# Contrast Sensitivity Function: A More Sensitive Index for Assessing Protective Effects of the Cilioretinal Artery on Macular Function in High Myopia

Ling Wei,[1–3] Jiaqi Meng,[1–3] Kaiwen Cheng,[1–3] Wenwen He,[1–3] Jiao Qi,[1–3] Zhong-Lin Lu,[4–6] Yi Lu,[1–3] and Xiangjia Zhu[1–3]

[1]Department of Ophthalmology and Eye Institute, Eye and Ear, Nose, and Throat Hospital of Fudan University, Shanghai, China
[2]Key Laboratory of Myopia (Fudan University), National Health Commission; Key Laboratory of Myopia, Chinese Academy of Medical Science; and Shanghai Key Laboratory of Visual Impairment and Restoration, Shanghai, China
[3]State Key Laboratory of Medical Neurobiology, Fudan University, Shanghai, China
[4]Division of Arts and Sciences, New York University Shanghai, Shanghai, China
[5]Center for Neural Science and Department of Psychology, New York University, New York, New York, United States
[6]NYU-ECNU Institute of Brain and Cognitive Science, New York University Shanghai, Shanghai, China

Correspondence: Xiangjia Zhu, Department of Ophthalmology and Eye Institute, Eye and Ear, Nose, and Throat Hospital, Fudan University, 83 Fenyang Road, Shanghai 200031, China; zhuxiangjia1982@126.com.
Yi Lu, Department of Ophthalmology and Eye Institute, Eye and Ear, Nose, and Throat Hospital, Fudan University, 83 Fenyang Road, Shanghai 200031, China; luyieent@163.com.

LW and JM contributed equally to this work as co-first authors.

**Received:** July 27, 2022
**Accepted:** December 8, 2022
**Published:** December 29, 2022

Citation: Wei L, Meng J, Cheng K, et al. Contrast sensitivity function: A more sensitive index for assessing protective effects of the cilioretinal artery on macular function in high myopia. *Invest Ophthalmol Vis Sci.* 2022;63(13):25. https://doi.org/10.1167/iovs.63.13.25

**Purpose.** To assess the benefits of the cilioretinal artery on macular function in high myopia using the quantitative contrast sensitivity function (qCSF) method.

**Methods.** This cross-sectional study was conducted at the Eye and Ear, Nose, and Throat Hospital of Fudan University. In total, 137 highly myopic patients (with axial length [AL] ≥ 26.00 mm) were enrolled and divided into cilioretinal artery absent and present groups based on their fundus photographs. One eye in each patient was randomly selected. Choroid thickness was measured using macular optical coherence tomography. The best-corrected visual acuity (BCVA) was evaluated by Early Treatment Diabetic Retinopathy Study charts, and the area under the log CSF (AULCSF), CSF acuity, and CS at six spatial frequencies were evaluated with the qCSF method.

**Results.** Although no significant BCVA difference was found between the cilioretinal artery absent (97 patients) and present (40 patients) groups, choroid thickness, AULCSF, CSF acuity, and CSF at low and intermediate spatial frequencies (1–6 cycles per degree) were all significantly higher in the cilioretinal artery present group than in the absent group (all $P < 0.05$). In addition, eyes with temporal cilioretinal arteries exhibited significantly higher AULCSF, CSF acuity, and CSFs at 3 and 6 cycles per degree (all $P < 0.05$) than those with a nasal one (all $P < 0.05$). Multivariate analysis showed that better AULCSF was associated with the presence of cilioretinal artery and the interaction of AL and choroid thickness.

**Conclusions.** The cilioretinal artery may associate with the larger choroid thickness in highly myopic eyes and may play a role in preserving qCSF outcomes, which are more sensitive than chart-based acuity tests.

Keywords: high myopia, cilioretinal artery, macular function, contrast sensitivity, choroid thickness

High myopia has become one of the leading causes of blindness worldwide,[1] and an estimated 9.8% of the global population is expected to be affected by 2050.[2] Due to the elongation of axial length (AL) of the eye and extreme thinning of the choroid and retina, the fundus vasculature of highly myopic eyes is reportedly attenuated and may negatively impact macular functions.[3,4] Exploring and identifying potential protective factors for macular functions may help preserve vision in eyes with high myopia.

The cilioretinal artery has a reported 20% to 40% prevalence in the general population.[5–7] Some studies have shown that it may be involved in preventing the development of age-related macular degeneration (AMD) and preserving visual functions in central retinal artery occlusion.[8–10] Studies have attempted to uncover the role of cilioretinal arteries in high myopia. For example, Watanabe et al.[11] demonstrated the derivation of cilioretinal arteries in high myopia, including short posterior ciliary arteries and Zinn–Haller arterial rings. Our group has previously proposed a photographic classification system of the cilioretinal artery in high myopia that is clinically relevant to visual acuity (VA).[12,13] However, previous evaluations of the protective effects of the cilioretinal artery on macular functions in high myopia have been based on blood flow analysis and/or VA assessment, which are not very sensitive measures of functional vision and may not reflect the real visual performance of eyes.[14]

The contrast sensitivity function (CSF) is a more comprehensive measure of spatial vision. Whereas VA assesses the spatial resolution of the eye in high contrast, CSF measures the minimum amount of contrast necessary for the eye to discern objects across a wide range of sizes or spatial frequencies,[15] and it has been shown to better correlate with daily visual functions such as driving and reading.[16,17] Recently, with the development of the quantitative contrast sensitivity function (qCSF) method, CSF can be measured very efficiently with high precision and accuracy in the clinic.[18] The qCSF method has been used to detect relevant functional vision changes in many eye diseases, including amblyopia[19] and AMD.[20–22] However, no study has applied qCSF to evaluate the effects of cilioretinal artery on macular functions in high myopia. In this study, we aimed to apply qCSF to evaluating the role of the cilioretinal artery in macular functions in highly myopic eyes across different AL ranges and cilioretinal artery morphological categories.

