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ORIGINAL RESEARCH

The Characteristics of Quick Contrast Sensitivity Function in Keratoconus and Its Correlation with Corneal Topography

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ABSTRACT

Introduction: To characterize quick contrast sensitivity function (qCSF) in keratoconus and its correlation with corneal topographic parameters.

Methods: Patients with keratoconus (n = 120) who visited the Fudan Eye and ENT Hospital between April and June 2021 were enrolled in our study. A total of 215 eyes were subdivided into three groups according to maximum keratometry (K_{max}): Group 1 ($K_{max} \leq 48$ D, 74 eyes), Group 2 (48 D $< K_{max} \leq 55$ D, 64 eyes), and Group 3 ($K_{max} > 55$ D, 77 eyes). Manifest refraction, best corrected distance visual acuity (BCVA), corneal topography, and the qCSF test were examined. Intergroup comparisons and correlations among various corneal topographic parameters and qCSF were analyzed.

Results: Significant differences in the area under the log CSF (AULCSF) and CSF Acuity among the three groups were found, which decreased with an increase in K_{max}. Contrast sensitivity (CS) between spatial frequencies of 3.0 to 18.0 cpd was significantly different (all $P < 0.05$) between Groups 1 and 2. The CS at all spatial frequencies was significantly different (all $P < 0.05$) between Group 3 and other two groups. At 3.0–18.0 cpd, CS decreased significantly (all $P < 0.05$) in Groups 1–3. Manifest

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refraction and topographic indices correlated significantly with qCSF parameters (all $P < 0.05$). Multivariable linear regression analysis showed that cylindrical refraction, logMAR BCVA, and index of surface variance had good predictive values for AULCSF and CSF Acuity.
Conclusions: The use of qCSF test can serve as a feasible tool to evaluate visual quality and severity of keratoconus, since changes in CS significantly correlated with keratoconus severity.

Keywords: Contrast sensitivity; Corneal topography; Keratoconus; Photokeratoscopy; Quick CSF

Key Summary Points
Why carry out this study?
Keratoconus is a corneal ectatic disease characterized by decreased corneal thickness, corneal protrusion, and increased irregular astigmatism.
Visual acuity and manifest refraction are insufficient to reflect the visual quality of keratoconus.
The quick contrast sensitivity function (qCSF) test can comprehensively evaluate different contrast sensitivities under a series of spatial frequencies.
What was learned from the study?
The changes of contrast sensitivity were significantly correlated with the severity of keratoconus.
The qCSF test can serve as a feasible tool to evaluate the visual quality and severity of keratoconus.

INTRODUCTION

Keratoconus (KC) is a corneal ectatic disease characterized by decreased corneal thickness, corneal protrusion, and increased irregular astigmatism, resulting in corneal edema, and scarring at the late stage. The prevalence of keratoconus is approximately 1 in 2000 patients, who can suffer from irreversible damage of visual function [1]. In early keratoconus, photokeratoscopy or corneal topography can be used to detect abnormal corneal morphology, including increased corneal curvature, front and back elevations, and irregular astigmatism [2].

Visual acuity (VA) is the most commonly used and basic index to evaluate ophthalmic disease; however, it merely represents the best spatial frequencies that humans can distinguish under high contrast ratio, which is insufficient to assess the spatial visual function of the human eye and reflect the patients' subjective perception. For example, some patients with early keratoconus may complain of visual blur or distortion, yet their best corrected distance visual acuity (BCVA) can remain normal. In fact, their visual function cannot meet the needs of daily life, and manifest refraction outcomes may fluctuate significantly because of irregular corneal astigmatism.

The contrast sensitivity (CS) test can comprehensively evaluate the ability of the human eye to distinguish between different contrast ratios under a series of spatial frequencies. The quick contrast sensitivity function (qCSF) test is a novel method developed by Lesmes et al. [3] for assessing CS. Compared to conventional methods such as the Pelli–Robson chart and CVS-1000 series chart, the qCSF test utilizes the Bayesian adaptive test strategy as the optimization algorithm and the 10-digit identification task to obtain a faster testing speed, good accuracy, and high test–retest reliability that has been clinically validated [4–6].

We believe that evaluating the visual quality of keratoconus with qCSF parameters would theoretically be more accurate and objective. To date, the application of qCSF in keratoconus has not been reported, and the distribution characteristics of qCSF in keratoconus are unclear. Moreover, the correlation between CS of keratoconus and commonly used methods, such as VA and corneal topography, is worth studying. Therefore, this study aimed to explore the

characteristics of qCSF and analyze the relationship between qCSF and the corneal topographic features of keratoconus, thus providing new perspectives for monitoring the progress of keratoconus and therapeutic strategies in clinical practice.

METHODS

Patients

This cross-sectional study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committee of the Eye and ENT Hospital of Fudan University (ky2012-017). Informed consent was obtained from all patients.

The inclusion criterion was diagnosis of keratoconus without corneal cross-linking or keratoplasty.

