Vision Parameters Most Important to Functionality in Glaucoma

Ahmed F. Shakarchi,[1] Aleksandra Mihailovic,[1] Sheila K. West,[1] David S. Friedman,[2] and Pradeep Y. Ramulu[1]

[1]The Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, United States
[2]Department of Ophthalmology, Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, United States

Correspondence: Pradeep Y. Ramulu, Maumenee B110, Johns Hopkins Hospital, 600 N Wolfe Street, Baltimore, MD 21287, USA; pramulu1@jhmi.edu.

Submitted: July 24, 2019
Accepted: September 9, 2019

Citation: Shakarchi AF, Mihailovic A, West SK, Friedman DS, Ramulu PY. Vision parameters most important to functionality in glaucoma. *Invest Ophthalmol Vis Sci*. 2019;60:4556–4563. https://doi.org/10.1167/iovs.19-28023

Purpose. To determine the importance of various vision parameters to functionality in glaucoma.

Methods. Vision was measured using seven parameters: visual acuity (VA), contrast sensitivity (CS), integrated visual field (IVF), area under the log CS function (AULCSF), color vision, stereoacuity, and VA with noise (ViN). Likelihood ratio testing (LRT) determined if the full set of visual parameters significantly explained variability in 10 functional outcomes. For outcomes where the visual contribution was significant, dominance analysis determined the relative importance of the various visual parameters.

Results. The analysis included 151 glaucoma patients. Mean age was 70 ± 6.8 years, and 47% were men. Significant visual contributions (LRT $P < 0.05$) were noted for glaucoma quality of life (GQL-15), reading speed, driving cessation, daily steps, and base of support while walking, but not for fear of falling, balance, gait velocity, stride velocity, and stride length while walking (LRT $P > 0.05$). The most important parameter (and percent contribution) to vision-explained variability were AULCSF for daily steps (45%), IVF for base of support (35%), VA for reading speed (34%), CS for GQL-15 (30%), and VA for driving cessation (26%).

Conclusions. Measures of visual ability are important for several aspects of quality of life and functionality. The most important vision parameter for functionality differs depending on the domain studied. Reading and driving were explained by VA and IVF sensitivity. On the other hand, GQL-15 and daily steps were more heavily influenced by CS and AULCSF, which are rarely performed clinically.

Keywords: functionality, vision parameters, dominance analysis

Vision loss from glaucoma can adversely affect function, including mobility, driving, and reading.[1] Visual field (VF) testing is commonly used to monitor glaucoma progression, but glaucoma can affect visual acuity (VA), contrast sensitivity (CS), and color vision as well.[2–6] Although VF sensitivity is an important tool to diagnose and monitor patients with glaucoma, other vision parameters may be as, or more, important for everyday function and quality of life.[6,7] We have previously shown that more than one visual parameter is required to optimally explain variability in glaucoma-related quality of life.[2]

A common clinical and research question relates to which visual parameter(s) are most relevant to functionality for a specific task or quality of life measure. In determining vision parameters most relevant to function, previous research utilized correlation coefficients to rank predictor importance[7–9]; however, this approach does not account for predictor intercorrelation. Relative importance analysis encompasses statistical techniques that rank predictor importance; this is accomplished by decomposing the variability explained in statistical models according to the different predictors.[10] Dominance analysis is one such technique that has been used in psychology and management science, and it is well-suited to answer our research question.[11,12]

The purpose of this article is to study the importance of vision to several subjective and objective functional outcomes in glaucoma patients and suspects. First, we identify a set of functional outcomes where a significant visual contribution is noted (i.e., where vision explains a statistically significant degree of the observed variability). Next, using dominance analysis, we determine the relative importance of seven vision parameters—VA, CS, integrated VF (IVF), area under the log CS function (AULCSF), color vision, stereoacuity, and VA with noise (ViN)—for the functional outcomes where there is a significant visual contribution. Knowledge from this study will identify the measures of vision that should be explored further in research and monitored clinically to properly understand and identify decreased functionality in glaucoma patients.

Methods

We conducted this analysis as part of the Falls in Glaucoma Study (FIGS). The study protocol was approved by the Johns Hopkins University School of Medicine Institutional Review Board and adhered to the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Study Participants

Participants were recruited between September 2013 and March 2015 from the glaucoma clinic at the Wilmer Eye Institute of Johns Hopkins University. Participants were eligible if they were 57 years or older (turning 60 during the 3-year study period) and had a diagnosis of primary open angle, primary angle closure, pseudoexfoliative, or pigmentary glaucoma. Glaucoma suspects based on intraocular pressure elevation, family history, narrow angles, presence of pseudoexfoliative material, or pigment dispersion syndrome were also included. Participants were excluded if they had any concurrent eye disease resulting in VA worse than 20/40 in the better eye. Additional exclusion criteria have been described previously.[13]

Assessment of Vision

We used seven vision parameters to evaluate visual ability: VA, CS, IVF, AULCSF, color vision, stereoacuity, and ViN. All vision parameters except VA and IVF were tested binocularly.