## Materials and Methods

This cross-sectional study was carried out at the Eye and Ear, Nose, and Throat (ENT) Hospital of Fudan University. The design and conduct of the study were consistent with the tenets of the Declaration of Helsinki and approved by the Institutional Review Board of the hospital (no. 2013021). This study was conducted as part of a larger project, the Shanghai High Myopia Study, registered at www.clinicaltrials.gov (accession number NCT03062085). Signed informed consent regarding usage of their clinical data was obtained from each participant.

### Patients

Patients with eyes with AL $\geq$ 26.00 mm and credible and clear fundus photographs and who did not meet any of the exclusion criteria were included and called back for qCSF assessment. The exclusion criteria included (1) other ocular comorbidities, such as strabismus, corneal diseases, glaucoma, and uveitis; (2) severe fundus lesions, such as severe macular atrophy and choroidal neovascularization, or myopic maculopathy (MMD) grading > 3 as defined by the international Meta-Analysis for Pathologic Myopia (META-PM) classification system,[23] due to their inability to finish the qCSF assessment; (3) other fundus pathologic features related to high myopia; and (4) previous trauma or ocular surgery or systematic diseases such as diabetes. Eyes were then classified into the cilioretinal artery absent and present groups based on their fundus photography. If a patient was bilaterally eligible, one eye was randomly selected for the analysis. A total of 137 highly myopic eyes from 137 patients were analyzed, with 97 eyes in the cilioretinal artery absent group and 40 eyes in the cilioretinal artery present group. Eyes were further divided into two subgroups according to AL: 26.00 to 28.00 mm ($n$ = 66) and >28.00 mm ($n$ = 71).

### Routine Ophthalmic Examinations

All participants received ophthalmic examinations including slit-lamp microscopy, fundoscopy, and B-scan ultrasonography. MMD grading was assessed by the International META-PM Classification System using fundoscopy photographs.[23] AL was measured using the IOLMaster 700 (ZEISS, Oberkochen, Germany).

### Fundus Photographs

Fundus photographs were collected with a Canon CR-2 retinal camera (Canon, Tokyo, Japan). Three experienced doctors (LW, WH, and JM) independently determined the presence or absence of the cilioretinal artery and its classification, and disagreements were resolved by discussions. The definition and classification of a cilioretinal artery were in accordance with our prior publications.[12,13] Briefly, a cilioretinal artery can be identified by the sharp hook-like appearance at the optic disc margin and must not have any visible communication with the central retinal artery. The classifications of arteries include the following: category 1, temporal "cake-fork," which has two main branches; category 2, temporal "ribbon," which has no obvious branches; category 3, "multiple," which has two or more cilioretinal arteries; and category 4, "nasal," which refers to the cilioretinal artery that emerges from the nasal border of the optic disc (Fig. 1).

### Choroid Thickness Measurements

Images of the choroid were collected using enhanced depth imaging with spectral-domain optical coherence tomography (EDI SD-OCT; Heidelberg Engineering, Heidelberg, Germany). Horizontal sections going directly through the center of the fovea were selected to measure the thickness of the choroid, and the measurements were performed using with Heidelberg Eye Explorer 1.5.12.0. Figure 1E demonstrates example measurements of the subfoveal choroid thickness (SFCT) and thickness at 1 and 3 mm temporally and nasally to the fovea, as previously described.[24] The measurements were conducted by two independent doctors who were blinded to other clinical features. If their difference exceeded 15% of the mean of the two values, a senior doctor would help with determining the thickness.

### Visual Acuity Assessment and qCSF Test

The best-corrected visual acuity (BCVA) logarithm of the minimal angle of resolution (logMAR) was assessed with a back-lit Early Treatment of Diabetic Retinopathy Study (ETDRS) chart at 4 meters (m). The qCSF test was conducted without pupil dilation in a 25-trial setting at a 4-m testing distance using the Manifold Contrast Vision Meter (Adaptive Sensory Technology, San Diego, CA, USA), which uses a computerized adaptive Bayesian algorithm to assess CSF across a range of spatial frequencies and models CSF as a function of stimulus spatial frequency.[18] All participants were tested monocularly with their individual best-corrected habitual glasses following measurement of BCVA; the untested eye was covered with a patch. The area under the logCSF curve (AULCSF) was computed by integrating the estimated CSF from 1 to 18 cycles per degree (cpd). CFS acuity was defined as the spatial frequency at which CS = 1.0. CS values at 1, 1.5, 3, 6, 12, and 18 cpd were also computed from the qCSF test.