Exclusion criteria were history of other eye diseases (such as glaucoma, cataract, and macular degeneration), history of eye surgery, history of systemic diseases (such as hypertension, diabetes, and connective tissue disease), pregnancy, and inability to cooperate with the examination.

This study included consecutive patients with keratoconus who visited the Eye and ENT Hospital of Fudan University from April to June 2021. Keratoconus eyes of the included participants were classified into three groups according to the maximum curvature of the anterior corneal surface (K_{max}): Group 1 ($K_{max} \leq 48$ D), Group 2 ($48\ \text{D} < K_{max} \leq 55\ \text{D}$), and Group 3 ($K_{max} > 55$ D).

Examinations

The following examinations were performed and parameters were assessed: (1) subjective refraction: the patient's spherical diopter, cylindrical diopter, cylindrical axis, and BCVA were examined by an experienced optometrist; (2) corneal topography by the Pentacam HR (Oculus Optikgerate Wetzlar, Germany) was used to assess the following: flat keratometry (K1), steep keratometry (K2), mean keratometry (K_{mean}), K_{max} of the anterior corneal surface, the index of surface variance (ISV), index of vertical asymmetry (IVA), keratoconus index (KI), central keratoconus index (CKI), index of highest asymmetry (IHA), index of highest dencentralization (IHD), minimum sagittal curvature (RsagMin), thinnest pachymetry (TCT), front elevation of the thinnest point (FETh), and back elevation of the thinnest point (BETh).

Contrast Sensitivity Test

The qCSF test was conducted in a mesopic environment at a test distance of 3 m while the participants wore spectacles for the best distance correction. The display used in the test was an NEC P403 monitor (Gension & Waltai Digital Video System Co. Ltd. China), size 116.84×77.89 cm, resolution 1920×1080 pixels, maximum brightness 700 cd/m^2. The standard brightness in the test was 550 cd/m^2 and the contrast ratio was 4000:1. Ten digits filtered by a raised cosine filter were used as the test stimuli in a 10-alternative forced choice identification task (10AFC) [6, 7], and the spatial frequencies were between 1.4 and 36.2 cpd. In each trial, three filtered digits of the same size but of successively lower contrast ratios were displayed on the screen; the participants were required to report the number they saw or that they could not see it clearly. The technician then entered the corresponding results on a tablet computer. Only one eye was tested at a time and the contralateral eye was covered with an eye patch. After 25 trials, the area under log CSF (AULCSF), cutoff spatial frequencies (CSF Acuity), and log contrast sensitivity (log CS) at spatial frequencies of 1.0, 1.5, 3.0, 6.0, 12.0, and 18.0 cpd would be automatically calculated by the software.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS v26.0, IBM Corp., Armonk, NY, USA) was used for statistical analysis. Descriptive analysis (mean ± standard error) was used to display the baseline and qCSF values for the different groups. To adjust for interocular correlation, the

generalized estimating equation (GEE) models were used to test the differences in baseline parameters and qCSF among the three groups, and to examine the differences among all qCSF values for each group, in which the sequential Šidák was the post hoc test. Pearson's correlations were used to determine the relationship between qCSF values and other variables. Multivariable linear regression with the forward stepwise method was used to predict the qCSF parameters, and variables with $P > 0.1$ were excluded.

RESULTS

Demographic Data

Participants' age, subjective refraction, BCVA, and corneal topographic parameters are shown in Table 1. This study included 215 keratoconus eyes of 120 patients (average age 23.22 ± 6.67 years, range 8–41 years), with 74 eyes in Group 1 ($K_{max} \leq 48$ D), 64 eyes in Group 2 (48 D $< K_{max} \leq 55$ D), and 77 eyes in Group 3 ($K_{max} > 55$ D). Except for age, the other parameters were significantly different among the three groups ($P < 0.01$).

Characteristics of qCSF Distribution

Table 2 shows the qCSF results for the three groups. There were significant differences in AULCSF and CSF Acuity among the three groups ($P < 0.001$), the values of which decreased with the severity of keratoconus (Fig. 1a, b).

Intergroup comparison (Table 2) showed that the CS at low spatial frequencies (1.0 and 1.5 cpd) was significantly lower in severe keratoconus (Group 3) than in mild and moderate keratoconus (Group 1, Group 2) ($P < 0.05$). The CS at medium and high spatial frequencies (3.0–18.0 cpd) decreased with the severity of keratoconus ($P < 0.05$).

Intragroup comparisons (Fig. 1c) revealed that CS showed a downward trend with an increase in spatial frequency, in which CS of the three groups decreased significantly from 3.0 cpd (all $P < 0.05$). In severe keratoconus (Group 3), CS at 12.0 cpd was not significantly different from that at 18.0 cpd ($P > 0.05$).

Correlation Analysis

Correlation analysis between various parameters is represented in Table 3. There was no correlation between age and qCSF parameters ($P > 0.05$), nor between IHA and CS at 18.0 cpd ($P > 0.05$). Other parameters were significantly correlated with qCSF parameters ($P < 0.05$). Figure 2 shows the correlations between the various parameters and qCSF.

