無虹彩症（aniridia） 診断基準

概念

PAX6 遺伝子変異により胎生期に虹彩がほとんど形成されず虹彩欠損を呈する疾患

主要所見

１．虹彩欠損

部分的から完全まで様々な程度の先天的虹彩欠損。通常両眼性で程度より羞明を訴える。

さらに、以下の眼合併症を認め、視力低下を呈することがある。

２．黄斑低形成

３．緑内障

４．白内障

５．小眼球

６．眼球振盪症

７．角膜輪部疲弊症や角膜混濁などの角膜症

除外

１．ICE（iridocorneal endothelial、虹彩角膜内皮）症候群

２．外傷後または眼内手術後虹彩欠損

留意点

１．遺伝子異常

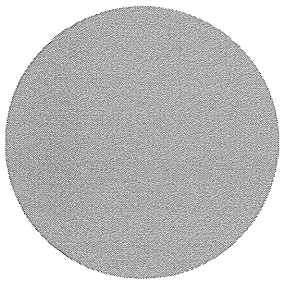
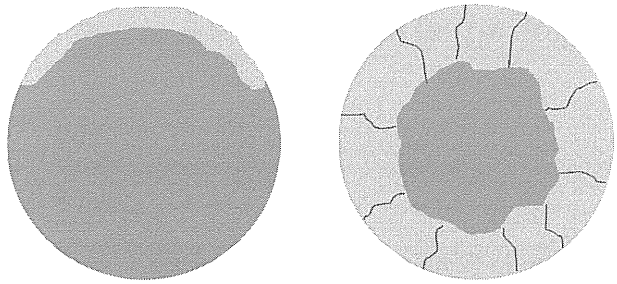
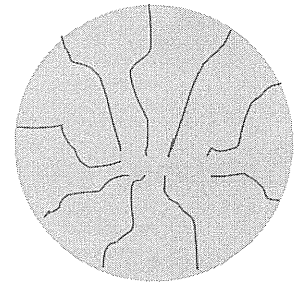
11 番染色体遺伝子短腕に存在する転写因子 PAX6 遺伝子変異により生じる。常染色体優性遺伝、劣性遺伝、散発性などの遺伝形式をとる。

２．全身合併症

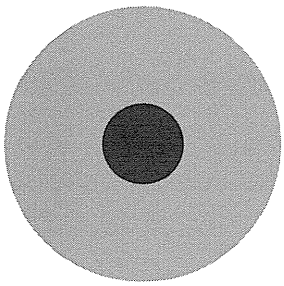
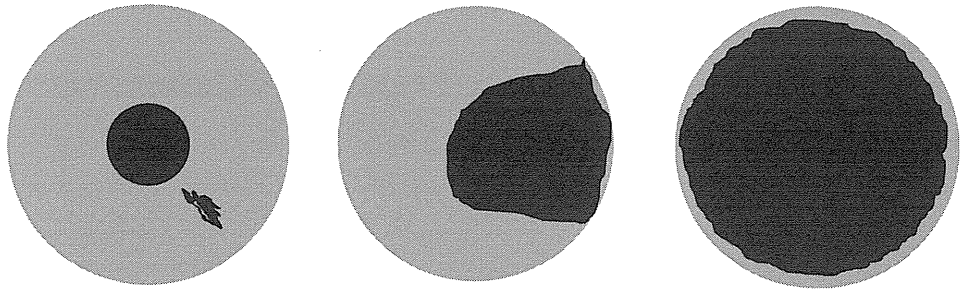
PAX6 遺伝子の隣接遺伝子症候群として Wilms 腫瘍など合併する（WAGR 症候群）ことがある。PAX6 遺伝子は神経外胚葉の発達に関与するため、脳形成不全などの脳神経異常を合併することがある。