Investigative Ophthalmology & Visual Science

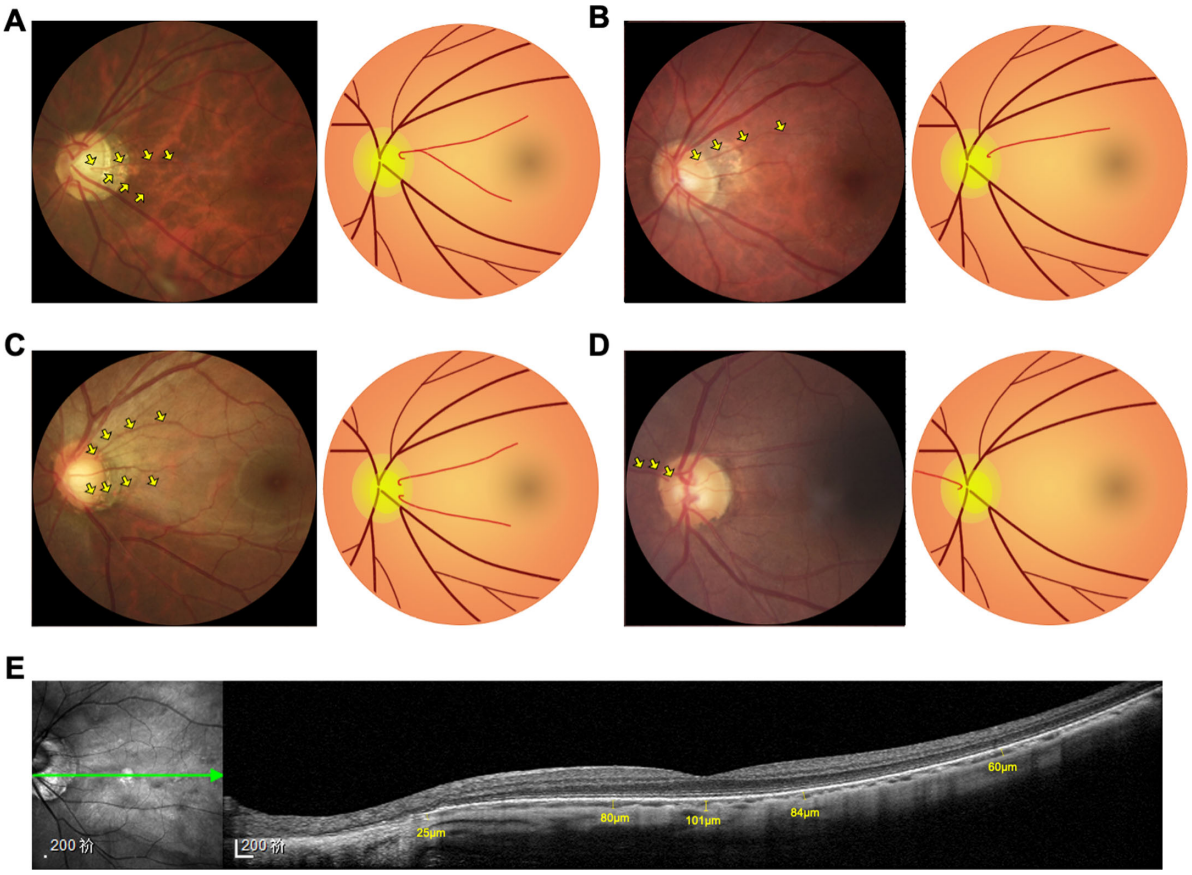


**Figure 1.** Morphological classifications of the cilioretinal artery and measurements of choroid thickness. (**A**) Category 1, temporal "cake-fork," a cilioretinal artery with two main branches; (**B**) category 2, temporal "ribbon," a cilioretinal artery without obvious branches; (**C**) category 3, "multiple" cilioretinal arteries, two or more with separate origins; and (**D**) category 4, a "nasal" cilioretinal artery, which emerges from the nasal border of the optic disc. The *yellow arrow* marks the cilioretinal artery. (**E**) EDI SD-OCT scans show the CT measurements in the horizontal scan. *Left*, nasal; *right*, temporal. The EDI SD-OCT image shows SFCT and T1 mm, N1 mm, T3 mm, and N3 mm CTs, with CTs of 101, 84, 80, 60, and 25 μm, respectively.

### Statistical Analyses

Continuous variables were summarized as mean ± standard deviation, and categorical variables were summarized as frequencies. Data distributions were assessed graphically and with the Shapiro–Wilk test for normality. Normally distributed data in two groups were compared using two-tailed independent samples *t*-tests. One-way ANOVA was used to compare outcomes in three or more groups, with Tukey's honest significance test (HSD) post hoc analysis. Two-way repeated-measures ANOVA with post hoc Bonferroni analysis was used to compare sensitivity across multiple spatial frequencies. Two-tailed Pearson's correlation was used to evaluate the direction and magnitude of relationships among the qCSF outcomes and AL. Backward stepwise multivariate linear regression analysis was used to determine the significant predictors for SFCT. Multiple linear regression with interaction terms was used to determine the significant predictors for AULCSF.[25] Continuous variables were centered around the mean to better demonstrate interaction effects between two continuous variables. Simple slope analysis was used to further interpret significant interaction terms. All data analyses were conducted using SPSS Statistics 25.0 (IBM, Chicago, IL), with $P < 0.05$ defined as statistically significant.

## Results

### Patient Characteristics

There was no significant difference in age, gender, eye laterality, AL, or MMD grading between the cilioretinal artery present and absent groups (Table 1).

### Choroid Thickness

Table 2 shows the CT measurements in highly myopic eyes with or without cilioretinal arteries. The cilioretinal artery present group demonstrated significantly larger SFCTs ($P = 0.016$) and CTs at 1 mm temporally (T1; $P = 0.046$), 3 mm temporally (T3; $P = 0.002$), and 3 mm nasally to the fovea (N3; $P = 0.007$). Furthermore, the cilioretinal artery present eyes were further divided into four categories according to our previous morphological classifications (Fig. 1). SFCT and T1, N1, T3, and N3 CTs were not significantly different among eyes in the four subgroups of cilioretinal artery categories (Supplementary Table S1).

We further conducted a backward stepwise multivariable regression analysis on SFCT using the presence of cilioretinal artery, AL, and MMD grading as predictors. It demonstrated that larger SFCT was significantly associated with

**Table 1.** Patient Characteristics

| Characteristics | Cilioretinal Artery Absent | Cilioretinal Artery Present | *P* |
|---|---|---|---|
| Number of eyes | 97 | 40 | — |
| Age (y), mean ± SD | 60.12 ± 8.64 | 58.65 ± 11.71 | 0.193 |
| Female, *n* (%) | 54 (55.67) | 20 (50.00) | 0.545 |
| Eye laterality, right eye, *n* (%) | 58 (59.79) | 23 (57.50) | 0.804 |
| Axial length (mm), mean ± SD | 28.15 ± 1.37 | 28.69 ± 1.89 | 0.067 |
| Myopic maculopathy grading,* *n* (%) | | | 0.699 |
| Grade 0 (no macular lesions) | 2 (2.06) | 2 (5.00) | |
| Grade 1 (tessellated fundus) | 35 (36.08) | 16 (40.00) | |
| Grade 2 (diffuse atrophy) | 35 (36.08) | 14 (35.00) | |
| Grade 3 (patchy atrophy) | 25 (25.77) | 8 (20.00) | |
| Grade 4 (macular atrophy)† | 0 | 0 | |

* Myopic macular degeneration as defined by the International META-PM Classification System.[23]
† Patients with macular atrophy were excluded in this study because they failed to get credible qCSF results due to low vision.