Multivariable Linear Regression Analysis

Table 4 shows the predictors of qCSF parameters analyzed using multivariable linear regression. In terms of predicting AULCSF and CSF Acuity, the regression equation composed of Cyl, logMAR BCVA, and ISV obtained an adjusted R^2 of 0.585 and 0.529, respectively. The results showed that BCVA and irregularity of the cornea had a relatively strong predictive value for qCSF. However, the goodness of fit was low in predicting CS at 12.0 and 18.0 cpd (adjusted R^2 = 0.311 and 0.104).

DISCUSSION

Keratoconus can cause irregular corneal astigmatism and impair visual function. Although some patients with keratoconus may have a normal BCVA, some still complain of blurred vision, indicating that the abnormal visual performance of keratoconus requires a more comprehensive and accurate evaluation. In 2010, Lesmes et al. introduced the qCSF method [3]. Traditional CS tests, such as the Pelli–Robson chart, use coarse quantization and sampling, and are limited to a fixed spatial frequency [8], while the qCSF test can identify and measure disproportionate reductions in CS at specific spatial frequencies through depicting a complete CSF curve. The qCSF has been applied to measure CSF in several clinical populations, including amblyopia [9], multiple

Table 1 Baseline situation among three groups

Variables	Overall (N = 215)	Group 1 (N = 74)	Group 2 (N = 64)	Group 3 (N = 77)	Wald chi-square*	P*
Age (years)	23.22 ± 6.67	23.85 ± 6.51	22.75 ± 6.93	23.00 ± 6.63	1.041	0.594
Sph (D)	− 4.43 ± 3.66	− 3.72 ± 3.16[b]	− 3.61 ± 2.90[c]	− 5.80 ± 4.27[bc]	14.269	**0.001**
Cyl (D)	− 2.84 ± 2.56	− 1.60 ± 1.76[ab]	− 3.01 ± 2.01[ac]	− 3.89 ± 3.05[bc]	27.555	< **0.001**
SE (D)	− 5.83 ± 4.21	− 4.51 ± 3.33[b]	− 5.07 ± 3.19[c]	− 7.73 ± 4.99[bc]	20.348	< **0.001**
logMAR BCVA	0.23 ± 0.24	0.06 ± 0.13[ab]	0.19 ± 0.18[ac]	0.42 ± 0.23[bc]	123.423	< **0.001**
Corneal keratometry, pachymetry, and elevations						
K1 (D)	45.1 ± 4.61	41.57 ± 2.06[ab]	43.98 ± 1.73[ac]	49.40 ± 4.62[bc]	200.425	< **0.001**
K2 (D)	47.89 ± 5.32	43.01 ± 2.06[ab]	47.10 ± 2.03[ac]	53.24 ± 4.41[bc]	302.396	< **0.001**
K_{mean} (D)	46.44 ± 4.87	42.27 ± 2.01[ab]	45.48 ± 1.74[ac]	51.23 ± 4.40[bc]	297.480	< **0.001**
K_{max} (D)	53.68 ± 9.31	44.92 ± 1.58[ab]	51.33 ± 2.17[ac]	64.06 ± 7.03[bc]	978.938	< **0.001**
TCT (μm)	470.87 ± 51.94	507.97 ± 43.14[ab]	473.91 ± 38.9[ac]	432.69 ± 41.58[bc]	104.312	< **0.001**
FETh (μm)	18.73 ± 17.19	3.74 ± 4.52[ab]	15.56 ± 7.36[ac]	35.75 ± 15.71[bc]	317.570	< **0.001**
BETh (μm)	43.39 ± 34.36	12.36 ± 10.68[ab]	37.25 ± 14.48[ac]	78.30 ± 28.93[bc]	366.493	< **0.001**
Topographic indices						
ISV	72.11 ± 47.17	29.16 ± 14.35[ab]	59.14 ± 21.78[ac]	124.16 ± 31.52[bc]	564.678	< **0.001**
IVA	0.74 ± 0.53	0.29 ± 0.22[ab]	0.64 ± 0.35[ac]	1.25 ± 0.42[bc]	314.999	< **0.001**
KI	1.18 ± 0.16	1.05 ± 0.05[ab]	1.14 ± 0.08[ac]	1.35 ± 0.13[bc]	324.077	< **0.001**
CKI	1.06 ± 0.07	1.01 ± 0.01[ab]	1.03 ± 0.03[ac]	1.13 ± 0.07[bc]	307.922	< **0.001**
IHA	22.95 ± 21.84	11.01 ± 8.60[ab]	22.86 ± 19.83[ac]	34.49 ± 25.94[bc]	83.418	< **0.001**
IHD	0.10 ± 0.08	0.03 ± 0.02[ab]	0.08 ± 0.04[ac]	0.19 ± 0.07[bc]	396.245	< **0.001**
RSagMin	6.46 ± 1.00	7.52 ± 0.26[ab]	6.59 ± 0.28[ac]	5.33 ± 0.53[bc]	1216.286	< **0.001**