VA was tested on back-lit Early Treatment of Diabetic Retinopathy Study (ETDRS) charts at 4 meters using presenting correction. The logarithm of the minimum angle of resolution (logMAR) in the better-seeing eye was used for this analysis. CS was assessed using the Mars chart illuminated under standard fluorescent light (Mars Perceptrix, Chappaqua, NY, USA). CS was measured at 40 cm with habitual correction and converted to log contrast units (logCS) for analysis. Unilateral VFs were assessed using the Humphrey Field Analyzer II with the SITA standard 24-2 test (Carl Zeiss Meditec, Inc., Dublin, CA, USA). A glaucoma specialist (PR) reviewed all VFs for reliability, that is, the absence of artifacts and consistency with prior test results. Unreliable VFs, such as tests with unusually dramatic changes inconsistent with the patient's clinical course, were excluded.[14] Binocular integrated VFs (IVFs) were estimated as previously described.[14] AULCSF was estimated from the quick CS function (qCSF) test (Adaptive Sensory Technology, San Diego, CA, USA), which assesses CS across a range of spatial frequencies and models logCS as a function of stimulus size.[15] Color vision was tested using the Hardy-Rand-Rittler (HRR) (OttLite Technology, Tampa, FL, USA) under standard full spectrum lighting with habitual correction. Stereoacuity was tested using the Distance Randot Stereotest (Stereo Optical, Chicago, IL, USA) at 3 meters and reported as the minimum level of disparity as greater than 400 (no stereoacuity), 400, 200, 100, or 60 arcseconds.[16] ViN was assessed with the Pelli-Levi Dual Acuity Chart, which consists of a standard Snellen VA chart in one half and white noise (14.5 square checks per letter size) set on the letters of a Snellen chart in the other half. The test was administered in a dimmed room at 3 meters with habitual correction. We used number of letters read on the noise half of the chart to reflect ViN in this analysis.[17]

Functional Outcomes

Outcome measures evaluated in this analysis included patient self-reported measures: glaucoma quality of life-15 (GQL-15), fear of falling, and driving cessation; and objective functional outcomes: reading speed, daily steps, balance, and four gait parameters (gait speed, stride length, stride velocity and base of support).

GQL-15 is a validated 15-item questionnaire that assesses function in glaucoma patients across the domains of central and near vision, peripheral vision, glare and dark adaptation, and outdoor mobility. Participants are asked to rate their difficulty with each task as none, a little bit, some, quite a lot, severe, or not applicable (do not perform for nonvisual reasons).[18,19] As previously described,[2] Rasch analysis using the Winsteps Rasch statistical package version 3.91.2 (Winsteps, Chicago, IL, USA) was used to obtain item and person measures. The item measure score denotes task difficulty, with lower scores denoting more difficult tasks. Person measure scores were calculated for each participant based on the reported difficulty with each task and the task's item score. Higher person measure scores indicate more difficulty in performing tasks. Person and item measure scores were expressed along a log-odds (logits) scale. Person measure scores were used for this analysis. Fear of falling was assessed using the University of Illinois at Chicago Fear of Falling Questionnaire[20] with two added questions: "If you were to walk outside at night when icy, how worried are you of falling?" and "If you were to walk on uneven terrain, how worried are you of falling?" Participants rated how much fear they would have if they were to perform any of the 18 tasks as: not worried, a little/moderately worried, or very worried.[20] Rasch analysis was used to obtain person measure scores as described above for the GQL-15. Driving cessation was reported by study participants as a part of a questionnaire that evaluated their driving habits and was defined as a previous driver who has not driven over the last 3 months. Reading speed was calculated in words per minute (wpm) with nonlinear mixed effects models[21] using data collected via MNRead acuity chart.[22]

Daily steps were measured over 7 days using an accelerometer device (Actical, Respironics, Inc., Murrysville, PA, USA). Participants wore the accelerometer during a typical week from which average steps per day was derived as a measure of physical activity. Sway as a measure of balance was assessed using the Opal kinematic system (APDM, Inc., Portland, OR, USA). We evaluated sway as the root mean square (RMS) (m/s^2) of the acceleration vector length while the participant is standing on a foam surface with eyes open. Patients were instructed to maintain an upright standing posture with their arms crossed and feet approximately shoulder width apart for 30 seconds, as previously described.[23] We assessed four gait parameters: gait speed, stride length, stride velocity, and base of support. These gait parameters were obtained using the GAITRite Electronic Walkway (CIR System, Inc., Franklin, NJ, USA). Participants' gait parameters were collected barefoot at their usual-pace walking while wearing their habitual distance correction.[14]

Covariates

Standard questionnaires collected data on age, sex, race, marital status, living arrangements, employment status, and education. Polypharmacy was defined as having five or more noneyedrop prescriptions.[24] We asked patients about 15 comorbid medical conditions known to affect function (arthritis, broken or fractured hip, back problems, history of heart attack, history of angina/chest pain, congestive heart failure, peripheral vascular disease, high blood pressure, diabetes, emphysema, asthma, stroke, Parkinson's disease, cancer other than the skin cancer, and history of vertigo or Meniere's disease). Positive responses were totaled as part of a comorbidity index, whereas patients with more than five comorbid conditions ($n = 9$) were modeled as having five in our analyses.

Statistical Analysis

This analysis included participants with complete data for the demographic and vision variables used in our models. Driving cessation and daily steps were modeled using logistic and negative binomial regressions, respectively, and the remaining

Table 1. Demographics of Glaucoma Patients and Suspects in the Study

Demographics	*N* (%), Total = 151
Age, mean ± SD	70 ± 6.8
Male	72 (47)
African-American	41 (27)
Education	
High school or less	19 (13)
At least some college	58 (38)
Graduate education	74 (49)
Married	94 (62)
Living alone	31 (20)
Employed	57 (38)

eight functional outcomes using linear regression. We used R^2 to evaluate the percentage of variance explained in linear models and McFadden's pseudo-R^2 as the fit statistic in the logistic and negative binomial models.