**Table 2.** Choroid Thickness in Highly Myopic Eyes With or Without Cilioretinal Artery

| | Cilioretinal Artery Absent | Cilioretinal Artery Present | *P* |
|---|---|---|---|
| Number of eyes | 97 | 40 | — |
| SFCT (µm), mean ± SD | 88.95 ± 60.92 | 118.68 ± 72.92 | 0.016* |
| CT at T1 mm (µm), mean ± SD | 97.93 ± 64.46 | 123.20 ± 72.12 | 0.046* |
| CT at T3 mm (µm), mean ± SD | 106.82 ± 55.90 | 144.80 ± 78.29 | 0.002 |
| CT at N1 mm (µm), mean ± SD | 88.46 ± 59.31 | 103.05 ± 64.08 | 0.203* |
| CT at N3 mm (µm), mean ± SD | 42.22 ± 34.86 | 59.45 ± 30.88 | 0.007* |

* Significant difference using two-tailed independent samples *t*-test.

**Table 3.** BCVA and CSF Outcomes in Highly Myopic Eyes

| | Cilioretinal Artery Absent | Cilioretinal Artery Present | *P* |
|---|---|---|---|
| Eyes in entire AL range | | | |
| Number of eyes | 97 | 40 | — |
| BCVA (logMAR) | 0.20 ± 0.18 | 0.16 ± 0.17 | 0.318 |
| AULCSF (log unit) | 0.46 ± 0.40 | 0.76 ± 0.37 | <0.001* |
| CSF acuity (logMAR) | 0.79 ± 0.37 | 1.06 ± 0.30 | <0.001* |
| Eyes with AL 26.00 ~ 28.00 mm | | | |
| Number of eyes | 45 | 21 | — |
| BCVA (logMAR) | 0.15 ± 0.13 | 0.14 ± 0.16 | 0.892 |
| AULCSF (log unit) | 0.52 ± 0.40 | 0.70 ± 0.35 | 0.080 |
| CSF acuity (logMAR) | 0.85 ± 0.37 | 1.03 ± 0.24 | 0.022* |
| Eyes with AL > 28.00 mm | | | |
| Number of eyes | 52 | 19 | — |
| BCVA (logMAR) | 0.24 ± 0.21 | 0.19 ± 0.19 | 0.331 |
| AULCSF (log unit) | 0.41 ± 0.39 | 0.83 ± 0.40 | <0.001* |
| CSF acuity (logMAR) | 0.74 ± 0.37 | 1.10 ± 0.36 | 0.001* |

* Significant difference using two-tailed independent samples *t*-test.

the presence of cilioretinal artery (adjusted $\beta = 0.135$ in presence over absence; $P = 0.046$), shorter AL (adjusted $\beta = -0.251$ per 1-mm increase in AL; $P = 0.003$), and lower MMD grading (adjusted $\beta = -0.427$ per grading increase in META-PM system; $P < 0.001$; $R^2 = 0.399$).

## Visual Acuity and qCSF Outcomes

Table 3 shows the BCVA and qCSF outcomes of the two groups. Although there was no significant difference in BCVA between the cilioretinal artery absent and present groups ($P = 0.318$), the AULCSF and CSF acuity were both significantly higher in the cilioretinal artery present group than in the absent group (both $P < 0.001$). We further compared the qCSF outcomes in eyes with different AL ranges (Table 3). In eyes with AL from 26.00 to 28.00 mm, no significant differences were found in BCVA and AULCSF, although CSF acuity was significantly higher in the cilioretinal artery present than in the absent group ($P = 0.022$). In eyes with AL > 28.00 mm, although there was no significant difference in the BCVA, the differences in AULCSF and CSF acuity between the cilioretinal artery absent and present groups became more pronounced (0.41 ± 0.39 vs. 0.83 ± 0.40 and 0.74 ± 0.37 vs. 1.10 ± 0.36, respectively; both $P \leq 0.001$).

Figure 2 shows the CSFs of the different groups. The cilioretinal artery present group showed significantly higher CS at low and intermediate spatial frequencies than the cilioretinal artery absent group (two-way ANOVA $P < 0.001$, Bonferroni-corrected $P < 0.05$ at 1–6 cpd) (Fig. 2A). In eyes with AL from 26.00 to 28.00 mm (Fig. 2B), the CS was higher in the cilioretinal artery present group only at 3 cpd (two-way ANOVA $P = 0.065$, Bonferroni-corrected $P < 0.05$). In eyes with AL > 28.00 mm (Fig. 2C), the CS was higher in the cilioretinal artery present group at low and intermediate spatial frequencies than the cilioretinal artery absent group (two-way ANOVA $P < 0.001$, Bonferroni-corrected $P < 0.05$ at 1, 3, 6, and 12 cpd).