N number of eyes, *Sph* spherical refraction, *Cyl* cylindrical refraction, *SE* spherical equivalent, *logMAR BCVA* best corrected distance visual acuity (logMAR), *K1* flattest meridian keratometry, *K2* steepest meridian keratometry, K_{mean} mean keratometry, K_{max} maximum keratometry, *TCT* thinnest corneal thickness, *FETh* front elevation of the thinnest point, *BETh* back elevation of the thinnest point, *ISV* the index of surface variance, *IVA* index of vertical asymmetry, *KI* keratoconus index, *CKI* central keratoconus index, *IHA* index of highest asymmetry, *IHD* index of highest decentration, *RSagMin* minimum sagittal curvature, *D* diopter, *μm* micron

Bold indicates significant differences among the three groups ($p < 0.05$)

*Analyzed by the generalized estimating equation model

[a,b,c]Significant differences ($p < 0.05$) between Group 1 and Group 2, Group 1 and Group 3, and Group 2 and Group 3, respectively, in the pairwise comparison

sclerosis [10], glaucoma [11], early diabetic retinopathy [12], and aging [13] with great test–retest reliability and high sensitivity in detecting subtle changes in visual function [4, 5]. The present study is the first to report on qCSF in keratoconus.

Table 2 qCSF values among three groups

Variables	Group 1 (N = 74)	Group 2 (N = 64)	Group 3 (N = 77)	Wald chi-square*	P*
AULCSF	0.77 ± 0.34[ab]	0.59 ± 0.29[ac]	0.21 ± 0.19[bc]	171.182	< **0.001**
CSF Acuity	14.2 ± 6.61[ab]	10.42 ± 5.18[ac]	4.65 ± 2.55[bc]	154.729	< **0.001**
CS (1.0 cpd)	1.16 ± 0.28[b]	1.11 ± 0.27[c]	0.67 ± 0.38[bc]	86.384	< **0.001**
CS (1.5 cpd)	1.15 ± 0.31[b]	1.08 ± 0.27[c]	0.60 ± 0.38[bc]	95.898	< **0.001**
CS (3.0 cpd)	1.02 ± 0.38[ab]	0.87 ± 0.35[ac]	0.33 ± 0.32[bc]	158.037	< **0.001**
CS (6.0 cpd)	0.72 ± 0.42[ab]	0.46 ± 0.38[ac]	0.08 ± 0.19[bc]	159.585	< **0.001**
CS (12.0 cpd)	0.27 ± 0.29[ab]	0.11 ± 0.19[ac]	0.00 ± 0.02[bc]	69.315	< **0.001**
CS (18.0 cpd)	0.06 ± 0.13[ab]	0.02 ± 0.05[ac]	0.00 ± 0.00[bc]	21.206	< **0.001**

N number of eyes, *qCSF* quick contrast sensitivity function, *AULCSF* area under log CSF, *CSF Acuity* cutoff spatial frequencies of CSF, *CS* contrast sensitivity, *cpd* cycle per degree

Bold indicates significant differences among the three groups ($p < 0.05$)

*Analyzed by the generalized estimating equation model

[a,b,c]Significant differences ($p < 0.05$) between Group 1 and Group 2, Group 1 and Group 3, and Group 2 and Group 3, respectively, in the pairwise comparison

Early screening and assessment of visual abnormalities in keratoconus are important for detecting the progression of keratoconus and making therapeutic decisions. This study showed that AULCSF and CSF Acuity significantly decreased with keratoconus severity. Our findings showed that the decrease in CS was significantly correlated with an increase in irregular corneal astigmatism in keratoconus. The BCVA also decreased with the severity of keratoconus, which was consistent with AULCSF and CSF Acuity. In clinical practice, VA is currently considered the gold standard for evaluating the visual function of patients, and ophthalmologists routinely examine the patient's subjective refraction to evaluate the impact of keratoconus on visual function. However, with an increase in disease severity, irregular corneal astigmatism leads to increased examination time and decreased credibility of the VA test, as it is difficult for patients to recognize optotypes. Therefore, VA may not be ideal for assessing patients with keratoconus. Previous studies indicated that CS seems to correlate better with subjective visual impairment and vision-related quality of life compared to VA [14–17], and may detect more subtle changes in visual function [14]. The time for test completion is 2–5 min per eye [3], which is easy for patients to cooperate with. Thus, qCSF may be a promising visual function endpoint for patients with keratoconus.

