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Association of Contrast Sensitivity with Eye Disease and Vision-Related Quality of Life

Kathryn Flaharty, BA¹, Leslie M. Niziol, MS², Maria A. Woodward, MD, MSc², Angela Elam, MD², Amanda Bicket, MD², Olivia J. Killeen, MD, MS², Jason Zhang, MD², Leroy Johnson, MD³, Martha Kershaw, MD⁴, Denise A. John, MD², Sarah K. Wood, OD, MS², David C. Musch, PhD, MPH^{2,5}, Paula Anne Newman-Casey, MD, MS²

¹University of Michigan Medical School, Ann Arbor, MI

²Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, MI

³Hamilton Community Health Network, Flint, MI

⁴Hope Clinic, Ypsilanti, MI

⁵Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI

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Introduction

Screening for eye disease currently takes place primarily in specialty eye clinics, yet these clinics are not easily accessible for everyone in the United States. In 2011, a review of the geographic distribution of eye care providers showed that 24% of counties in the United States had no advanced practice eye care provider (ophthalmologist or optometrist), and 61% of counties had no ophthalmologist.¹ Further, uninsured and underinsured patients often have a harder time accessing eye clinics due to an increased distance from those individual's homes to eye care offices.¹ Insidious diseases, such as diabetic retinopathy and glaucoma, can lead to blindness if people do not get screened and treated appropriately. One structural mechanism for improving access to eye care for populations at higher risk of disease is through telemedicine, where the specialist provider and the patient do not need to be co-located to provide high-quality care. The Michigan Screening and Intervention for Glaucoma and Eye Health through Telemedicine (MI-SIGHT) program is a telemedicine-based glaucoma and eye disease screening program that operates in a free clinic and a Federally Qualified Health Center (FQHC) that serve communities with high levels of poverty and large proportions of residents who identify as Black and Hispanic/Latino.

Visual acuity (VA) is the most common measure used to screen for eye disease in primary care and community clinic settings. The ubiquity of VA testing in primary care offices,

however, does not ensure that everyone with eye disease will get appropriately flagged and referred for treatment because many diseases do not impact VA until late in their course.² In addition, patients with early stages of eye diseases, such as glaucoma, diabetic retinopathy, and age-related macular degeneration, report increasing difficulty with vision while VA measures remain unchanged or remain within normal ranges. Some have postulated that CS may be a measure responsible for some of the self-reported difficulties in vision that are not detectable via VA measurement.^{2–5} Although not included in most routine eye exams, CS is an important aspect of visual function that relays additional information not captured by VA.⁶ CS refers to the ability to visually discern objects from their backgrounds and is a critical component of mobility,⁷ stability^{8,9} and safe driving.¹⁰ CS is a critical components of visual quality, and determines the amount of illumination, contrast, and magnification needed to see.¹¹

Deficiencies in CS may precede deficiencies in VA measurements because VA is measured using a high-contrast test. Additionally, CS shows quantitatively different patterns for different ocular pathologies.¹² This distinction suggests that measuring CS may represent a separate and complementary measure to VA for screening, detecting, and triaging eye disease. In fact, a laboratory study in 1984 showed evidence that CS, measured by an oscilloscope, was a robust measure for the detection of perceived visual disability in a small sample of glaucoma patients, particularly early in the disease process when visual fields are still largely unaffected.¹³ The study found that CS measurement was highly correlated with self-reported visual disturbance as well as early glaucoma disease state. To that end, this study aims to investigate the role of CS as a possible screening measure for eye disease, and its relationship to vision-related quality of life (VRQOL) in a medically underserved cohort recruited from two primary care clinics. We hypothesized that CS may have utility both in detecting the presence of eye disease as well as assessing impact on VRQOL.

Methods

This study was approved by the Institutional Review Board at the University of Michigan (UM) and adhered to all Tenets of the Declaration of Helsinki. The clinical trial component of the study is registered at [clinicaltrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT04274764) (NCT04274764), but this analysis is not part of the clinical trial. The MI-SIGHT program is being conducted in two clinics serving primarily low-income communities with large proportions of people who identify as Black and Hispanic/Latino, including a free clinic in Ypsilanti, MI and a FQHC in Flint, MI. Community residents were recruited by various methods including advertising in the communities and directly calling existing patients, and our community outreach strategies have been detailed in the cited publication.¹⁴ At the free clinic, study personnel called patients who were referred by clinicians at the free clinic for a variety of reasons, and at the FQHC, study personnel called patients with diabetes who were overdue for their annual eye exam. The cohort for this study consists of participants recruited during the program's first year in each clinic, from June 2020-June 2021 at the free clinic and from January 2021-January 2022 at the FQHC.

Community residents at least 18 years of age were eligible to participate. Exclusion criteria included those with any of the following eye symptoms: significant eye pain, sudden

decrease in vision within one week, or binocular diplopia. People with these symptoms were referred directly to an eye care provider. Additionally, anyone with cognitive impairment (assessed as inability to answer screening questions), or who was currently pregnant, incarcerated, or moving outside of driving distance to the clinic within 6 months was also excluded.