For each outcome, a model was fitted with the covariates only (Covar Only) and one with the covariates plus the seven vision measures (Covar + Vision). All covariates, or covariates and vision measures, were included in the respective multivariable models regardless of univariable associations. Linear variables were modeled continuously, and categorical variables were modeled using indicator variables. Likelihood ratio testing (LRT) was then performed to compare the extended and nested models, and to determine if adding all seven vision measures contributed significantly to the degree of variance explained for each outcome. For each linear outcome, we calculated the contribution of vision to explained variability in the final model as $([R^2_{\text{Covar + Vision}} - R^2_{\text{Covar Only}}]/R^2_{\text{Covar + Vision}})$. This cannot be done for nonlinear models, as pseudo-R^2 is not a true measure of explained variability in an outcome. Pseudo-R^2 is useful for comparing different models of the same outcome in the same data set, as was done in our dominance analysis.[25,26]

Next, dominance analysis was performed across vision parameters for each functional outcome where vision significantly contributed to explaining the variance, thus determining the relative importance of each vision parameter.[11] Dominance analysis ranks variables by their relative contribution to explaining outcome variability across models that include all combinations of predictors (in our case, visual parameters). There are three levels of dominance one variable can have over another: complete, conditional, and general dominance.[12] Complete dominance of factor A over factor B indicates that adding A to a model increases the fit statistic (R^2 or McFadden's pseudo-R^2) to a greater extent than adding B across all possible models (i.e., all possible combinations of predictor variables). Conditional dominance indicates that the average increase in fit statistic is higher for a variable than another across all orders of models. Model order is defined as the number of predictor variables in a model; several models can have the same order if they have a different combination, but the same number, of predictor variables. Finally, general dominance statistic measures the average change in fit statistic across all possible models, and A generally dominates B if the average increase in fit statistic across all models is higher for A than B. These dominance designations operate hierarchically, such that complete dominance indicates conditional and general dominance, and conditional dominance indicates general dominance. Confidence intervals of general dominance statistics were calculated by bootstrapping 1000 cohort samples with replacement.[12]

Dominance analysis was repeated to determine the most important vision parameter in each question in GQL-15. In sensitivity analyses, the likelihood ratio test was repeated while excluding marital status, living arrangement, and employment status from the covariate list as these may act as mediators of the association between glaucomatous visual loss and function. We additionally assessed the relative importance of vision parameters using constrained dominance analysis, where the nonvisual predictors were included in all models.[12] P value < 0.05 was used to denote statistical significance. We used STATA 15 for this analysis (Stata Statistical Software: Release 15; StataCorp LP, College Station, TX, USA).

Table 2. Health of Glaucoma Patients and Suspects in the Study

Health	*N* (%), Total = 151
Comorbidities	
None	22 (15)
1 or 2	78 (51)
3 or 4	40 (26)
5 or more	12 (8)
Polypharmacy*	43 (28)

* Five or more noneyedrop medications.

Results

Participant Characteristics

The FIGS cohort included 245 individuals. Of them, 151 had complete data on the covariates and all vision measures and were included in this analysis (Tables 1–3). Glaucoma was primary open angle in 95 patients (63%), primary angle closure in 12 (8%), pseudoexfoliative in 7 (5%), and pigmentary in 2 (1%); 35 patients (23%) were glaucoma suspects. Mean age was 70 (±6.8) years, 72 (47%) were men, and 41 (27%) were African-American. Ninety-four (62%) were married and 57 (38%) were employed. Our study cohort is generally well-educated with roughly half (49%) having graduate-level education. Approximately half (51%) had 1 or 2 comorbidities, and 43 (28%) had 5 or more noneyedrop prescriptions (polypharmacy). The only significant difference between FIGS cohort members included in the analysis and members not included was polypharmacy (χ^2 P value = 0.04).

Variability in the Functional Outcomes Explained by Vision

The number of participants completing functional tests and their results are shown in Table 4. Models including both

Table 3. Vision Characteristics of Glaucoma Patients and Suspects in the Study

Vision Parameters	Mean ± SD	Median [IQR]
VA, logMAR	0.92 ± 1.4	0.6 [0 to 1.6]
CS, logCS	−11.1 ± 1.4	−11.5 [−11.7 to −10.9]
IVF, mean deviation	−5.5 ± 0.8	−5.7 [−6.0 to −5.4]
Color	17.7 ± 5.1	20 [18.5 to 20]
AULCSF	−11.3 ± 3.1	−11.6 [−13.8 to −11.6]
ViN, number of letters	−15.5 ± 5.3	−16 [−20 to −13]
Stereoacuity, *N* (%)		
None, >400 arcseconds	116 (76%)	
400 arcseconds	7 (5%)	
200 arcseconds	14 (9%)	
100 arcseconds	9 (6%)	
60 arcseconds	6 (4%)	

IQR, interquartile range.

Table 4. The Number of Participants Completing Each Functional Outcome Test and Their Results

Outcome	*N* Completed Test	Mean ± SD	Median [IQR]
Quality of life (GQL-15), logits*	151	−2.4 ± 1.6	−2.2 [−3.2 to −1.4]
Fear of falling, logits*	151	−3.2 ± 2.4	−3.1 [−5.2 to −1.6]
Reading speed, WPM	149	179.4 ± 33.6	179.9 [156.4 to 199.2]
Balance (RMS Sway), m/s^2	147	0.1 ± 0.1	0.1 [0.1 to 0.2]
Gait velocity, cm/s	150	100.6 ± 18.9	99.7 [86.9 to 116.4]
Base of support, cm	150	10.2 ± 3.2	10.1 [7.9 to 11.8]
Stride velocity, cm/s†	150	101.7 ± 18.7	101.2 [88.3 to 117.3]
Stride length, cm	150	114.1 ± 16.0	114.4 [103.1 to 124.8]
Driving cessation, *N* (%)	148	14 (9.5%)	
Daily steps, steps/day	148	4116 ± 2495	3742 [2215 to 5327]

IQR, interquartile range.
* Difficulty score based on the Rasch analysis.
† Stride length (in centimeters) divided by time to complete stride (in seconds).

covariates and vision parameters (Covar + Vision) explained significantly more of the variance in the data as compared with covariate-only (Covar Only) models for three functional outcomes modeled with linear regression (GQL-15, reading speed, and base of support while walking; $P < 0.05$ for all) and two outcomes modeled by other forms of regression (driving cessation and daily steps; $P < 0.05$ for both) (Fig. 1; Table 5). The addition of vision parameters did not statistically significantly explain more variance for the remaining five linear functional outcomes (fear of falling, balance, gait velocity, stride length, and stride velocity; $P > 0.05$ for all).