The qCSF test presents patients with spatially filtered optotypes that modify both spatial frequency and contrast, in order to efficiently estimate CSF across multiple spatial frequencies in parallel [18]. Patients may have CSF impairments even when their VA seems normal, suggesting that the CSF is more sensitive than letter acuity in identifying spatial vision deficits [19]. This study showed that the CS at low spatial frequencies (1.0 and 1.5 cpd) was not significantly different between mild and moderate keratoconus, but that of the two groups was significantly different from that of severe keratoconus. The CS at medium and high spatial frequencies (3.0–18.0 cpd) was significantly different among the three groups (Table 2). The results indicated that the severity of keratoconus could be detected by CS at different spatial frequencies, and that the impairment of CS at a lower spatial frequency suggests a more

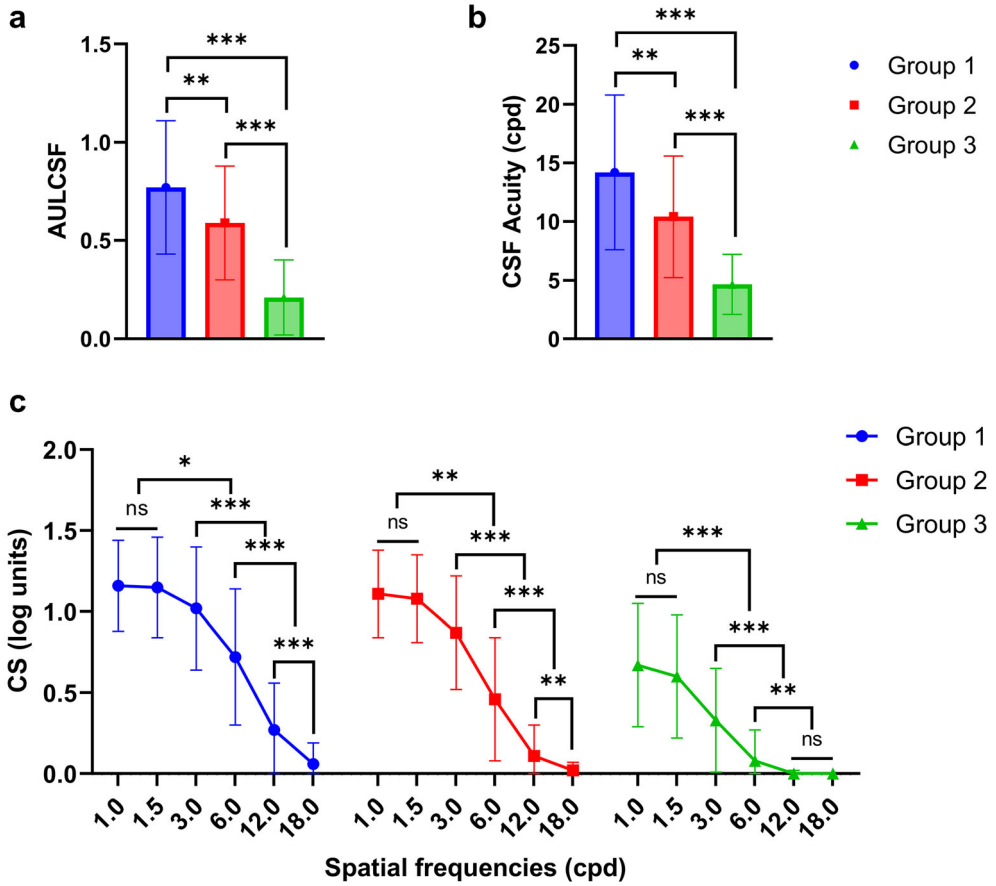

Fig. 1 Characteristics of quick contrast sensitivity function (qCSF) in keratoconus of different severities. **a** AULCSF and **b** CSF Acuity among the three groups, and significant differences were found ($P < 0.05$). **c** Distribution of contrast sensitivity (log units) at different spatial frequencies (cpd) in the three groups. *AULCSF* area under the log contrast sensitivity function, *CS* contrast sensitivity, *cpd* cycle per degree. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$

severe stage of keratoconus. In patients with the same BCVA or unreliable visual outcomes, CS at different spatial frequencies through the qCSF test can help identify the impact of keratoconus on visual functions.

Furthermore, the results of this study showed that the CS in the three groups of keratoconus decreased significantly by 3.0 cpd (Fig. 1c). In normal eyes, the CS appeared to decrease significantly by 6.0 cpd [12, 13], which was different from that in keratoconus as shown in our study. A previous study showed that a CS threshold of 6.0 cpd was closely correlated with patient's ability to identify traffic signs and objects, reflecting the visual function in daily life [3]. When compared to VA, the CSF appears to have a better correlation with everyday activities, like mobility [20], target and face recognition [21], driving [22], walking [23], and reading [24]; and subjectively perceived visual impairment [25]. This study indicated that even in patients with mild keratoconus and relatively good BCVA, the damaged visual functions would significantly affect activities of daily living. Thus, this study provides clues regarding the importance of early diagnosis and intensive monitoring of keratoconus. And the qCSF test would be a more valuable addition to the guidelines for clinical judgement on initiating and evaluating therapeutic interventions, especially in early keratoconus with an apparent decrease in VA yet impaired visual function.