Comparison of BCVA and qCSF outcomes was further conducted among four categories of cilioretinal artery (Table 4). Although the BCVA was not significantly different among eyes in the four subgroups ($P = 0.318$), the AULCSF and CSF acuity were both significantly lower in eyes in the nasal subgroup compared to eyes in the other subgroups ($P = 0.011$ and $P = 0.006$, respectively; all $P < 0.05$ for post hoc Turkey's HSD test) (Table 4). However, the AULCSF and CSF acuity were not significantly different among the temporal "cake-fork," temporal "ribbon," and "multiple" arteries subgroups (all paired $P > 0.10$ in post hoc Tukey's HSD test). In addition, the nasal artery subgroup also exhibited significantly lower CS at intermediate spatial frequencies

Investigative Ophthalmology & Visual Science

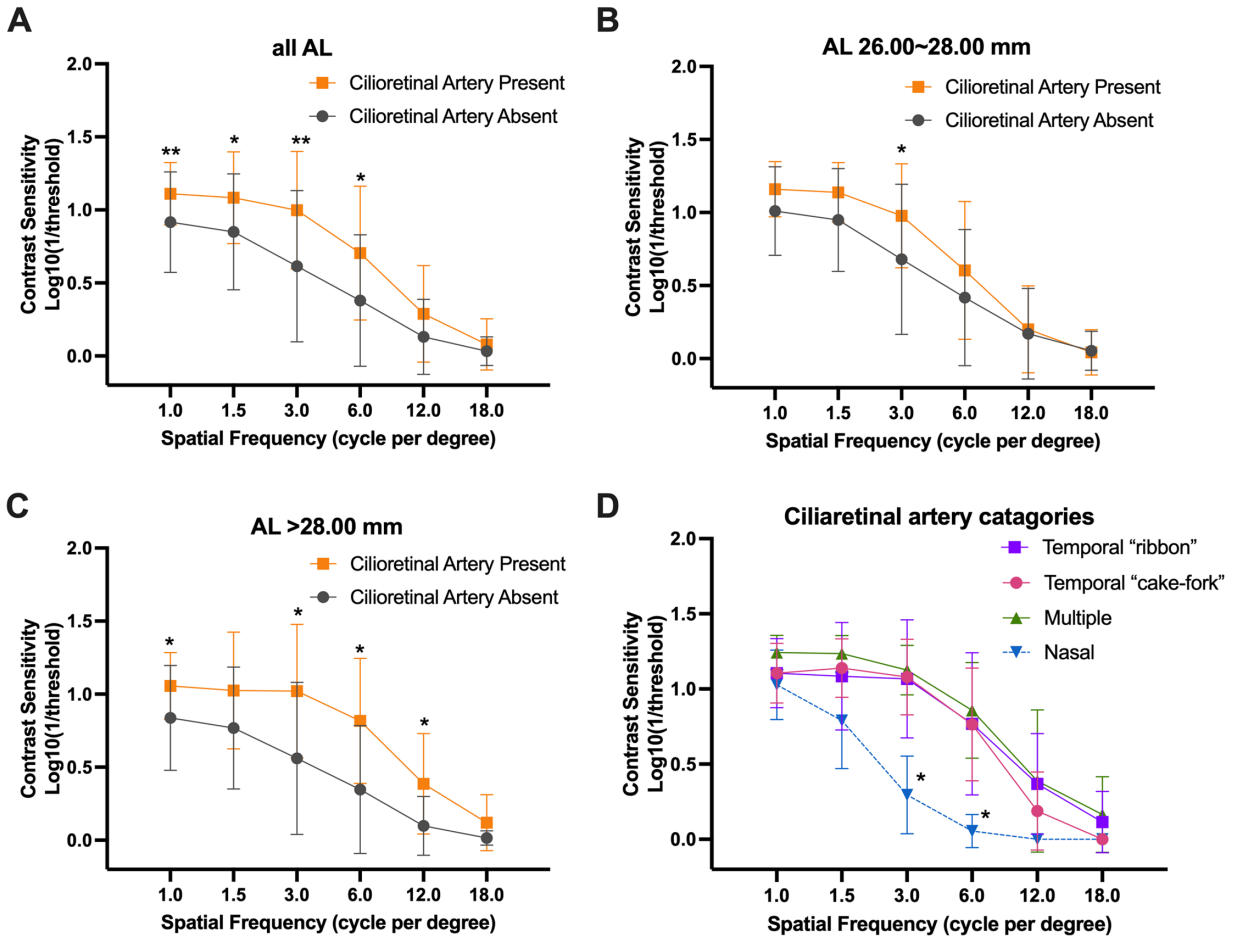


**Figure 2.** CSFs of different groups. (**A**) CSFs in the cilioretinal artery present and absent groups among all highly myopic eyes. (**B**) CSFs in the cilioretinal artery present and absent groups among eyes with AL from 26.00 to 28.00 mm. (**C**) CSFs in the cilioretinal artery present and absent groups among eyes with AL > 28.00 mm. (**D**) CSFs in the four cilioretinal artery categories. Two-way ANOVA and post hoc Bonferroni analysis were used. $^{*}P < 0.05$ and $^{**}P < 0.001$ for post hoc Bonferroni analysis comparing CSF at each spatial frequency.

**Table 4.** BCVA and qCSF Outcomes in the Four Cilioretinal Artery Present Subgroups

| Category of Cilioretinal Artery | Category 1 (Temporal "Cake-Fork") | Category 2 (Temporal "Ribbon") | Category 3 (Multiple) | Category 4 (Nasal) | *P* |
|---|---|---|---|---|---|
| Number of eyes (%) | 10 (25.0) | 22 (55.0) | 4 (10.0) | 4 (10.0) | — |
| Axial length (mm), mean ± SD | 28.01 ± 1.02 | 28.40 ± 1.37 | 27.47 ± 1.00 | 27.82 ± 2.43 | 0.576 |
| BCVA (logMAR), mean ± SD | 0.19 ± 0.15 | 0.16 ± 0.19 | 0.12 ± 0.12 | 0.24 ± 0.22 | 0.318 |
| AULCSF (log unit), mean ± SD | 0.74 ± 0.23* | 0.80 ± 0.37* | 0.90 ± 0.27* | 0.20 ± 0.16 | 0.011† |
| CSF acuity (logMAR), mean ± SD | 1.09 ± 0.13* | 1.11 ± 0.32* | 1.21 ± 0.17* | 0.59 ± 0.26 | 0.006† |

* Significant difference in post hoc Tukey's HSD test with nasal cilioretinal artery category.
† Significant difference in one-way ANOVA analysis.

compared to the other three subgroups (two-way ANOVA $P = 0.029$, Bonferroni-corrected $P < 0.05$ at 3 and 6 cpd) (Fig. 2D).