For the outcomes modeled with linear regression, and for which there was a significant visual contribution to the explained variance, explained variabilities (R^2) in the final model including covariates and vision were 36% for GQL-15 and 22% for both reading speed and base of support. Vision parameters contributed 54% of total explained variability in the final model for GQL-15 ($P < 0.0001$), 38% for reading speed ($P = 0.03$), and 48% for base of support ($P = 0.01$) (Table 5).

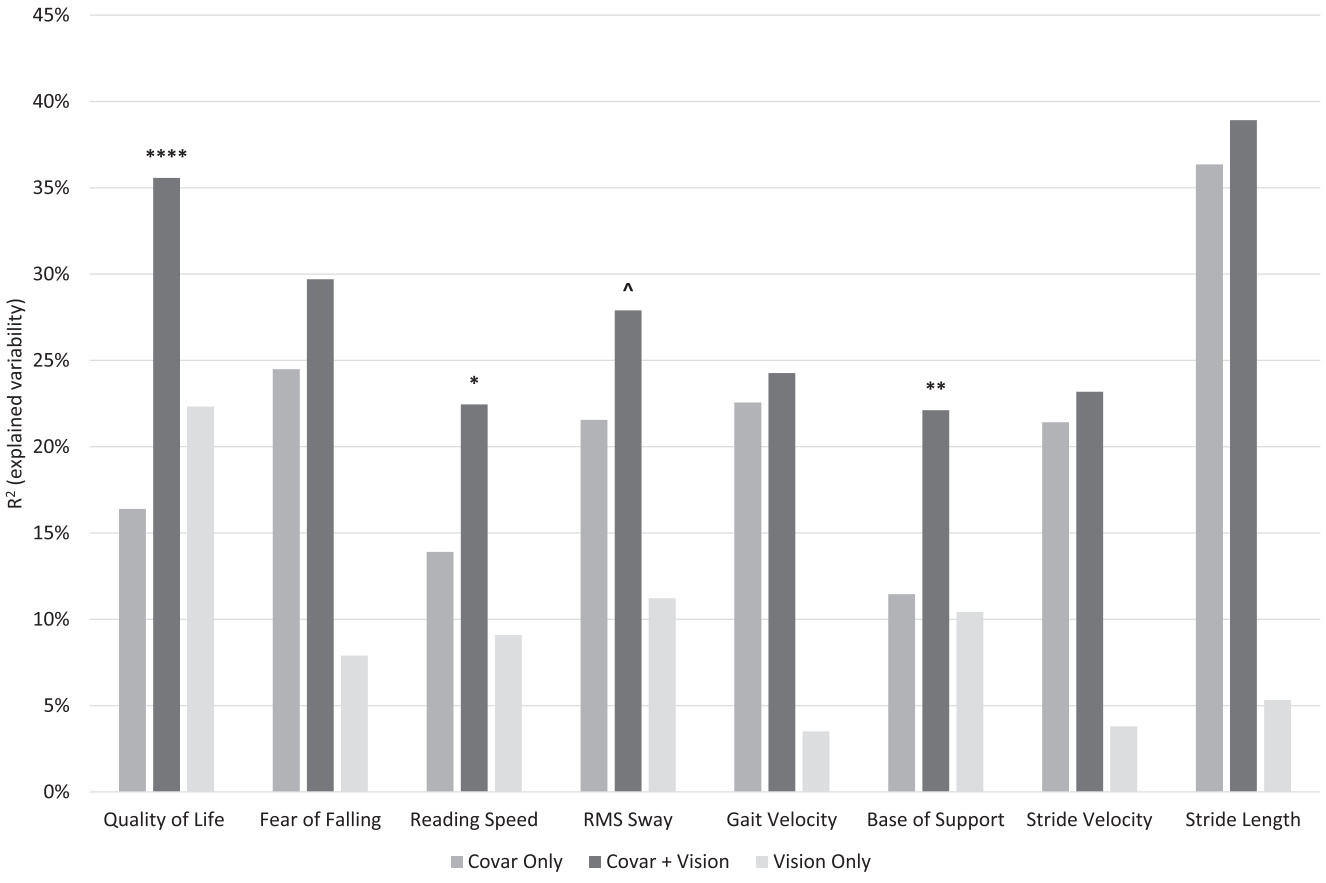

Figure 1. The variability in linear functional outcomes explained by the covariates (age, sex, race, marital status, living alone, employment, education, comorbidities, and polypharmacy), vision (VA, CS, VF, color vision, stereoacuity, AULCSF, and vision-noise), and covariates and vision combined. Statistical significance annotations (^0.1, *0.05, **0.01, ****0.0001) are for the log-likelihood ratio test comparing Covar + Vision model to Covar Only model.

Investigative Ophthalmology & Visual Science

Table 5. Variability Explained by Vision Parameters in Linear Functional Outcomes

Outcome	R^2 (Explained Variability)			
	Covar Only*	Covar + Vision†	Contribution of Vision‡	*P* Value§
GQL-15	0.16	0.36	54%	**< 0.0001**
Fear of falling	0.25	0.30	18%	0.15
Reading speed	0.14	0.22	38%	**0.03**
Balance (RMS Sway)	0.22	0.28	23%	0.09
Gait velocity	0.23	0.24	7%	0.85
Base of support	0.12	0.22	48%	**0.01**
Stride velocity	0.21	0.23	8%	0.85
Stride length	0.36	0.39	7%	0.52
Driving cessation||				**0.001**
Daily steps||				**0.01**

Bold values indicate $P < 0.05$.