Table 3 Correlation between qCSF values and other variables

Variables	AULCSF	CSF Acuity	CS (1.0 cpd)	CS (1.5 cpd)	CS (3.0 cpd)	CS (6.0 cpd)	CS (12.0 cpd)	CS (18.0 cpd)
Age (years)	− 0.019	− 0.03	− 0.05	− 0.05	− 0.00	− 0.03	− 0.02	− 0.01
Sph (D)	0.28**	0.28**	0.27**	0.29**	0.30**	0.23**	0.20**	0.15*
Cyl (D)	0.45**	0.47**	0.30**	0.33**	0.42**	0.47**	0.38**	0.22**
SE (D)	0.38**	0.38**	0.33**	0.35**	0.38**	0.34**	0.30**	0.19**
logMAR BCVA	**− 0.69****	**− 0.66****	**− 0.60****	**− 0.65****	**− 0.69****	**− 0.66****	− 0.48**	− 0.29**
Corneal keratometry, pachymetry, and elevations								
K1 (D)	**− 0.50****	− 0.46**	**− 0.50****	**− 0.52****	**− 0.51****	− 0.44**	− 0.34**	− 0.21**
K2 (D)	**− 0.58****	**− 0.55****	**− 0.54****	**− 0.56****	**− 0.58****	**− 0.54****	− 0.41**	− 0.25**
K_{mean} (D)	**− 0.55****	**− 0.51****	**− 0.53****	**− 0.55****	**− 0.56****	**− 0.50****	− 0.38**	− 0.23**
K_{max} (D)	**− 0.65****	**− 0.60****	**− 0.60****	**− 0.63****	**− 0.66****	**− 0.60****	− 0.45**	− 0.27**
TCT (μm)	0.46**	0.43**	0.42**	0.43**	0.45**	0.44**	0.32**	0.26**
FETh (μm)	**− 0.60****	**− 0.56****	**− 0.53****	**− 0.56****	**− 0.61****	**− 0.56****	− 0.42**	− 0.25**
BETh (μm)	**− 0.63****	**− 0.59****	**− 0.59****	**− 0.61****	**− 0.64****	**− 0.59****	− 0.44**	− 0.26**
Topographic indices								
ISV	**− 0.69****	**− 0.64****	**− 0.65****	**− 0.67****	**− 0.69****	**− 0.64****	− 0.48**	− 0.29**
IVA	**− 0.61****	**− 0.56****	**− 0.56****	**− 0.59****	**− 0.61****	**− 0.58****	− 0.44**	− 0.27**
KI	**− 0.62****	**− 0.57****	**− 0.61****	**− 0.62****	**− 0.63****	**− 0.57****	− 0.42**	− 0.24**
CKI	**− 0.62****	**− 0.57****	**− 0.58****	**− 0.61****	**− 0.65****	**− 0.56****	− 0.40**	− 0.24**
IHA	− 0.30**	− 0.28**	− 0.29**	− 0.29**	− 0.30**	− 0.28**	-0.21**	− 0.12
IHD	**− 0.63****	**− 0.58****	**− 0.59****	**− 0.62****	**− 0.64****	**− 0.59****	-0.44**	− 0.26**
RSagMin	**0.67****	**0.64****	**0.59****	**0.61****	**0.67****	**0.64****	**0.50****	0.31**

Bold fonts: absolute values of Pearson correlation coefficients ≥ 0.5

N number of eyes, *Sph* spherical refraction, *Cyl* cylindrical refraction, *SE* spherical equivalent, *logMAR BCVA* best corrected distance visual acuity (logMAR), *K1* flattest meridian keratometry, *K2* steepest meridian keratometry, Kmean mean keratometry, K_{max} maximum keratometry, *TCT* thinnest corneal thickness, *FETh* front elevation of the thinnest point, *BETh* back elevation of the thinnest point, *ISV* index of surface variance, *IVA* index of vertical asymmetry, *KI* keratoconus index, *CKI* central keratoconus index, *IHA* index of highest asymmetry, *IHD* index of highest decentration, *RSagMin* minimum sagittal curvature, *D* diopter, *μm* micron, *qCSF* quick contrast sensitivity function, *AULCSF* area under log CSF, *CSF Acuity* cutoff spatial frequencies of CSF, *CS* contrast sensitivity, *cpd* cycle per degree

*$p < 0.05$; **$p < 0.01$

This study showed that topographical indices were correlated with qCSF parameters; ISV, IVA, KI, CKI, IHA, and IHD were negatively correlated, and RSagMin was positively correlated with qCSF parameters, which indicated that qCSF parameters decreased with corneal irregularity. This proves that qCSF is closely correlated with corneal morphological