## Associations of qCSF Outcomes, AL, SFCT, and Presence of Cilioretinal Artery

In eyes with all AL ranges and in the 26.00- to 28.00-mm subgroup, no significant correlation was found between AL and AULCSF or CSF acuity (Spearman's correlation, all $P >$ 0.10). In eyes with AL > 28.00 mm, the AULCSF was significantly and negatively correlated with AL (Spearman's rank correlation $r = -0.275$, $P = 0.020$) (Fig. 3). CSF acuity tended to be negatively correlated with AL but was only marginally significant ($r = -0.218$, $P = 0.068$).

We then conducted a multivariate regression analysis on AULSCF using age, AL, MMD grading, SFCT, and the presence of cilioretinal arteries as predictors, as well as the interaction of AL with the cilioretinal artery and the interaction of AL with SFCT (continuous variables AL and SFCT were centered as [AL – AL mean] and [SFCT – SFCT mean] in the model). Supplementary Table S2 shows the multivari-

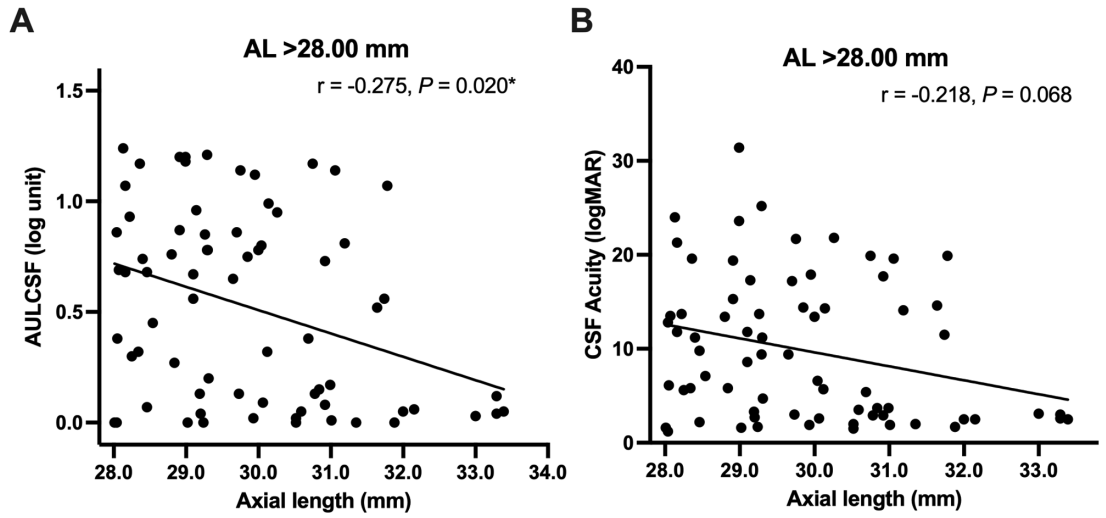


**Figure 3.** Correlation between AL and CSF outcomes in eyes with AL > 28.00 mm. (**A**) A scatterplot of AULCSF and AL. (**B**) A scatterplot of CSF acuity and AL. $^{*}P < 0.05$ for Pearson's correlation analysis.

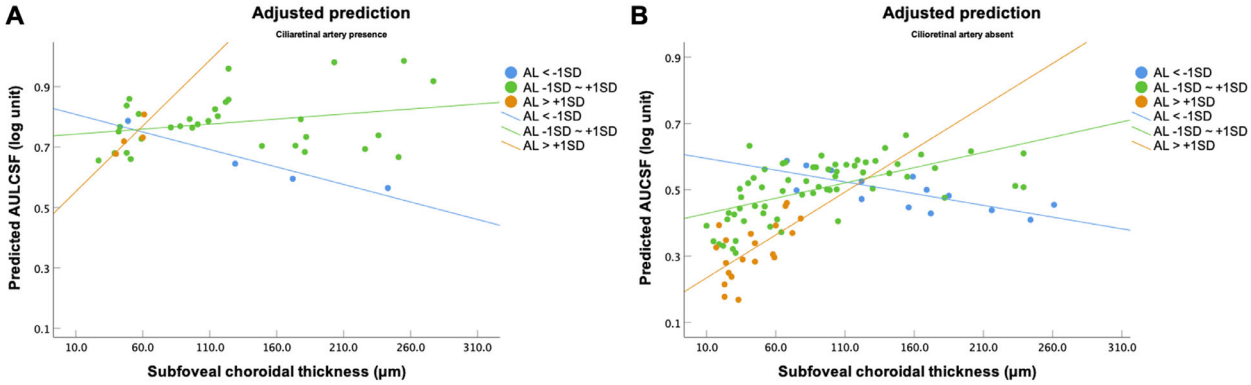


**Figure 4.** Simple slope analyses demonstrating the effect of interaction between AL and SFCT on AULCSF. (**A**) The adjusted prediction of AULCSF against SFCT in the cilioretinal artery present group. (**B**) The adjusted prediction of AULCSF against SFCT in the cilioretinal absent present group. Scatterplots were divided by AL < −1 SD (*blue*), AL from –1 SD to +1 SD (*green*), and AL > +1 SD (*orange*).

able analysis outcomes, which demonstrated that a higher AULCSF was significantly associated with the presence of a cilioretinal artery (adjusted $\beta = 0.305$ in presence over absence; $P < 0.001$), AL (adjusted $\beta = -0.327$ per 1-mm increase in AL; $P = 0.044$), and a centered AL × centered SFCT interaction (adjusted $\beta = 0.371$ per interaction, $P = 0.045$; $R^2 = 0.177$).