For those community members who were eligible to participate, enrollment began with obtaining written informed consent. Full consent forms were provided in English, Spanish, and Arabic, and short form consents were provided in Albanian, Chinese, French, Hindi, Korean, Igbo, and Tagalog. After obtaining informed consent, an ophthalmic technician completed a health history and questionnaires with the patient. This included the 9-item National Eye Institute Visual Function Questionnaire (VFQ-9) to assess visual function and VRQOL.¹⁵ This shortened version of the original questionnaire¹⁶ assesses visual function across 7 domains (general vision, near and distance activities, mental health, role difficulties, driving, and peripheral vision). Each question is asked on a 5- or 6-point Likert scale, that is then coded from 0 to 100 with larger values indicating better visual function. The questionnaire was scored for an overall composite score as a mean of all 9 questions, and a mean score for each of the 7 sub-domains was also calculated.

Following completion of the history and questionnaires, an ophthalmic technician completed an eye screening testing with the patient, including: 1. Near and distance VA assessment; 2. Auto refraction (NIDEK autorefractor) and Manifest Refraction (manual using phoropter); 3. CS measurements for each eye using the Pelli-Robson chart¹⁷; 4. Eyeglass measurement if wearing, with a lensometer and inter-pupillary distance (pupilometer); 5. Eye examination including pupillary response, anterior chamber angle assessment by penlight, extraocular motility and alignment, and intraocular pressure (IOP) measurement; 6. Dilation with 0.5% tropicamide only¹⁸ for those participants without a narrow angle on penlight exam¹⁹ and IOP less than 30 mmHg to mitigate the potential risk of acute angle closure; 7. Mydriatic imaging of the posterior pole by fundus photography (three images focused on the disc, the macula, and the superotemporal arcade²⁰) and Retinal Nerve Fiber Layer Optical Coherence Tomography imaging.²¹ If images were not of sufficient quality, the ophthalmic technician would repeat the imaging as time allowed. The ophthalmic technician entered the screening data and imaging data into the electronic health record (EHR). If urgent or emergent conditions such as severely elevated IOP were identified, a UM ophthalmologist and/or the ophthalmologist at the FQHC or the Medical Director at the free clinic were paged to ensure that the participant was offered timely, appropriate care.

The ophthalmic technician measured CS in each eye of participants using the Pelli-Robson chart¹⁷ from a distance of 1 meter with the room lighting at 269.1 lumens (standard illumination) in a room without a windows. Corrective lenses were used if participants presented with contacts or glasses. The clinically significant values that are reported from the Pelli-Robson chart are logarithmic measures of the participants' CS, or logCS (hereafter referred to as just CS) that range from 0.00–2.25 log units with higher numbers indicating better CS performance. The chart uses triplets of letters to assess CS, with two triplets (6 total letters) on each line. Each triplet of letters fades in contrast, so that there are two distinct levels of CS on each line. Each triplet a participant reports correctly represents a

0.15 log unit increase in the CS value, and each line increase represents a 0.3 log unit increase in the CS value. The patient's CS is determined by the best triplet, for which two of the three letters are correct.

Remote ophthalmologists at the UM reviewed the MI-SIGHT participant data through the EHR and designated whether fundus photographs and optical coherence tomography (OCT) images were gradable or ungradable. The remote ophthalmologists assessed whether the following eye diseases were present or absent for the following most common eye diseases through protocol-specified criteria:²¹ visual impairment (best corrected visual acuity $\leq 20/40$ in the better seeing eye), refractive error, cataract, diabetic retinopathy, macular degeneration, and glaucoma, alongside any other incidental findings. The ophthalmologists assessed any signs of cataract seen on anterior segment photograph as requiring or not requiring referral for surgical consultation based on visualization of a cataract on anterior segment photographs combined with level of best-corrected visual acuity. The ophthalmologists assessed for the presence and stage of diabetic retinopathy with/without macular edema according to the English National Health Service criteria.²² The ophthalmologists assessed for macular degeneration using Age-Related Eye Disease Study (AREDS) criteria.²³ Glaucoma or suspected glaucoma was assessed by the grading ophthalmologist using the following criteria:²⁰ 1. Patient previously treated for glaucoma (e.g. already taking glaucoma medications or previous glaucoma surgery); 2. Narrow angle on penlight exam; 3. Cup-to-disc (c/d) ratio ≥ 0.7 ;²⁴ 4. Asymmetry of the cup-to-disc by ≥ 0.2 where the larger cup is ≥ 0.6 ;²⁰ 5. Abnormal high-quality OCT (overall retinal nerve fiber layer thickness < 80 microns or thinning at $< 1\%$ certainty (RED-damaged tissue) in the inferior or superior quadrants);^{20,25} 6. IOP > 21 mmHg (median of the 3 measures taken), interpreted according to the following criteria: if the IOP is 22–24 mmHg and the c/d ratio is < 0.35 with no other risk factors, there is no referral but if the c/d is ≥ 0.35 , refer within 6 months; IOP 25–29 mmHg, refer within 1 month; IOP 30–40 mmHg, refer within one week; IOP > 40 , refer within 24 hours or immediately. Each ophthalmologist used clinical judgment to determine whether the participant's diagnosis was glaucoma or glaucoma suspect. Each of the six ophthalmologists on the team met with the study PI individually to go over diagnostic criteria prior to beginning to interpret examinations and group meetings were held quarterly to address issues and inconsistencies. Any other eye disease identified was also noted and recommendations for appropriate care and follow-up interval were made. A templated letter was sent to the patient and their primary care physician, if the patient wanted it sent, with the assessment and plan.