無虹彩症（aniridia） 重症度分類

角膜病変

Grade 0	Grade 1	Grade 2
結膜上皮の侵入を認めない	結膜上皮の侵入を認めるが、角膜上皮が残存する	結膜上皮が角膜全体を覆う
		

虹彩病変

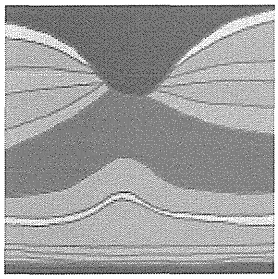
Grade 0	Grade 1
虹彩の欠損を認めない	虹彩の欠損を認める
	

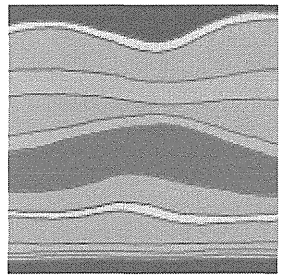
隅角形成不全

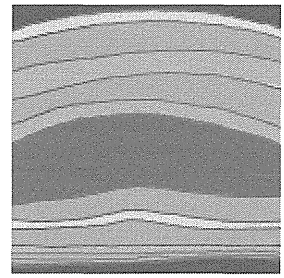
Grade 0	Grade 1
緑内障を認めない	緑内障を認める

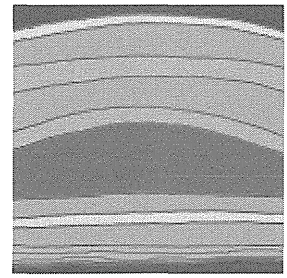
黄斑形成の異常

Grade 0	Grade 1
黄斑低形成を認めない	黄斑低形成を認める


OCT では異常を認めない


網状層の突出の消失


中心窩の陥凹の消失


視細胞外節の伸長の消失

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班会議議事録

平成27年度 厚生労働科学研究費補助金
難治性疾患克服研究事業
「希少難治性角膜疾患の疫学調査」
第三回班会議 議事録

作成：西田希

日時：2015年7月11日（土）12時～13時
場所：グランフロント大阪（北館）タワーC　8階C06会議室
参加者：21名（敬称略）
西田　幸二、山上　聡、島﨑　潤、山田　昌和、新谷　歩、川崎　諭、外園　千恵、鄭　暁東、原　祐子、林　康人、羽藤　晋、松田　彰、舟木　俊成、佐竹　良之、子島　良平、重安　千花、山本　紘司、辻川　元一、橋田　徳康、相馬　剛至、大家　義則

1. 開会の挨拶
研究代表者の西田 幸二より、本研究事業についての再説明が行われた。

2. 研究全体の進捗報告および今年度の予定
研究分担者の川崎 諭より、研究全体の進捗報告および今年度やるべき事についての説明が行われた。

3. 各ワーキンググループの進捗報告および今年度の予定

WG1：角膜内皮症（リーダー：西田 幸二、サブリーダー：山上 聡）
コアメンバーの辻川 元一と、グループリーダーの西田 幸二より、昨年度の進捗および今年度の予定について報告が行われた。

WG2：角膜形状異常症（リーダー：島﨑 潤、サブリーダー：前田 直之）
グループリーダーの島﨑 潤より、昨年度の進捗および今年度の予定について報告が行われた。

WG3：先天性角膜混濁（リーダー：山田 昌和、サブリーダー：宮田 和典）
グループリーダーの山田 昌和より、昨年度の進捗および今年度の予定について報告が行われた。

・診断基準などの作成には小児眼科学会および緑内障学会との折衝が必要なため、グループリーダーの山田 昌和と、サブリーダーの宮田 和典とで案（たたき台）を作成し、角膜学会と日本眼科学会から小児眼科学会および緑内障学会に審議をお願いすることとした。