* Covar Only models are adjusted for covariates only: age, sex, African-American race, marital status, living alone, employment, education, comorbidities, and polypharmacy.

† Covar + Vision models are adjusted for covariates plus vision parameters: VA, CS, IVF, color, stereo, AULCSF, and ViN.

‡ (R^2Covar + Vision − R^2Covar Only) / (R^2Covar + Vision). Applying the formula to numbers from column 1 and 2 may not exact match the result in column 3 because of rounding.

§ *P* value from log likelihood test comparing Covar + Vision to Covar Only models.

|| R^2 cannot be calculated for logistic (driving cessation) and negative binomial (daily steps) regression.

Relative Importance of Vision Parameters in Functional Outcomes—Dominance Analysis

One vision parameter completely dominated all others in four of the five functional outcomes where vision significantly contributed to the explained final-model variability. The completely dominating vision parameter was CS for GQL-15, VA for both reading speed and base of support while walking, and AULCSF for daily steps. For driving cessation, VA completely dominated all other parameters except CS, which VA conditionally dominated (Fig. 2). Adding CS to all possible models of GQL-15 incorporating other vision parameters increases R^2 by an average of 0.07. Similarly, VA increased model R^2 by an average of 0.03 for reading speed and IVF by an average of 0.04 for base of support. VA increased McFadden's pseudo-R^2 for driving cessation by an average of 0.07, and AULCSF increased McFadden's pseudo-R^2 for daily steps by an average of 0.004 (Table 6).

Across the five functional outcomes where vision contributed significantly to explained variability, IVF contributed $\geq$ 15% (range, 16%–35%) to vision-explained variability in all outcomes, whereas stereoacuity contributed at most 7% (range, 1%–7%). The remaining vision parameters contributed $\geq$ 15% of vision-explained variability in some, but not all, outcomes: CS contributed $\geq$ 15% in GQL-15, reading speed, and driving cessation; AULCSF contributed $\geq$ 15% in base of support and daily steps; VA contributed $\geq$ 15% in reading speed and driving cessation; ViN contributed $\geq$ 15% in GQL-15 only; and color vision contributed $\geq$ 15% in reading speed and base of support (Table 6).

Subanalysis and Sensitivity Analyses

The subanalysis of the 15 questions in GQL-15 demonstrated complete dominance of CS in six questions and its general dominance in additional three questions, with other parameters (IVF sensitivity, VA, and ViN) dominating for the remaining six questions (Table 7).

After excluding marital and employment statuses and living arrangement from the covariate list, the likelihood ratio test comparing models of covariates and vision (Covar + Vision) to covariates only (Covar Only) became borderline significant ($P = 0.05$) for reading speed and was statistically significant ($P = 0.03$) for balance. Furthermore, constrained dominance analysis yielded the same inferences regarding functional outcomes; however, CS now generally, instead of completely, dominated ViN for GQL-15, and VA completely, instead of conditionally, dominated CS for driving cessation.

Discussion

Vision parameters significantly predicted functional outcomes for glaucoma-related quality of life, daily steps, driving cessation, reading speed, and base of support while walking. However, the most important visual parameter predicting these outcomes differed across the outcomes studied, suggesting that there is no universal "best visual measure" to capture the impact of visual damage from glaucoma on functionality. Additionally, for two functional domains, the most predictive visual parameter was neither IVF nor VA, the parameters most commonly tested clinically. Clinicians and researchers should be aware that the relationship between visual parameters and functional outcomes in glaucoma is complex, with the visual parameter(s) most predictive of function changing across functional domains, or even across the various questions contained within a questionnaire.

Glaucoma's combined impact on all the vision parameters assessed explained variability in some, but not all, functional outcomes. Specifically, in LRT analyses of models with and without visual parameters, vision was significantly predictive in quality of life, daily steps, driving cessation, reading speed, and base of support while walking and was not significantly predictive in fear of falling, balance, gait velocity, stride length, and stride velocity. Previous research has linked glaucomatous visual loss to fear of falling,[27,28] balance,[29] and gait,[14] and we may not have found a significant visual contribution to these outcomes here because of limited sample size, or statistical features of our LRT,[30] in which we evaluated the importance of seven visual parameters combined rather than one or few parameters as had been done previously. Prior groups have focused on creating a "battery" of objective tests that can be used to evaluate the impact of glaucoma,[31,32] and our findings here can inform the specific elements likely to demonstrate a strong visual contribution, thus meriting inclusion in such a battery.

Surprisingly, IVF sensitivity was not the dominant visual predictor for several functional outcomes, though it was at least somewhat important for all functional outcomes. IVF sensitivity contributed over 15% of vision-explained variability across all five functional outcomes where visual contribution was significant (Table 6). Still, IVF was only completely dominant for base of support while walking, and other vision parameters dominated IVF in the other four outcomes. That is, glaucoma's effect on IVF contributes to reduced function across multiple domains, but glaucomatous IVF loss explained only 15% to 35% of the visual component of functional impairment. Although assessing VF remains an important clinical tool to diagnose and monitor glaucoma, a more comprehensive assessment of vision should be considered in research aimed at capturing the full impact of glaucomatous visual loss on function. Indeed, in conversations with patients, physicians should be aware that VF damage only partially accounts for their functional difficulties.