Statistical Methods

The sample of MI-SIGHT participants recruited during the first year of the program who also had CS measured were identified. Demographic characteristics of the sample were summarized with descriptive statistics. CS was measured per eye and summarized overall, for the better or worse eye, and for the difference between eyes with means, standard deviations (SD), medians, and interquartile ranges (IQR). For the few patients in our sample who had a CS measurement from only one eye, a difference score was unable to be obtained, and their single CS value was used for both better and worse eye calculations. The

associations of CS with eye disease (glaucoma, cataract, DR, AMD) and self-reported visual function were explored.

Using eye as the unit of analysis (analyzing data from each eye), CS was summarized with descriptive statistics between eyes with and without disease and compared for differences using repeated measure linear regression accounting for the correlation between eyes of a subject. Further, logistic regression with generalized estimating equations (GEE) was used to investigate the effect of CS on the probability of each eye disease (cataract, glaucoma, DR, AMD) while accounting for the correlation between eyes of a patient.²⁶ Models were run with adjustment for participant age and presenting VA. Results are reported with odds ratio (OR) and 95% confidence intervals (CI) for a 0.3 log unit decrease in CS to contextualize the effect of missing an entire line of contrast (two sets of triplet letters) on the Pelli-Robson chart. The ability of CS to predict eye disease was also explored using logistic regression with GEE. Cut points to the model predicted probabilities were chosen to maximize Youden's statistic and prediction diagnostics including sensitivity, specificity, and area under the curve (AUC) are reported with 95% CIs.²⁷

Using patient as the unit of analysis (aggregating data between eyes to the patient-level), patient-based measures of CS (better eye, worse eye, difference between eyes) were summarized with descriptive statistics between those patients with and without eye disease and compared for differences with 2-sample Wilcoxon tests. The ability of patient-based CS measures to predict eye disease was explored using logistic regression (without GEE) and prediction diagnostics are reported with 95% CIs. The association between self-reported visual function and patient-based measures of CS was assessed with Spearman correlation (r_s). Linear regression was also used to estimate the effect of patient-based CS measures on self-reported visual function adjusting for age and presenting VA. Depending on the CS measure investigated, VA was adjusted for accordingly such that if better eye CS was investigated the VA of the eye with the better CS was used for adjustment, if worse eye CS was investigated the VA of the eye with the worse CS was used for adjustment, and if difference in CS between eyes was investigated then the difference in VA was used for adjustment. Model estimates are reported with 95% CIs also for a 0.3 log unit decrease in CS. All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

Results

There were 1171 patients enrolled in the first-year cohort of the MI-SIGHT program. Nearly all patients had CS measured for both eyes ($n=1138$, 97%), but 12 patients did not have CS measurements for either eye (1%), and 21 patients had CS measured for only one eye (2%). Therefore, 1159 patients were included in the analysis. These patients were on average 54.9 years old at time of program enrollment ($SD=14.5$), 62% identified as female, 34% as White, 54% as Black, 4% as Asian, 8% as Other race, and 10% as Hispanic/Latino. In our sample, the average logCS (hereafter referred to as CS) observed over all eyes was 1.54 log units ($SD=0.24$; range=0 to 1.95; median=1.65, IQR=1.50 to 1.65), whereas the average CS measure for the better eye was 1.58 log units ($SD=0.20$) and for the worse eye was 1.50 log units ($SD=0.27$). For patients who had CS measurements from both eyes, the difference between eyes was on average 0.08 log units ($SD=0.19$; range=0 to 1.95; median=0; IQR=0

to 0.15), where 63% of patients had no difference between eyes. However, when patients' eyes did differ, that difference showed a wide distribution of values (Figure 1). Specifically, when the worse eye still had CS in the normal range (>1.5 log units), the better eye is the same or better, and the participant has two eyes with normal CS. However, as the worse eye CS value decreases, there is a larger spectrum of CS values possible for the better eye, so that a participant can have either two eyes with severe CS loss (≤ 1.0 log units) or one eye with moderate (1.05 to 1.5 log units) or severe CS loss and the other with normal CS.¹¹

Eye Disease

Eye disease screening revealed 21% of total eyes in the sample (479 eyes from 280 different patients) had glaucoma. DR was present in 6% of eyes (144 eyes from 85 different patients), cataract in 19% of eyes (438 eyes from 243 different patients), and AMD in 2% of eyes (42 eyes from 23 different patients). CS was significantly worse in patients or eyes who screened positive for disease versus those that did not (Table 1). Specifically, eyes that screened positive for glaucoma had an average CS of 1.48 log units versus 1.56 log units in those that did not ($p<0.0001$). Eyes that screened positive for DR versus those that screened negative had an average CS of 1.39 log units versus 1.55 log units ($p<0.0001$). Eyes that screened positive for cataract versus those that screened negative had an average CS of 1.45 log units versus 1.56 log units ($p<0.0001$). Eyes that screened positive for AMD versus those that screened negative had an average CS of 1.38 log units versus 1.54 log units ($p=0.0006$). Similar results were observed for patient-based better and worse eye measures of CS. Patients who screened positive for glaucoma or cataract also showed a larger difference in CS between eyes than patients that screened negative for those conditions (average CS difference between eyes of 0.13 log units in those screened positive for glaucoma versus 0.07 log units who screened negative, $p=0.0002$; average CS difference between eyes of 0.12 log units in those screened positive for cataract versus 0.07 log units in those screened negative, $p<0.0001$).