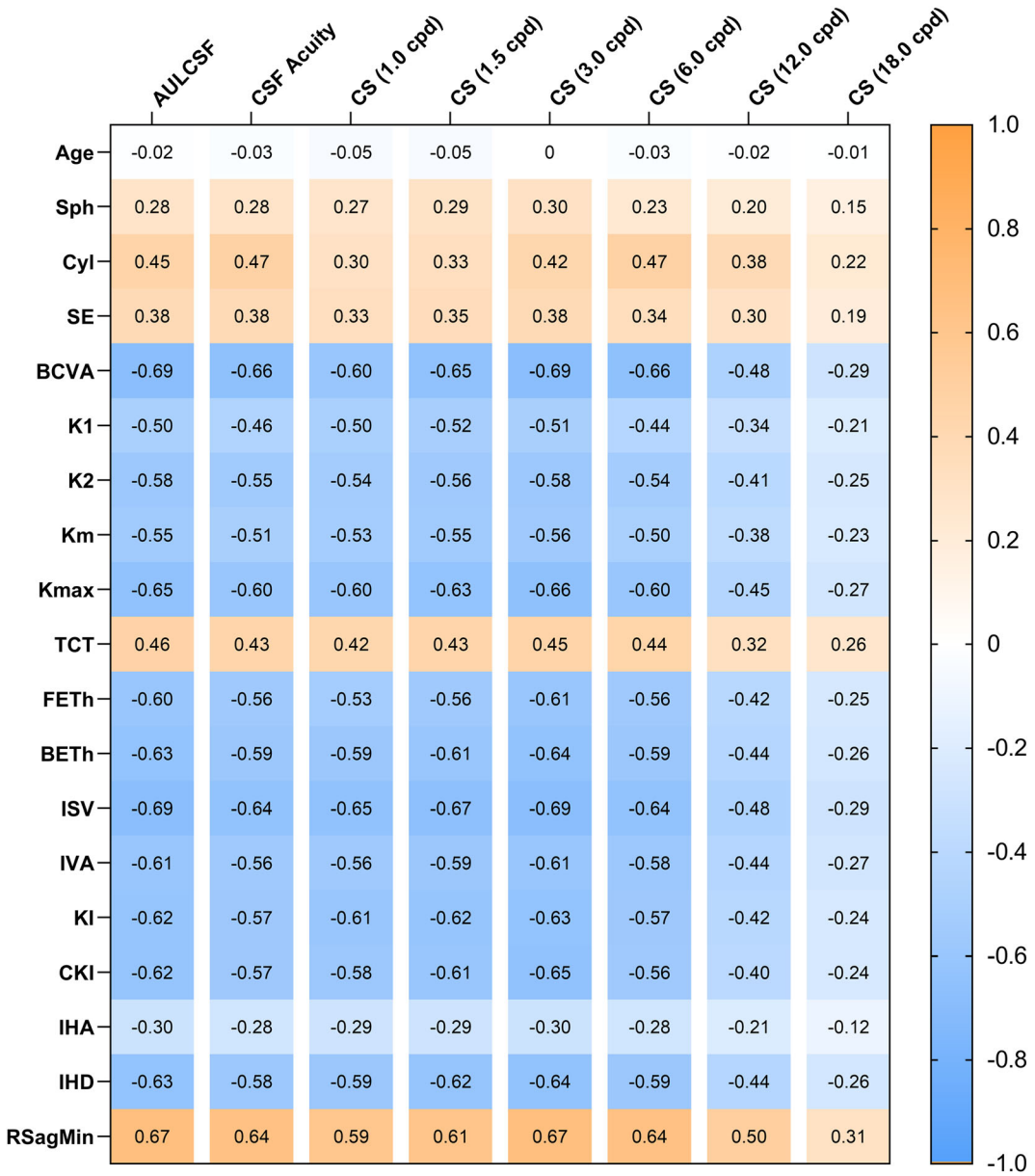

Fig. 2 Correlation between age, refraction, corneal topography, and quick contrast sensitivity function (qCSF). Each cell depicts the relationship between the corresponding parameters and the correlation coefficients. *Sph* spherical refraction, *Cyl* cylindrical refraction, *SE* spherical equivalent, *BCVA* best corrected distance visual acuity (logMAR), *K1* flattest meridian keratometry, *K2* steepest meridian keratometry, *Km* mean keratometry, K_{max} maximum keratometry, *TCT* thinnest corneal thickness, *FETh* front elevation of the thinnest point, *BETh* back elevation of the thinnest point, *ISV* index of surface variance, *IVA* index of vertical asymmetry, *KI* keratoconus index, *CKI* central keratoconus index, *IHA* index of highest asymmetry, *IHD* index of highest decentration, *RSagMin* minimum sagittal curvature, *AULCSF* area under log CSF, *CSF* Acuity cutoff spatial frequencies of CSF, *CS* contrast sensitivity, *cpd* cycle per degree

changes and the development of keratoconus, and qCSF could also be applied to evaluate the clinical outcomes and visual quality after corneal collagen cross-linking (CXL). It has been