Investigative Ophthalmology & Visual Science

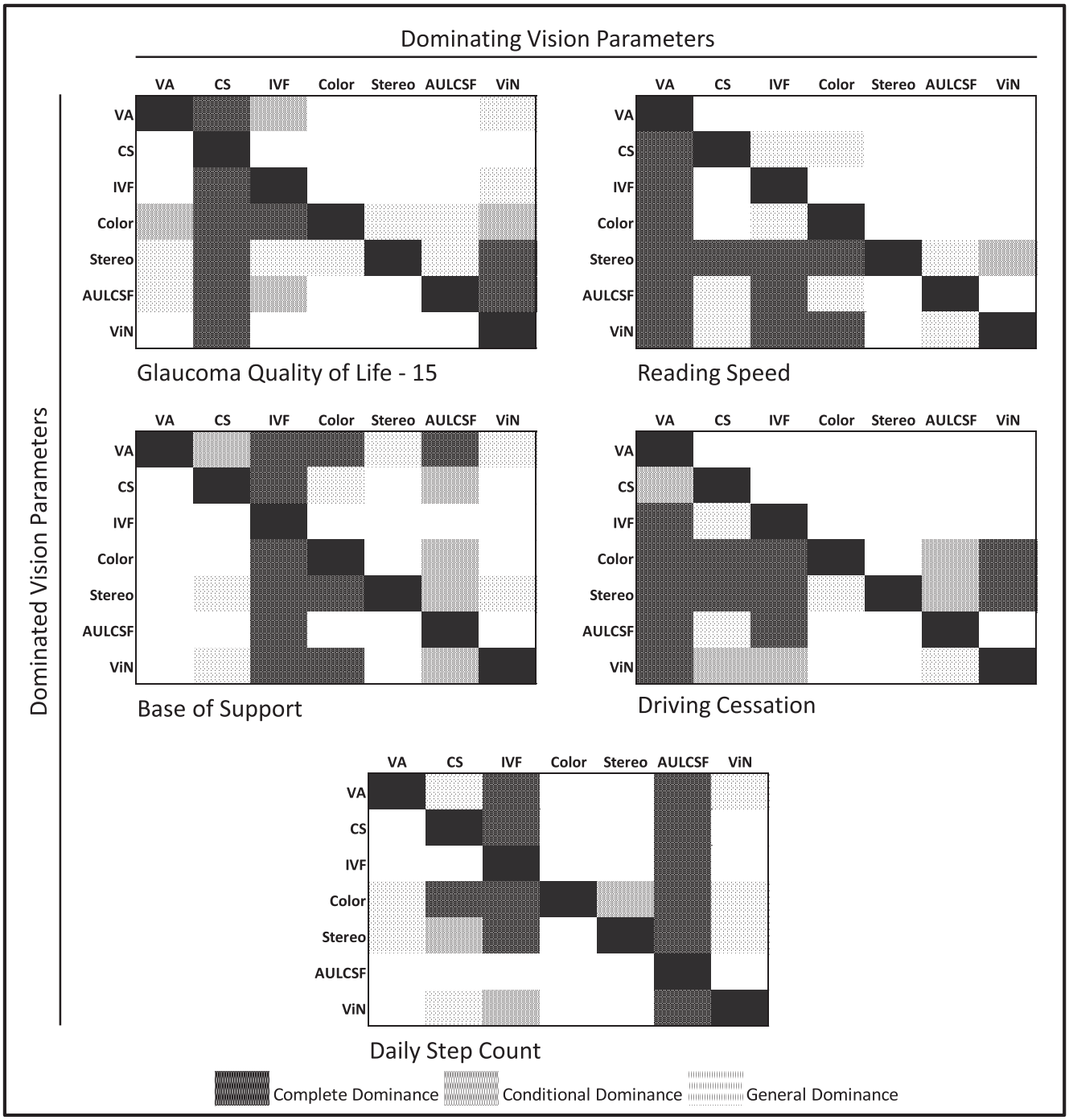

Figure 2. Dominance analysis of vision parameters in functional outcomes where vision significantly contributed to explaining variability in glaucoma patients. Empty cells indicate no dominance designation between the two vision parameters. Color, color vision; Stereo, stereoacuity.

In addition to IVF, VA (dominant parameter for reading speed and driving cessation), CS (dominant parameter for GQL-15 scores), and AULCSF (dominant parameter for daily steps) were also important for our studied outcomes, consistent with previous research.[6–8] In fact, the combination of IVF, VA, CS, and AULCSF consistently contributed 70% or more to vision-explained variability across our studied outcomes. Therefore, when studying glaucoma's association with function, these four parameters should be most strongly considered as measures of vision. Outside the research setting, it is possible, in theory, to measure all four of these visual parameters in two tests—a VF test and a CS function test, which simultaneously captures VA, CS, and AULCSF.[33]

Patient-reported functional limitations as measured by the GQL-15 questionnaire were strongly predicted by vision. Although VF assessment has traditionally been used in studying the impact of glaucoma on quality of life,[34] CS was the most important, completely dominant, vision parameter in our analysis. Furthermore, a subanalysis of the 15 questions in GQL-15 demonstrated dominance of CS in nine questions, with other parameters (IVF sensitivity, VA, and ViN) dominating in the other six questions. The fact that different parameters

Investigative Ophthalmology & Visual Science

Investigative Ophthalmology & Visual Science

Table 6. General Dominance and Standardized* General Dominance Statistics of Vision Parameters for Functional Outcomes Where Vision Significantly Explains Part of the Variance