A significant relationship was observed between CS and screening positive for eye disease, after adjusting for patient age and presenting VA (Table 2). For eye-based analyses, a 0.3 log unit decrease in CS was associated with increased odds of screening positive for glaucoma (OR=1.42, 95% CI: 1.18, 1.72) and screening positive for DR (OR=1.39, 95% CI: 1.21, 1.60). For patient-based analyses, a 0.3 log unit decrease in CS in the better eye was associated with an increased odds of screening positive for glaucoma (OR=1.35, 95% CI: 1.09, 1.67), DR (OR=2.05, 95% CI: 1.51, 2.77), cataract (OR=1.35, 95% CI: 1.05, 1.72), and AMD (OR=2.08, 95% CI: 1.10, 3.91). Furthermore, larger differences in CS between eyes was associated with increased odds of screening positive for glaucoma (OR=2.22, 95% CI: 1.63, 3.03) or cataract (OR=1.45, 95% CI: 1.07, 1.97). However, there was no significant association between the difference in CS between eyes and the odds of screening positive for DR or AMD (Table 2). Although measures of CS were found to be significantly associated with screening positive for disease, CS on its own was not a good predictor of those patients or eyes that did versus did not screen positive for disease (Table 3). At the most reliable CS cut-points (that maximized Youden's statistic), prediction diagnostics were low with AUC that ranged from 0.53 to 0.73, sensitivity that ranged from 0.34 to 0.83, and specificity that

ranged from 0.37 to 0.79. A similar investigation of the ability of CS and VA together to detect eye disease also showed poor prediction diagnostics (Supplemental Table 1).

Vision-Related Quality of Life (VFQ-9)

Patients reported an average overall composite visual function score of 79.7 (SD=15.3), and sub-scale scores ranging from 58.9 for mental health (SD=29.9) to 90.8 for driving (SD=19.8). Patient-based measures of CS showed significant correlation with self-reported visual function (Supplemental Table 2), including the VFQ-9 composite score, as well as every subscale. Larger (better) measures of CS were associated with better visual function with correlations ranging from 0.18 to 0.22 for the better eye CS and 0.07 to 0.23 for the worse eye CS (all $p < 0.05$). Additionally, 5 of 8 scales showed an inverse correlation with difference in CS measures between eyes. Larger between eye differences were associated with worse visual function (range r_s -0.08 to -0.06).

In linear regression models, after adjusting for age and presenting VA, a 0.3 log unit increase in CS in the patient's better eye was associated with an estimated increase in overall composite VRQOL of 5.9 (95% CI: 4.6, 7.3), and a 0.3 log unit increase in CS in the patient's worse eye was associated with an estimated increase of 3.9 (95% CI: 2.6, 5.2) (Table 4). In addition, CS measures in the better eye were significantly associated with VRQOL for each of the specific subscales of the VFQ-9 with regression estimates ranging from 2.8 to 6.4 (per 0.3 log unit increases in CS). In the worse eye, CS measures were significantly associated with VRQOL for six of the seven subscales of the VFQ-9 with regression estimates ranging from 3.6 to 4.8 (per 0.3 log unit increases in CS). Differences in CS measures between eyes of a patient were inversely associated with overall composite VRQOL such that for every 0.3 log unit increase in the difference in CS between eyes, patients had an estimated decrease in VRQOL of 3.1 (95% CI: -5.0, -1.2).

Discussion

CS is a very important dimension of visual function that is not often measured in routine eye examinations, and is rarely, if ever, measured in primary care settings. Our work showed that although CS measured with the Pelli-Robson chart was associated with the presence of eye disease (specifically glaucoma, DR, cataract, and AMD), it was neither sensitive nor specific enough to use alone as a screening tool for eye disease. Nonetheless, the data do demonstrate that measuring CS is important in understanding a patient's VRQOL, and picking up changes in visual function that may go unnoticed when assessing VA alone. Our data show that CS is correlated with the composite score on the VFQ-9, an association that remained significant even after adjustment for age and VA, indicating that CS is an important factor in understanding the complexity of a patient's experience with their vision. While these findings do not suggest that CS should be used for screening purposes, they do suggest that CS is a useful tool for understanding visual function.