WG4：特発性周辺部角膜潰瘍（リーダー：木下 茂、サブリーダー：坪田 一男）

サブメンバーの外園 千恵より、昨年度の進捗および今年度の予定について報告が行われた。

WG5：角膜ジストロフィ（リーダー：村上 晶、サブリーダー：川崎 諭）

サブリーダーの川崎 諭より、昨年度の進捗および今年度の予定について報告が行われた。

WG6：角膜上皮幹細胞疲弊症（リーダー：大橋 裕一、サブリーダー：川崎 諭）

グループリーダー 大橋 裕一の所属機関である愛媛大学の林 康人より、昨年度の進捗および今年度の予定について報告が行われた。

・アンケート調査の方法について、今後アンケート調査をする際にはREDCapを積極的に活用することとした。

3. REDCapデータベースについて ～ 閉会

・研究分担者の新谷 歩と、研究代表者の西田 幸二より、REDCapデータベースについての説明が行われた。

平成 27 年度 厚生労働科学研究費補助金
難治性疾患克服研究事業
「希少難治性角膜疾患の疫学調査」
第四回班会議 議事録

作成：西田希

日時：2016 年 2 月 18 日（木）12 時～13 時
場所：軽井沢プリンスホテルウエスト会議室（白樺）
参加者：18 名（敬称略）
山上　聡、木下　茂、川崎　諭、稲富　勉、白石　敦、榛村　重人、羽藤　晋、
舟木　俊成、山口　剛史、佐竹　良之、子島　良平、重安　千花、尾島　俊之、
山本　紘司、高　静花、相馬　剛至、大家　義則

1. 現在の進捗状況および今後の予定について
研究分担者の川﨑諭より、進捗状況についての説明があった。
また今後の予定についての説明があり、特に反対意見は出なかった。

2. 疾患レジストリ（REDCap）について
研究分担者の川﨑諭より、疾患レジストリについての説明があった。
REDCap データベースについて、進捗状況および今後の予定、問題点についての説明があった。

3. 診療ガイドラインの作成について
研究分担者の川﨑諭より、エビデンスに基づく診療ガイドラインの作成方法について、説明があった。

4. ワーキンググループ進捗報告および来年度の予定

①角膜内皮症グループ：研究協力者の大家義則より、進捗および今後の予定についての報告があった。

②先天性角膜混濁グループ：研究協力者の重安千花より、進捗および今後の予定についての報告があった。

③特発性周辺部角膜潰瘍グループ：研究分担者の木下茂より、進捗および今後の予定についての報告があった。

④角膜ジストロフィグループ：研究分担者の川﨑諭より、進捗および今後の予定についての報告があった。

⑤角膜上皮幹細胞疲弊症グループ：研究分担者の川﨑諭より、進捗および今後の予定についての報告があった。

5. 全体ディスカッション

・疾患によっては、日本人と外国人、あるいは国内と国外で、病因や治療法等に差が見られるものがある。そういった疾患について診療ガイドラインを作成する場合、海外のエビデンスを使用して問題はないのか？

→ 国内でのエビデンスがない場合は海外のエビデンスを頼りにするしかないが、臨床感覚に違和感があるようであれば「欧米でこういう報告があるけれども日本ではちょっと違うかもしれない」という使い方をするというのもあるのではないか。

・本研究終了後も疾患レジストリへの入力を続けていくという事になると、倫理審査はどのようにすれば良いのか？

→ 倫理審査は必要。その際、例えば期間を最長で申請したり、特定の疾患だけではなくある程度の疾患に対応できるような書き方をする等の工夫をするのが良いのではないか。

また倫理審査のほか、REDCap アカウントの作成も必要なので、入力はある程度コアの施設でやるしか仕方がない。それ以外の施設に患者が来院した場合には、コアの施設に紹介して貰って情報を入力するという形を取るのが良いのではないか。

・疾患レジストリへの入力について、項目が多いと入力の負担が大きくなり、なかなか症例数が伸びないという事になりがち。臨床研究の患者リクルートを主の目的とするのであれば、若干の項目ぐらいで登録して行き、必要に応じて入力項目を追加するというやり方もあるのではないか。