	GQL-15		Reading Speed		Base of Support		Driving Cessation		Daily Steps	
	Δ (95% CI)	ΔΣ	Δ (95% CI)	ΔΣ	Δ (95% CI)	ΔΣ	Δ (95% CI)	ΔΣ	Δ (95% CI)	ΔΣ
Color	0.021 (0.006–0.045)	9%	0.016 (0.001–0.066)	17%	0.016 (0.001–0.081)	17%	0.017 (0.002–0.047)	7%	0.0002 (0.00005–0.00037)	2%
Stereo	0.006 (0.001–0.028)	3%	0.001 (0–0.002)	1%	0.007 (0.001–0.043)	7%	0.007 (0–0.032)	3%	0.00034 (0.00006–0.00171)	4%
ViN	0.039 (0.008–0.096)	17%	0.004 (0.001–0.007)	4%	0.01 (0.002–0.044)	9%	0.028 (0.005–0.114)	12%	0.00059 (0.00016–0.00177)	7%
VA	0.03 (0.008–0.072)	14%	**0.03** (0.003–0.091)	**34%**	0.005 (0–0.01)	5%	**0.065** (0.012–0.163)	**26%**	0.00057 (0.00011–0.00114)	7%
AULCSF	0.023 (0.007–0.042)	10%	0.01 (0.001–0.026)	11%	0.023 (0.003–0.059)	18%	0.036 (0.007–0.072)	14%	**0.00387** (0.00122–0.00711)	**45%**
CS	**0.067** (0.023–0.125)	**30%**	0.013 (0.002–0.043)	15%	0.01 (0.001–0.019)	10%	0.049 (0.009–0.131)	20%	0.00081 (0.00017–0.00151)	9%
IVF	0.037 (0.009–0.086)	16%	0.016 (0.002–0.06)	17%	**0.034** (0.005–0.112)	**35%**	0.044 (0.006–0.133)	18%	0.00232 (0.00037–0.00703)	27%

Confidence intervals are obtained from 1000 bootstrapped subsamples. Bold numbers indicate vision parameter with highest dominance statistic. Δ, dominance statistic; ΔΣ, standardized dominance statistic (dominance statistics scaled to sum to 100%); CI, confidence interval.

* Standardized dominance statistic for a vision parameter can be interpreted as its contribution to vision-explained variability in the outcome.

Table 7. Dominance Analysis of Vision Parameters of the 15 Questions in GQL–15 Questionnaire

Question	Dominating Parameter	Strongest Dominance Designation*
How much trouble you have . . .		
with reading news online or print?	CS	Complete
walking after dark?	CS	General
seeing at night?	CS	Complete
walking on uneven ground?	IVF	Conditional
adjusting to bright lights?	CS	General
adjusting to dim lights?	CS	Complete
going from light to dark room or vice versa?	CS	Complete
tripping over objects?	IVF	Complete
seeing objects coming from the other side?	VA	General
crossing the road?	CS	Complete
walking on steps/stairs?	ViN	Complete
bumping into objects?	ViN	General
judging distance of foot/step to curb?	CS	Conditional
finding dropped objects?	CS	Complete
recognizing faces?	ViN	General

* Strongest dominance designation of dominating parameter (column 2) over all over vision parameters for each question. Complete dominance of a vision parameter over all other vision parameters indicates that adding this vision parameter to a model increases the fit statistic (R^2 or McFadden's pseudo-R^2) to a greater extent than adding any other vision parameter across all possible models. Conditional dominance indicates that the average increase in fit statistic is higher for a vision parameter than others across all orders of models. Model order is defined as the number of predictor variables in a model. General dominance indicates that the average increase in fit statistic across all models is higher for this vision parameter than all other vision parameters.

dominated different GQL-15 items raises the concern that it may not be appropriate to conclude that CS is most important to glaucoma-related quality of life, as the correct conclusion would appear to be that different aspects of vision are most relevant to different aspects of quality of life (as shown in Table 7).

Specific vision parameters likely dominated different outcomes based on their particular relevance to that functional task. VA may be most relevant for driving cessation because driving licensure requires good VA . On the other hand, VA may be most relevant for reading speed because reading is a task that relies on central foveal vision, which is measured by VA. The relevance of VF sensitivity to base of support suggests that balance in motion is facilitated by one's peripheral vision.

Importantly, when including the seven measures of visual ability with demographic and health predictors, vision contributed at most 54% of explained variability. Therefore, researchers must assess demographic and other comorbidities when studying the impact of glaucoma on functional outcomes. From a clinical standpoint, considerations about when or how to rehabilitate patients with glaucoma also need to take into account the entire patient and not merely the visual function.

Our analysis is limited by the use of cross-sectional data, and our findings need to be validated in a larger cohort with a longitudinal analysis. We looked at explained variability within glaucoma patients and suspects, and future studies can additionally explore the importance of vision and the relative importance of vision parameters to explaining variability in function between glaucoma and normal subjects. A large proportion of the original cohort was excluded from the

analysis because of incomplete data for the vision parameters; however, this is unlikely to affect our inference as the excluded individuals were comparable with participants included in the analysis. Our dominance analysis findings were robust as we included heath and demographic predictors in all subsets of models using constrained dominance analysis. Finally, our results help improve our big-picture understanding of glaucoma's impact on functionality, but we have to remain cognizant of the individual differences in visual experience and functionality among glaucoma patients.

In summary, visual loss in glaucoma is predictive for some, but not all, functional outcomes. The combination of IVF, VA, CS, and AULCSF consistently contributes 70% or more to the effect of vision on function, and should be most strongly considered as measures of vision in glaucoma research. The most important vision parameter for functionality differs depending on the functional domain studied, or even across functional domains queried as part of the same instrument.

Acknowledgments

Supported by the National Institutes of Health (Grant Number: EY022976).

Disclosure: **A.F. Shakarchi**, None; **A. Mihailovic**, None; **S.K. West**, None; **D.S. Friedman**, None; **P.Y. Ramulu**, None