The relationship between VRQOL and CS in our sample recapitulates evidence showing the importance of CS as it relates to VRQOL in eye diseases such as cataract,²⁸ AMD,²⁹ DR,³⁰ and glaucoma.³¹ In previous research among glaucoma patients, lower CS in the better eye was associated with worse VRQOL but lower CS in the worse eye was not,

meaning that if the better eye was more compromised in terms of CS, people felt more visually compromised.³² There has been more research into the relationship between VA and VRQOL depending on presence of eye disease. There is work showing that in eye disease with impairment of central vision, there was a better correlation between VRQOL and the level of acuity in the better seeing eye. In diseases with impairment of peripheral vision (i.e., glaucoma), there is evidence demonstrating correlation between VRQOL and both the better³³ and worse seeing eye.³⁴ For this reason as well as in light of the reported differences in VA's relationship to VRQOL by disease state, we chose to evaluate CS in both the better and the worse seeing eye in our heterogeneous sample.

We discovered that asymmetry plays a role in VRQOL, as a larger difference in CS between eyes was significantly correlated with a decrease in visual function measured by the VFQ-9 composite score. Additionally, larger asymmetry in CS was associated with worse VRQOL in five of the seven subscales of the VFQ-9 including general vision, distance activities, mental health, driving, and peripheral vision. To our knowledge, this is the first study that looks at differences between eyes in terms of CS and the association with visual function. The findings that a larger difference in CS between the better and worse eye is associated with decreased VRQOL suggests that CS is an important aspect of visual function that cannot necessarily be compensated for by the eye with a better CS. In clinical practice, it is common to focus attention on the better-seeing eye if a patient has a large difference in VA between eyes. These results give pause to that approach and may help inform choices in low vision rehabilitation in terms of focusing some efforts on rehabilitating the worse-seeing eye as well. Additionally, this may be an important consideration, for example, in cases where people have had unilateral cataract surgery and are qualitatively experiencing difficulties with their vision, even if their second eye has reasonably good VA.

Patients in the MI-SIGHT Program who screened positive for glaucoma, diabetic retinopathy, cataract or macular degeneration had significantly worse CS values in the better eye compared to those who screened negative for disease. This finding is consistent with previous studies^{2,35-37} and supports the notion that CS is a clinically important measure that is related to the presence of eye disease. However, though CS was significantly associated with disease status, CS by itself was not a good predictor of eyes that did versus did not have disease. Prediction diagnostics were low in terms of AUC, sensitivity, and specificity, meaning CS alone is not an appropriate screening test for eye disease such as glaucoma, diabetic retinopathy, cataract, or macular degeneration. Though CS is related to the presence of eye disease, its measurement may be more informative for assessing disease symptoms rather than disease prediction. One of the implications of this is to consider measuring CS in comprehensive eye exams. The Pelli-Robson CS assessment takes about two minutes to administer, making it a feasible addition to routine eye exams.

A few older studies with small samples of chronic open-angle glaucoma patients have explored the relationship between CS and presence of disease with varying results. A laboratory study in 1984 provided evidence that CS measurements can detect and quantify visual deficits in pre-perimetric glaucoma.¹³ However, this study measured CS in a laboratory with a time-intensive and in-depth analysis of CS using an oscilloscope. Our study, on the other hand, used a very widely available and easy to use measure of CS, the

Pelli-Robson chart, which takes around two minutes to administer. Therefore, though both studies looked at the relationship between CS and eye disease, we were asking a much broader question about the utility of a quick screening measure rather than the potential of in-depth analysis to detect disease.

Though VA and CS are distinct visual functions, they are also related. One study sought to disentangle the relationship between visual disturbances from cataract in terms of both CS and VA.³ VA is typically measured by small-letter high-contrast testing. However, this study measured CS in both small-letters and large-letters. They found that small letter CS was a more sensitive measure of early cataract than either VA or large letter CS. However, the practical value of small letter CS is restricted due to its very strong association with VA, which is the conventional and widely used measure of vision in assessing all patients, including patients being evaluated for cataract surgery. The CS measure we used in our study, the Pelli-Robson chart, measures large letter CS only, and is therefore separate, but related, to VA. Additionally, though VA and CS are related, we adjusted for VA and age in our logistic regression models demonstrating that CS has an independent association with eye disease status and VRQOL. Ultimately, the goal of this work was to investigate whether there was an independent effect of CS on our outcomes of eye disease and VFQ score, after adjusting for two well-documented predictors of our outcomes and two variables that are easy to assess in a screening capacity (age and VA). Univariate associations did show that CS was significantly associated with eye disease, yet in some adjusted models that effect disappeared. This indicates that CS did not account for any additional variability in these particular diseases that was not already accounted for by age and VA.

It is important to contextualize the magnitude of the relationship between CS and VRQOL. For example, in patients with newly-diagnosed open angle glaucoma, previous work has shown that the minimally important clinical difference in VA (a 10-letter difference on the Snellen chart) is associated with a 3.8 unit decrease in VFQ-9 score.³³ In terms of our findings, a 1-line decrease in better eye CS (0.3 log unit) was associated with a 5.9 unit decrease in the VFQ-9 composite score and a 1-line decrease in worse eye CS was associated with a 3.9 unit decrease in the VFQ-9 composite score, after adjusting for age and VA. A one-line reduction in CS in the better seeing eye has more impact on VRQOL than a two-line decrease in VA, demonstrating the importance of CS in people's visual function.