6. 来年度の班会議開催について

2016 年 7 月 1 日（金）～3 日（日）のフォーサム 2016（東京国際フォーラム）に合わせて開催予定

［VI］

研究成果の刊行に関する一覧表

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研究成果の刊行物・別刷

CrossMark

AMERICAN ACADEMY OF OPHTHALMOLOGY
The Eye M.D. Association

Relationship between Corneal Guttae and Quality of Vision in Patients with Mild Fuchs' Endothelial Corneal Dystrophy

Shinya Watanabe, MD, Yoshinori Oie, MD, PhD, Hisataka Fujimoto, MD, PhD, Takeshi Soma, MD, PhD, Shizuka Koh, MD, PhD, Motokazu Tsujikawa, MD, PhD, Naoyuki Maeda, MD, PhD, Kohji Nishida, MD, PhD

Purpose: To investigate the effect of the severity of corneal guttae on quality of vision (QOV) in patients with mild Fuchs' endothelial corneal dystrophy (FECD).

Design: Cross-sectional study.

Participants: Twenty-three eyes of 14 patients with mild FECD without corneal edema on slit-lamp examination (5 pseudophakic eyes and 18 phakic eyes with mild lens opacity; grade 1.0–2.0 nuclear opalescence, grade 1.0–2.0 nuclear color, grade 1.0 cortical cataract, and grade 1.0 posterior subcapsular cataract on the Lens Opacities Classification System, version III).

Methods: The area ratio of the corneal guttae (ARCG) in the endothelial cells was measured by multifocal specular microscopy. The QOV parameters, that is, corrected distance visual acuity (CDVA), letter contrast sensitivity (LCS), and intraocular straylight, also were measured. The correlations were assessed between the ARCG and QOV parameters and between the straylight and CDVA and LCS.

Main Outcome Measures: The ARCG, logarithm of the minimum angle of resolution CDVA, LCS, and straylight.

Results: Univariate analysis showed that the ARCG was correlated significantly with the CDVA, LCS, and straylight ($R^2 = 0.41$, $P = 0.001$; $R^2 = 0.55$, $P = 0.001$; and $R^2 = 0.39$, $P = 0.002$, respectively). Univariate analysis also showed that straylight was correlated significantly with the CDVA and LCS ($R^2 = 0.47$, $P = 0.001$ and $R^2 = 0.41$, $P = 0.001$, respectively).

Conclusions: Corneal guttae without edema caused the QOV to deteriorate in eyes with FECD. Patients with higher straylight had worse CDVA or LCS. Intraocular forward light scatter caused by corneal guttae may result in visual disturbances. Quantification of corneal guttae can be useful to evaluate the effect of guttae on the QOV and determine the surgical indications of endothelial keratoplasty for eyes with mild FECD. *Ophthalmology 2015;122:2103-2109 © 2015 by the American Academy of Ophthalmology.*

Fuchs' endothelial corneal dystrophy (FECD) is a bilateral corneal endothelial dysfunction characterized by deposition of extracellular matrix (guttae), thickening of Descemet's membrane, and progressive loss of corneal endothelial cells.[1–6] Fuchs' endothelial corneal dystrophy occurs most often in individuals in the fifth or sixth decade of life.[6] The prevalence in the United States is approximately 4% to 5% of the population older than 40 years.[6,7] Progressive endothelial cellular loss leads to corneal edema and impairs visual function. In eyes with FECD, corneal edema begins in the central cornea and expands into the periphery.[8] Fuchs' endothelial corneal dystrophy is the most common dystrophic reason for corneal transplantation in many countries, including the United States.[9]

Recent technologic advances have enabled quantitative measurement of guttae and intraocular forward light scatter, referred to as straylight, which impairs visual function. Straylight is caused by corneal or lenticular opacity, and the straylight value increases with aging.[10] The reliability of straylight measurements using the compensation comparison method has been reported.[11–14] Some studies have reported relationships between straylight and pseudophakic eyes or straylight and eyes that underwent corneal surgeries.[15–19]

Some patients report visual discomfort despite the absence of corneal edema. Intraocular forward light scatter impairs the quality of vision (QOV),[11] and corneal guttae associated with FECD may cause intraocular light scatter and glare, which can be extremely debilitating despite the absence of edema.[20,21] However, to the best of our knowledge, no study has confirmed that corneal guttae increase intraocular forward light scatter in eyes with FECD, resulting in visual deterioration. Therefore, we evaluated the relationship between the severity of corneal guttae and QOV.