References

1. Sotimehin A, Ramulu P. Measuring disability in glaucoma. *J Glaucoma*. 2018;27:939–949.
2. Lin S, Mihailovic A, West SK, et al. Predicting visual disability in glaucoma with combinations of vision measures. *Trans Vis Sci Tech*. 2018;7(2):22.
3. Sample PA, Boynton RM, Weinreb RN. Isolating the color vision loss in primary open-angle glaucoma. *Am J Ophthalmol*. 1988;106:686–691.
4. Hyman LG, Komaroff E, Heijl A, Bengtsson B, Leske MC. Treatment and vision-related quality of life in the early manifest glaucoma trial. *Ophthalmology*. 2005;112:1505–1513.
5. Goldberg I, Clement C, Chiang T, et al. Assessing quality of life in patients with glaucoma using the Glaucoma Quality of Life-15 (GQL-15) questionnaire. *J Glaucoma*. 2009;18:6–12.
6. Richman J, Lorenzana LL, Lankaranian D, et al. Importance of visual acuity and contrast sensitivity in patients with glaucoma. *Arch Ophthalmol*. 2010;128:1576–1582.
7. Ekici F, Loh R, Waisbourd M, et al. Relationships between measures of the ability to perform vision-related activities, vision-related quality of life, and clinical findings in patients with glaucoma. *JAMA Ophthalmol*. 2015;133:1377–1385.
8. Richman J, Lorenzana LL, Lankaranian D, et al. Relationships in glaucoma patients between standard vision tests, quality of life, and ability to perform daily activities. *Ophthalmic Epidemiol*. 2010;17:144–151.
9. Magacho L, Lima F, Nery AC, Sagawa A, Magacho B, Ávila M. Quality of life in glaucoma patients: regression analysis and correlation with possible modifiers. *Ophthalmic Epidemiol*. 2004;11:263–270.
10. Gromping U. Estimators of relative importance in linear regression based on variance decomposition. *Am Stat*. 2007;61:139–147.
11. Budescu DV. Dominance analysis: a new approach to the problem of relative importance of predictors in multiple regression. *Psychol Bull*. 1993;11:542–551.
12. Azen R, Budescu DV. The dominance analysis approach for comparing predictors in multiple regression. *Psychol Methods*. 2003;8:129–148.
13. Odden JL, Mihailovic A, Boland MV, Friedman DS, West SK, Ramulu PY. Evaluation of central and peripheral visual field concordance in glaucoma. *Invest Ophthalmol Vis Sci*. 2016;57:2797–2804.
14. Mihailovic A, Swenor BK, Friedman DS, West SK, Gitlin LN, Ramulu PY. Gait implications of visual field damage from glaucoma. *Transl Vis Sci Technol*. 2017;6(3):23.
15. Lesmes LA. Bayesian adaptive estimation of the contrast sensitivity function: the quick CSF method. *J Vis*. 2010;10(3):17.
16. Fu VLN, Birch EE, Holmes JM. Assessment of a new Distance Randot stereoacuity test. *J AAPOS*. 2006;10:419–423.
17. Pelli DG, Levi DM, Chung STL. Using visual noise to characterize amblyopic letter identification. *J Vis*. 2004;4:904–920.
18. Nelson P, Aspinall P, Papasouliotis O, Worton B, O'Brien C. Quality of life in glaucoma and its relationship with visual function. *J Glaucoma*. 2003;12:139–150.
19. Goldberg I, Clement CI, Chiang TH, et al. Assessing quality of life in patients with glaucoma using the Glaucoma Quality of Life-15 (GQL-15) questionnaire. *J Glaucoma*. 2009;18:6–12.
20. Velozo CA, Peterson EW. Developing meaningful fear of falling measures for community dwelling elderly. *Am J Phys Med Rehabil*. 2001;80:662–673.
21. Cheung S, Kallie CS, Legge GE, Cheong AMY. Nonlinear mixed-effects modeling of MNREAD data. *Invest Ophthalmol Vis Sci*. 2008;49:828–835.
22. Ramulu PY, Swenor BK, Jefferys JL, Rubin GS. Description and validation of a test to evaluate sustained silent reading. *Invest Ophthalmol Vis Sci*. 2013;54:673–680.
23. de Luna RA, Mihailovic A, Nguyen AM, Friedman DS, Gitlin LN, Ramulu PY. The association of glaucomatous visual field loss and balance. *Transl Vis Sci Technol*. 2017;6(3):8.
24. Gnjidic D, Hilmer SN, Blyth FM, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *J Clin Epidemiol*. 2012;65:989–995.
25. Long JS, Freese J. *Regression Models for Categorical Dependent Variables Using Stata*. 2nd ed. College Station, TX: Stata Press; 2006.
26. Long JS. *Regression Models for Categorical and Limited Dependent Variables*. Thousand Oaks, CA: Sage Publications; 1997.
27. Ramulu PY, van Landingham SW, Massof RW, Chan ES, Ferrucci L, Friedman DS. Fear of falling and visual field loss from glaucoma. *Ophthalmology*. 2012;119:1352–1358.
28. Adachi S, Yuki K, Awano-Tanabe S, et al. Factors associated with developing a fear of falling in subjects with primary open-angle glaucoma. *BMC Ophthalmol*. 2018;18:39.
29. Kotecha A, Richardson G, Chopra R, Fahy RTA, Garway-Heath DF, Rubin GS. Balance control in glaucoma. *Invest Ophthalmol Vis Sci*. 2012;53:7795–7801.
30. Brown C, Templin J, Cohen A. Comparing the two- and three-parameter logistic models via likelihood ratio tests. *Appl Psychol Meas*. 2015;39:335–348.
31. Lorenzana L, Lankaranian D, Dugar J, et al. A new method of assessing ability to perform activities of daily living: design, methods and baseline data. *Ophthalmic Epidemiol*. 2009;16:107–114.
32. Goh RLZ, Kong YXG, McAlinden C, Liu J, Crowston JG, Skalicky SE. Objective assessment of activity limitation in glaucoma with smartphone virtual reality goggles: a pilot study. *Trans Vis Sci Tech*. 2018;7(1):10.
33. Dorr M, Elze T, Wang H, Lu Z-L, Bex PJ, Lesmes LA. New precision metrics for contrast sensitivity testing. *IEEE J Biomed Health Inform*. 2018;22:919–925.
34. Gothwal VK, Reddy SP, Bharani S, et al. Impact of glaucoma on visual functioning in Indians. *Invest Ophthalmol Vis Sci*. 2012;53:6081–6092.