Some of the strengths of this study include the large sample of patients with heterogeneous disease status, and the representation of people identifying as racial and ethnic minorities, as people from these communities have been historically excluded from research. Because our study represents a large, heterogeneous sample of patients with multiple types of eye disease at various stages of severity, CS values in our sample likely span a wide range both within and between patients, giving large variability to the sample. Some of the limitations of our study include the use of the shorter VFQ-9 to assess VRQOL instead of the longer VFQ-25 or VFQ-52. Though the VFQ-9 has been shown to have high reliability and validity with respect to clinically relevant markers,¹⁵ it has not undergone a Rasch-model analysis. Other limitations include inherent challenges in CS testing such as maintaining consistent illumination and reflections on the chart's surface,³⁸ ungradable or poor quality images (1–2%) that did not allow for a screening result to be made that may have biased the results

towards the null as those with ungradable images may have been more likely to have both pathology and low contrast sensitivity but could not be included in our analysis, lack of generalizability since the study sample is not a population-based sample, and lack of a gold-standard diagnosis as participants were not examined in-person by an ophthalmologist. In terms of the model, a limitation of our study is that model estimates could be better estimated by adjusting for all known factors of eye disease instead of simply age and VA. Our sample included only 23 patients with AMD at various stages of disease, making it difficult to draw meaningful conclusions about AMD. In addition, this small sample size limited the number of variables we could include in the models. Lastly, the fact that our study sample is not a population-based sample is a limitation of the generalizability of this work and gives reason to interpret results with caution. Although sensitivity and specificity are regarded as disease prevalence invariant, there is emerging evidence that suggest these measures of diagnostic accuracy may not be stable with changing disease prevalence.³⁹ In our sample, with higher-than-average disease prevalence and perhaps more severe disease, testing may perform better and therefore overestimate accuracy diagnostics. However, even with possible overestimation, our results still showed low predictability.

In conclusion, CS is an important factor in understanding a patient's visual function and quality of life. While our study found that measuring CS using the Pelli-Robson chart was not sensitive or specific enough to be used in screening for eye disease, it was a valuable tool in assessing visual function. Additionally, we found that larger asymmetry in CS between the two eyes was associated with worse VRQOL. These findings highlight the potential utility in measuring CS in addition to VA in routine eye examinations or in times when visual complaints are not adequately captured by VA.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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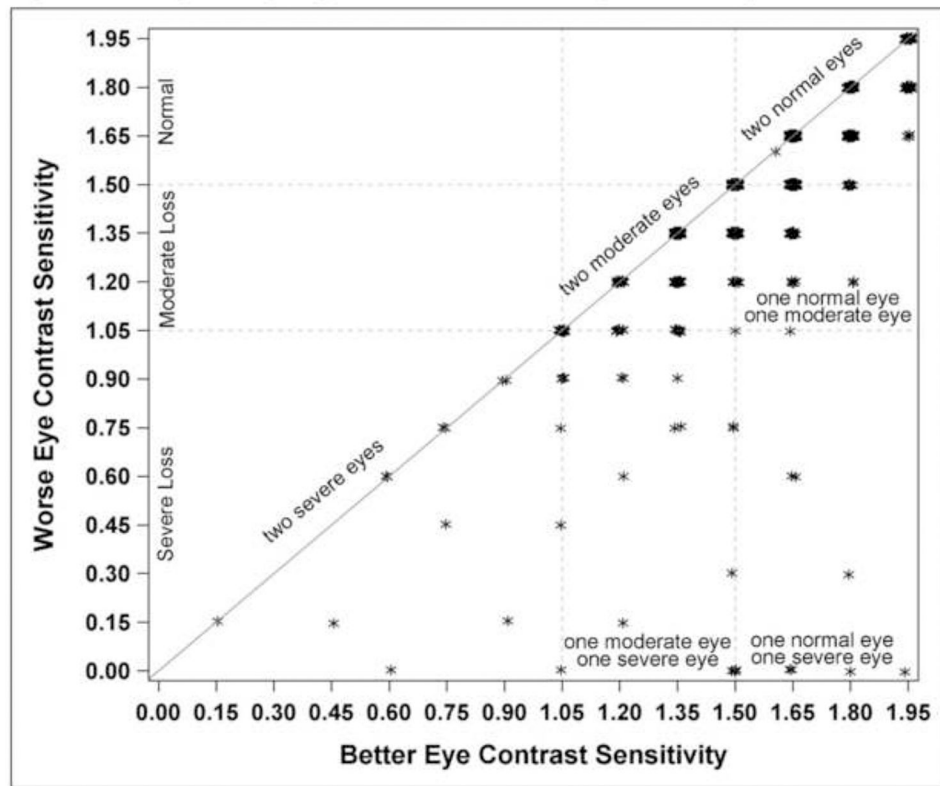


Figure 1.
Scatterplot comparing the distribution of better eye and worse eye contrast sensitivity.

Table 1.