Table 4 Multivariable linear regressions for qCSF values

Predictive variables	AULCSF		CSF Acuity		CS (1.0 cpd)		CS (1.5 cpd)	
	β	*P*	*β*	*P*	*β*	*P*	*β*	*P*
Intercept	0.935	< 0.001	16.666	< 0.001	1.358	< 0.001	1.355	< 0.001
Cyl	0.02	0.021	0.51	0.001				
logMAR BCVA	− 0.596	< 0.001	− 9.949	< 0.001	− 0.484	< 0.001	− 0.628	< 0.001
ISV	− 0.003	< 0.001	− 0.047	< 0.001	− 0.004	< 0.001	− 0.004	< 0.001
Adjust R^2	0.585		0.529		0.458		0.516	
Predictive variables	**CS (3.0 cpd)**		**CS (6.0 cpd)**		**CS (12.0 cpd)**		**CS (18.0 cpd)**	
	β	*P*	*β*	*P*	*β*	*P*	*β*	*P*
Intercept	2.637	< 0.001	0.887	< 0.001	− 0.234	< 0.001	− 0.072	0.173
Cyl			0.034	0.001	0.02	0.004		
logMAR BCVA	− 0.798	< 0.001	− 0.651	< 0.001	− 0.183	0.024	− 0.064	0.049
ISV	− 0.003	0.001	− 0.003	< 0.001				
CKI	− 1.45	0.009						
RSagMin					0.07	< 0.001	− 0.017	0.018
Adjust R^2	0.584		0.534		0.311		0.104	

Cyl cylindrical refraction, *logMAR BCVA* best corrected distance visual acuity (logMAR), *ISV* index of surface variance, *CKI* central keratoconus index, *RSagMin* minimum sagittal curvature, *AULCSF* area under log CSF, *CSF Acuity* cutoff spatial frequencies of CSF, *CS* contrast sensitivity, *cpd* cycle per degree, *β* coefficient, R^2 coefficient of determination

reported that the steepness and irregularity of corneas would decrease after CXL, while there may be no significant changes in the corneal curvature or VA, especially after transepithelial CXL [26, 27]. Therefore, researchers are still looking for a more sensitive index that can better reflect the effect of CXL. Previous studies have shown qCSF to be highly sensitive [4], and our findings indicate that it is highly correlated with ISV and IHD. Hence, we assume that the qCSF parameters may be improved when corneal irregularity decreases after CXL. Future studies are needed to clarify this assumption.

Additionally, our findings show that the correlation between IHA and qCSF was weaker than that between ISV, IVA, KI, and CKI. Possible reasons may be the relatively low sensitivity and specificity of IHA for classifying keratoconus [28, 29]; thus, the intergroup differences of IHA were less than those of other topographic indices. In this study, manifest refraction positively correlated with qCSF; the closer the refractive error is to emmetropia, the larger the qCSF parameter, which also indicates a correlation between CS and disease severity. However, the degree of correlation between refraction and qCSF was less than that of corneal asymmetric indices, which may be due to the influence of corneal irregular astigmatism and optometric errors on the accuracy of subjective refraction in patients with keratoconus.

In the multivariable linear regressions, the cylindrical refraction, BCVA, and ISV were the major predictors for qCSF parameters (Table 4). The ISV is the standard deviation of the axial radii of the eye from the mean anterior corneal curvature, and represents the irregularity of anterior corneal curvature [30]. Our findings manifested the significant influence of corneal irregularity on visual function, which was in

accordance with previous studies [31, 32]. However, the correlations between CS at high spatial frequencies (12.0 and 18.0 cpd) and other parameters were relatively weak (Table 3) and the goodness of fit of corresponding regression models was low (Table 4). The reason may be that it was difficult for patients to recognize the visual stimuli at high spatial frequencies because of visual impairments. Therefore, the CS at low and medium spatial frequencies (1.0–6.0 cpd) would be more accurate and valuable in assessing the visual function in keratoconus. Besides, the axial length, which may influence contrast sensitivity function [33], was not included as a parameter in the study. However, the correlation between axial length and severity of keratoconus was insignificant as reported by previous studies [34, 35], and thus it may not have a significant impact on the multivariable regression models for qCSF parameters. Overall, our findings indicate that the qCSF parameters, which reflect both visual acuity and corneal irregularity, are an appropriate indicator of visual function in keratoconus.

This study had some limitations. First, the sample size was small, which may have affected statistical efficacy. Therefore, we will continue to enroll more patients for further analysis. Second, this study compared the qCSF characteristics of patients with different degrees of keratoconus but did not include a normal control group. Compared with previous studies in the normal population, qCSF seemed to decrease in keratoconus [10, 36]. However, it cannot be compared directly as contrast sensitivity is correlated with age and refraction [13, 37]. Normal controls should be included in further studies to confirm changes in qCSF in keratoconus at early stage and provide reference to the clinical application of qCSF test in screening keratoconus.

CONCLUSION

This study shows that changes in contrast sensitivity in keratoconus are significantly correlated with disease severity, and qCSF can serve as a feasible tool to assess the visual quality and severity of keratoconus.

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recommendations of tenets of the Declaration of Helsinki with written informed consent from all subjects. All subjects gave written informed consent in accordance with the Declaration of Helsinki. The protocol was approved by the Ethics Committee of Fudan University Eye and ENT Hospital Review Board (Shanghai, China) (ky2012-017).

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