To further interpret the effect of the interaction between AL and SFCT, we conducted simple slope analyses stratified by AL ± 1 SD (Fig. 4) or AL < 26 mm, AL 26 ~ 28 mm, AL > 28 mm subgroups (Supplementary Fig. S1). The effect of the presence (Fig. 4A, Supplementary Fig. S1A) or absence (Fig. 4B, Supplementary Fig. S1A) of the cilioretinal artery on contrast sensitivity between SFCT and AL was explored. The findings suggest that the presence of the cilioretinal artery group showed relatively better predicted AULCSF compared to the absent group. As AL elongates, the associations of SFCT and AULCSF become more and more positive.

## Discussion

High myopia usually causes complications, including a spectrum of macular disorders that lead to irreversible vision loss.[26] Although our previous research documented the protective role of cilioretinal artery in alleviating progression of myopic macular degeneration,[13] its effects on functional vision were based on VA assessment, which is not very well correlated with subjective visual experience and daily visual functions. In this study, we showed that the qCSF method is a more sensitive index than VA assessment for assessing the protective effects of the cilioretinal artery on macular function in highly myopic eyes.

Due to the elongation of AL, mechanical stretching of the retinal pigment epithelium or Bruch's membrane in highly myopic eyes might introduce highly attenuated retinal and choroidal vasculature and impair macular functions.[27] High myopia was also associated with reduced vessel diameters at the retinal posterior pole and accelerated

Investigative Ophthalmology & Visual Science

capillary density loss.[4,28] Therefore, the presence of a cilioretinal artery may provide additional blood flow and oxygen to the macula,[29] resulting in potential preservation of macular functions.[12] However, previous evaluations based on VA assessment only partially assessed its effects on functional vision.[22] In this study, we revealed significantly better AULSCF and CSF acuity outcomes in highly myopic eyes with cilioretinal arteries, suggesting a role for the additional vasculature in the cilioretinal artery in protecting macular functions in high myopia. The results are consistent with those of Huber et al.,[30] who suggested that the increased retrobulbar blood flow and oxygen levels introduced by $CO_2$ breathing may result in improved contrast sensitivity.

The CSF has been shown to be better correlated with daily visual functions because it is necessary to identify objects of varying sizes and contrasts in daily life.[20] Although chart-based acuity tests, such as the ETDRS chart, are simple and can be quickly performed, they only provide very limited assessment of functional vision and do not have good correlations with the quality of subjective visual experience. In fact, subjective visual complaints are not uncommon even in highly myopic eyes with good BCVAs.[22] In the current study, we found no significant BCVA difference between highly myopic eyes with and without cilioretinal arteries, although a significant BCVA difference was found in our previous study.[13] The discrepancy might be caused by the smaller sample size in the current cross-sectional study. However, in situations where VA assessment revealed no significant effects, the higher sensitivity of qCSF may still make it possible to detect significant differences. The results suggest that the outcomes of the qCSF test explain the visual deficits and subjective complaints of highly myopic patients, especially those with pathologically affected macular functions but without VA disturbance. The qCSF test could become a routine examination for macular function evaluation in highly myopic patients.

Anatomical changes in fundus may have association with the functional performance. The cilioretinal artery, which originates from choroid, might also be affected by the thin choroid in highly myopic eyes. Here, we verified that SFCT was also significantly associated with AL, MMD, and the presence of a cilioretinal artery. Furthermore, we found reduced protection of CSF from the nasal-category cilioretinal artery, especially in intermediate spatial frequencies, which also verified the importance of increased macular vasculature from the cilioretinal artery emerging temporally. Diener et al.[31] also suggested that the temporal cilioretinal artery may increase vessel density in the peripapillary and macular superficial capillary plexus. In multivariable analyses of qCSF outcomes, the positive association between a cilioretinal artery and AULCSF was also confirmed. Also, more interestingly, the protective role of SFCT in preserving CSF might be more significant in extremely long eyes. Similarly, Shamsi et al.[32] reported an association between ganglion cell thickness and contrast sensitivity. Therefore, anatomical changes in the retina or choroid may play an important role in functional performance. The preservation of SFCT might be more beneficial in protecting macular functions, especially against the barren environment of extremely stretched eyeballs in extreme myopia. The results could help us to better estimate and explain macular function deficits in extremely myopic eyes.

In conclusion, the qCSF method is a more sensitive index for assessing the protective effects of cilioretinal artery on macular function in highly myopic eyes compared to VA assessment. It can provide important clinical evidence to explain subjective visual complaints and should be recommended as a routine functional examination for highly myopic eyes.

## Acknowledgments

Supported by research grants from the National Natural Science Foundation of China (82122017, 82271069, 81870642, 81970780, 81470613, and 81670835), Science and Technology Innovation Action Plan of Shanghai Science and Technology Commission (19441900700 and 21S31904900), Clinical Science and Technology Innovation Project of Shanghai Shenkang Hospital Development Center (SHDC12019x08 and SHDC2020CR4078), Double-E Plan of Eye and ENT Hospital (SYA202006), and Shanghai Municipal Key Clinical Specialty Program (shslczdzk01901).

Disclosure: **L. Wei**, None; **J. Meng**, None; **K. Cheng**, None; **W. He**, None; **J. Qi**, None; **Z.-L. Lu**, P, Adaptive Sensory Technology, Inc. (F); **Y. Lu**, None; **X. Zhu**, None