Comparison of contrast sensitivity between those eyes or patients with and without disease in the year 1 MI-SIGHT program cohort

CS Measure	N	Mean (SD)	Median (IQR)	N	Mean (SD)	Median (IQR)	P-value*
No Glaucoma				Glaucoma			
Eye-Based							
All Eyes	1808	1.56 (0.21)	1.65 (1.50–1.65)	479	1.48 (0.29)	1.50 (1.35–1.65)	<0.0001
Patient-Based							
Better Eye	874	1.59 (0.19)	1.65 (1.50–1.65)	280	1.54 (0.22)	1.65 (1.35–1.65)	0.0002
Worse Eye	874	1.53 (0.22)	1.50 (1.50–1.65)	280	1.41 (0.35)	1.50 (1.35–1.65)	<0.0001
Difference	862	0.07 (0.14)	0.00 (0.00–0.15)	272	0.13 (0.27)	0.00 (0.00–0.15)	0.0002
No Diabetic Retinopathy				Diabetic Retinopathy			
Eye-Based							
All Eyes	2147	1.55 (0.23)	1.65 (1.50–1.65)	144	1.39 (0.28)	1.43 (1.35–1.50)	<0.0001
Patient-Based							
Better Eye	1071	1.59 (0.19)	1.65 (1.50–1.65)	85	1.46 (0.24)	1.50 (1.35–1.65)	<0.0001
Worse Eye	1071	1.51 (0.26)	1.50 (1.35–1.50)	85	1.37 (0.28)	1.35 (1.35–1.50)	<0.0001
Difference	1052	0.08 (0.18)	0.00 (0.00–0.15)	83	0.09 (0.15)	0.00 (0.00–0.15)	0.1732
No Cataract				Cataract			
Eye-Based							
All Eyes	1853	1.56 (0.23)	1.65 (1.50–1.65)	438	1.45 (0.24)	1.50 (1.35–1.65)	<0.0001
Patient-Based							
Better Eye	913	1.60 (0.19)	1.65 (1.50–1.65)	243	1.51 (0.21)	1.50 (1.35–1.65)	<0.0001
Worse Eye	913	1.52 (0.26)	1.65 (1.50–1.65)	243	1.39 (0.28)	1.50 (1.35–1.50)	<0.0001
Difference	897	0.07 (0.17)	0.00 (0.00–0.15)	238	0.12 (0.20)	0.00 (0.00–0.15)	<0.0001
No Age-Related Macular Degeneration				Age-Related Macular Degeneration			
Eye-Based							
All Eyes	2249	1.54 (0.23)	1.65 (1.50–1.65)	42	1.38 (0.29)	1.35 (1.35–1.50)	0.0006
Patient-Based							
Better Eye	1133	1.58 (0.19)	1.65 (1.50–1.65)	23	1.41 (0.26)	1.50 (1.35–1.65)	<0.0001
Worse Eye	1133	1.50 (0.27)	1.50 (1.35–1.50)	23	1.36 (0.31)	1.35 (1.35–1.50)	0.0017
Difference	1113	0.08 (0.18)	0.00 (0.00–0.15)	22	0.05 (0.09)	0.00 (0.00–0.15)	0.6381

MI-SIGHT, Michigan Screening and Intervention for Glaucoma and Eye Health through Telemedicine; CS, Contrast Sensitivity; SD, Standard Deviation; IQR, InterQuartile Range

* P-values obtained from repeated measures linear regression for eye-based measures and from 2-sample Wilcoxon tests for patient-based measures

Note: some participants had missing data for contrast sensitivity measures and/or disease status

Table 2.

Logistic regression models for the association of contrast sensitivity with the probability of eye disease, adjusting for age and presenting visual acuity

Outcome	Eye-Based Effect of Any Eye CS		Patient-Based Effect of Difference CS	
	OR ^a (95% CI)	P-value	OR ^b (95% CI)	P-value
Glaucoma	1.42 (1.18, 1.72)	0.0003	2.22 (1.63, 3.03)	<0.0001
Diabetic Retinopathy	1.39 (1.21, 1.60)	<0.0001	1.33 (0.84, 2.10)	0.2289
Cataract	1.07 (0.87, 1.31)	0.5331	1.45 (1.07, 1.97)	0.0171
AMD	1.06 (0.99, 1.13)	0.1063	0.54 (0.13, 2.17)	0.3810
	Patient-Based Effect of Better Eye CS		Patient-Based Effect of Worse Eye CS	
	OR ^c (95% CI)	P-value	OR ^c (95% CI)	P-value
Glaucoma	1.35 (1.09, 1.67)	0.0065	1.67 (1.36, 2.04)	<0.0001
Diabetic Retinopathy	2.05 (1.51, 2.77)	<0.0001	1.54 (1.17, 2.03)	0.0020
Cataract	1.35 (1.05, 1.72)	0.0177	1.38 (1.10, 1.73)	0.0049
AMD	2.08 (1.10, 3.91)	0.0236	1.57 (0.88, 2.79)	0.1250

CS, Contrast Sensitivity; OR, Odds Ratio; CI, Confidence Interval; AMD, Age-Related Macular Degeneration

^aORs and CIs obtained from a repeated measures logistics regression using GEE methodology, ORs are reported for a 0.3-unit decrease

^bORs and CIs obtained from a logistics regression (without GEE), ORs are reported for a 0.3-unit increase

^cORs and CIs obtained from a logistics regression (without GEE), ORs are reported for a 0.3-unit decrease

Table 3.

