCT-RNFL for more definitive answers on the structure–function decline in advanced glaucoma cases. In addition, in current COVID scenario, online resources for remote testing become more valid for detecting deterioration in elderly glaucoma patients with moderate to advanced disease (at-risk population for COVID). The chief limitations of the study include a small sample size, excluding patients who were started on medications or required surgery, and the need for a longer follow-up to ascertain true progression. We are continuing to monitor these patients and in the next phase plan to do a sub-analysis of patients with and without adjustment in treatment plan.

Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

The study was approved by the institutional review board and was performed in compliance with the Declaration of Helsinki.

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