## References

1. Morgan IG, French AN, Ashby RS, et al. The epidemics of myopia: aetiology and prevention. *Prog Retin Eye Res*. 2018;62:134–149.
2. Saw SM, Matsumura S, Hoang QV. Prevention and management of myopia and myopic pathology. *Invest Ophthalmol Vis Sci*. 2019;60(2):488–499.
3. Devarajan K, Sim R, Chua J, et al. Optical coherence tomography angiography for the assessment of choroidal vasculature in high myopia. *Br J Ophthalmol*. 2020;104(7):917–923.
4. Lin F, Zhao Z, Li F, et al. Longitudinal macular retinal and choroidal microvasculature changes in high myopia. *Invest Ophthalmol Vis Sci*. 2021;62(15):1.
5. Justice J, Lehmann RP. Cilioretinal arteries. A study based on review of stereo fundus photographs and fluorescein angiographic findings. *Arch Ophthalmol*. 1976;94(8):1355–1358.
6. Liu L, Liu LM, Chen L. Incidence of cilioretinal arteries in Chinese Han population. *Int J Ophthalmol*. 2011;4(3):323–325.
7. Ohno-Matsui K, Akiba M, Ishibashi T, Moriyama M. Observations of vascular structures within and posterior to sclera in eyes with pathologic myopia by swept-source optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2012;53(11):7290–7298.
8. Kim DI, Yoon CK, Yu HG. Unilateral cilioretinal artery and advanced age-related macular degeneration: a retrospective cross-sectional study. *Am J Ophthalmol*. 2021;237:204–210.
9. Snyder K, Yazdanyar A, Mahajan A, Yiu G. Association between the cilioretinal artery and choroidal neovascularization in age-related macular degeneration: a secondary analysis from the Age-Related Eye Disease Study. *JAMA Ophthalmol*. 2018;136(9):1008–1014.
10. Ebraheem A, Uji A, Saleh Abdelfattah N, Gupta Nittala M, Sadda S, Le PV. Relationship between the presence of a cilioretinal artery and subretinal fluid in neovascular age-related macular degeneration. *Ophthalmol Retina*. 2018;2(5):469–474.
11. Watanabe T, Kasahara K, Futagami S, et al. Cilioretinal arteries and cilioretinal veins in eyes with pathologic myopia. *Sci Rep*. 2019;9(1):2451.
12. Meng J, Wei L, Zhang K, He W, Lu Y, Zhu X. Cilioretinal arteries in highly myopic eyes: a photographic classification system and its association with myopic macular degeneration. *Front Med (Lausanne)*. 2020;7:595544.
13. Zhu X, Meng J, Wei L, Zhang K, He W, Lu Y. Cilioretinal arteries and macular vasculature in highly myopic

eyes: an OCT angiography-based study. *Ophthalmol Retina*. 2020;4(10):965–972.
14. Marmor MF. Contrast sensitivity versus visual acuity in retinal disease. *Br J Ophthalmol*. 1986;70(7):553–559.
15. Richman J, Spaeth GL, Wirostko B. Contrast sensitivity basics and a critique of currently available tests. *J Cataract Refract Surg*. 2013;39(7):1100–1106.
16. Brussee T, van den Berg T, van Nispen RMA, de Boer I, van Rens G. Association between contrast sensitivity and reading with macular pathology. *Optom Vis Sci*. 2018;95(3):183–192.
17. Freeman EE, Muñoz B, Turano KA, West SK. Measures of visual function and time to driving cessation in older adults. *Optom Vis Sci*. 2005;82(8):765–773.
18. Zheng H, Wang C, Cui R, et al. Measuring the contrast sensitivity function using the qCSF method with 10 digits. *Transl Vis Sci Technol*. 2018;7(6):9.
19. Hou F, Huang CB, Lesmes L, et al. qCSF in clinical application: efficient characterization and classification of contrast sensitivity functions in amblyopia. *Invest Ophthalmol Vis Sci*. 2010;51(10):5365–5377.
20. Ou WC, Lesmes LA, Christie AH, Denlar RA, Csaky KG. Normal- and low-luminance automated quantitative contrast sensitivity assessment in eyes with age-related macular degeneration. *Am J Ophthalmol*. 2021;226:148–155.
21. Vingopoulos F, Wai KM, Katz R, Vavvas DG, Kim LA, Miller JB. Measuring the contrast sensitivity function in non-neovascular and neovascular age-related macular degeneration: the quantitative Contrast sensitivity function test. *J Clin Med*. 2021;10(13):2768.
22. Wai KM, Vingopoulos F, Garg I, et al. Contrast sensitivity function in patients with macular disease and good visual acuity. *Br J Ophthalmol*. 2022;106(6):839–844.
23. Ohno-Matsui K, Kawasaki R, Jonas JB, et al. International photographic classification and grading system for myopic maculopathy. *Am J Ophthalmol*. 2015;159(5):877–883.e7.
24. Zhou M, Wang W, Ding X, et al. Choroidal thickness in fellow eyes of patients with acute primary angle-closure measured by enhanced depth imaging spectral-domain optical coherence tomography. *Invest Ophthalmol Vis Sci*. 2013;54(3):1971–1978.
25. Berman H.B. Interaction effects in regression. Available at: https://stattrek.com/multiple-regression/interaction. Accessed October 25, 2022.
26. Lesmes LA, Lu ZL, Baek J, Albright TD. Bayesian adaptive estimation of the contrast sensitivity function: the quick CSF method. *J Vis*. 2010;10(3):17.1–21.
27. Leveziel N, Marillet S, Dufour Q, et al. Prevalence of macular complications related to myopia - results of a multicenter evaluation of myopic patients in eye clinics in France. *Acta Ophthalmol*. 2020;98(2):e245–e251.
28. Bailey ST. Does the cilioretinal artery preserve vision in high myopia? *Ophthalmol Retina*. 2020;4(10):963–964.
29. La Spina C, Corvi F, Bandello F, Querques G. Static characteristics and dynamic functionality of retinal vessels in longer eyes with or without pathologic myopia. *Graefes Arch Clin Exp Ophthalmol*. 2016;254(5):827–834.
30. Huber KK, Adams H, Remky A, Arend KO. Retrobulbar haemodynamics and contrast sensitivity improvements after $CO_2$ breathing. *Acta Ophthalmol Scand*. 2006;84(4):481–487.
31. Diener R, Leclaire MD, Eckardt F, et al. Cilioretinal arteries influence optic nerve head, peripapillary, and macular vessel densities in healthy eyes: an optical coherence tomography angiography study. *Retina*. 2021;41(11):2399–2406.
32. Shamsi F, Liu R, Owsley C, Kwon M. Identifying the retinal layers linked to human contrast sensitivity via deep learning. *Invest Ophthalmol Vis Sci*. 2022;63(2):27.