Diagnostics for predicting disease status from contrast sensitivity.

Outcome	Predictor	AUC (95% CI)	P-value *	ROC Curve Diagnostics at CS Cut-Point that Maximizes Youden Index		
				Cut-Point	Sensitivity (95% CI)	Specificity (95% CI)
Glaucoma	Eye-based All Eyes CS	0.58 (0.55, 0.61)	<0.0001	≤1.35	0.34 (0.29, 0.39)	0.79 (0.77, 0.82)
	Patient-based Better CS	0.57 (0.53, 0.61)	0.0003	≤1.60	0.48 (0.42, 0.54)	0.65 (0.62, 0.68)
	Patient-based Worse CS	0.61 (0.57, 0.65)	<0.0001	≤1.35	0.42 (0.36, 0.48)	0.75 (0.73, 0.78)
	Patient-based Difference CS	0.56 (0.53, 0.60)	0.0003	≥0.15	0.44 (0.39, 0.50)	0.66 (0.63, 0.69)
Diabetic Retinopathy	Eye-based All Eyes CS	0.70 (0.66, 0.74)	<0.0001	≤1.50	0.76 (0.68, 0.83)	0.56 (0.53, 0.58)
	Patient-based Better CS	0.68 (0.62, 0.73)	<0.0001	≤1.50	0.65 (0.55, 0.75)	0.64 (0.61, 0.67)
	Patient-based Worse CS	0.69 (0.63, 0.74)	<0.0001	≤1.50	0.82 (0.74, 0.90)	0.47 (0.44, 0.50)
	Patient-based Difference CS	0.54 (0.48, 0.60)	0.1801	≥0.15	0.43 (0.33, 0.54)	0.64 (0.61, 0.67)
Cataract	Eye-based All Eyes CS	0.66 (0.63, 0.68)	<0.0001	≤1.50	0.68 (0.63, 0.73)	0.59 (0.56, 0.62)
	Patient-based Better CS	0.63 (0.59, 0.67)	<0.0001	≤1.50	0.57 (0.51, 0.63)	0.67 (0.64, 0.70)
	Patient-based Worse CS	0.68 (0.64, 0.71)	<0.0001	≤1.50	0.77 (0.72, 0.83)	0.51 (0.48, 0.55)
	Patient-based Difference CS	0.59 (0.55, 0.63)	<0.0001	≥0.15	0.49 (0.43, 0.56)	0.67 (0.64, 0.70)
Age-related Macular Degeneration	Eye-based All Eyes CS	0.71 (0.64, 0.78)	<0.0001	≤1.50	0.79 (0.59, 0.90)	0.54 (0.52, 0.57)
	Patient-based Better CS	0.73 (0.64, 0.82)	<0.0001	≥1.50	0.74 (0.56, 0.92)	0.63 (0.60, 0.66)
	Patient-based Worse CS	0.68 (0.59, 0.78)	0.0002	≤1.50	0.83 (0.67, 0.98)	0.46 (0.43, 0.49)
	Patient-based Difference CS	0.53 (0.43, 0.63)	0.5603	=0.00	0.68 (0.49, 0.88)	0.37 (0.34, 0.40)

ROC, Receiver Operator Curve; AUC, Area Under Curve; CI, Confidence Interval; CS, Contrast Sensitivity

* test of AUC significantly different from 0.5

Table 4.

Separate linear regression models estimating the effect of patient-based measures of contrast sensitivity on self-reported visual function (VFQ overall score and subscale scores), adjusting for age and presenting visual acuity.

Outcome	Patient-Based Better Eye CS		Patient-Based Worse Eye CS		Patient-Based Difference CS	
	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value	Estimate (95% CI)	P-value
General Vision	6.2 (4.5, 7.9)	<0.0001	4.1 (2.5, 5.6)	<0.0001	-3.9 (-6.2, -1.5)	0.0011
Near Activities	6.2 (4.4, 8.0)	<0.0001	3.6 (2.0, 5.3)	<0.0001	-2.3 (-4.7, 0.2)	0.0706
Distance Activities	6.2 (4.1, 8.3)	<0.0001	4.5 (2.6, 6.4)	<0.0001	-3.5 (-6.3, -0.7)	0.0137
Mental Health	6.4 (3.6, 9.2)	<0.0001	4.3 (1.7, 6.9)	0.0012	-3.5 (-6.3, -0.7)	0.0137
Role Difficulties	2.8 (0.2, 5.3)	0.0348	1.2 (-1.1, 3.5)	0.3074	-0.7 (-4.1, 2.6)	0.6723
Driving	4.9 (2.9, 7.0)	<0.0001	3.6 (1.8, 5.5)	0.0001	-3.0 (-5.7, -0.3)	0.0301
Peripheral Vision	5.5 (3.8, 7.2)	<0.0001	4.8 (3.2, 6.3)	<0.0001	-4.9 (-7.2, -2.6)	<0.0001
Composite	5.9 (4.6, 7.3)	<0.0001	3.9 (2.6, 5.2)	<0.0001	-3.1 (-5.0, -1.2)	0.0017

VFQ, Visual Function Questionnaire; CS, Contrast Sensitivity; CI, Confidence Interval