Methods

Subjects with FECD were recruited at the outpatient clinic of the Department of Ophthalmology at Osaka University Hospital. Cornea specialists diagnosed all cases of FECD based on the

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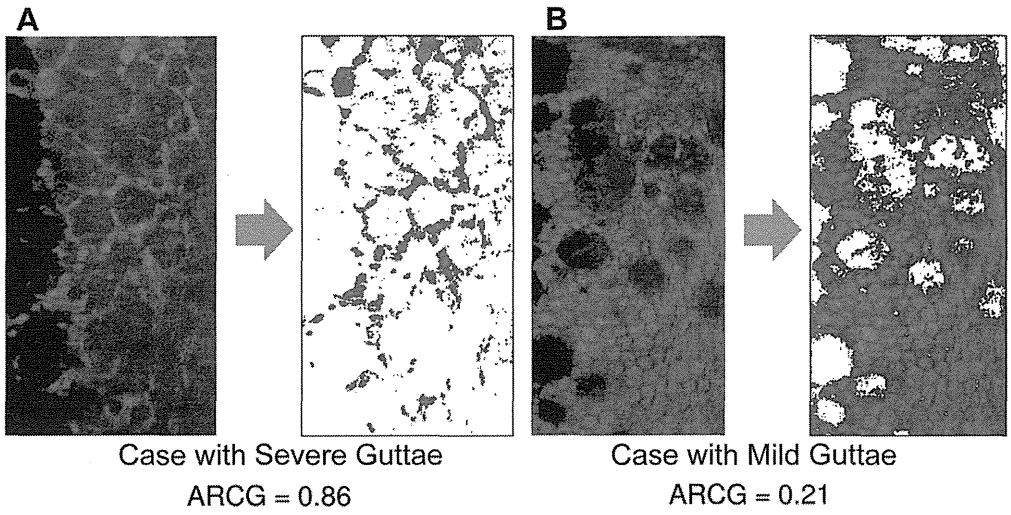

Figure 1. Evaluation of corneal guttae using multifocal specular microscopy images. The captured images are 0.55 mm high and 0.25 mm wide. The area ratio of the corneal guttae (ARCG) in the endothelial cells is measured. **A**, In a severe case, ARCG in the endothelial cells is 0.86. **B**, In a mild case, the ARCG is 0.21.

presence of longstanding bilateral corneal guttae or a beaten metal appearance without other corneal abnormalities. All eyes had central or paracentral guttae, and there was no corneal edema defined by epithelial and stromal edema or Descemet's folds detected by slit-lamp examination. In the current study, the eyes without corneal edema observed on slit-lamp examination were diagnosed with mild FECD. To minimize the effect of lens opacity, pseudophakic eyes or phakic eyes with mild lens opacity were included. The extent of the cataracts in the phakic eyes was grade 1.0 to 2.0 nuclear opalescence, grade 1.0 to 2.0 nuclear color, grade 1.0 cortical cataract, and grade 1.0 posterior subcapsular cataract on the Lens Opacities Classification System, version III.[22] Pseudophakic eyes with posterior capsule opacification and eyes with other ocular disorders were excluded.

The Institutional Review Board of Osaka University Hospital approved this study. The research adhered to the tenets of the Declaration of Helsinki. All subjects provided informed consent after they received an explanation of the nature and possible consequences of the study before any measurements were performed.

In the current study, we calculated the area ratio of the corneal guttae (ARCG) in eyes with FECD using the same method we reported previously to quantify the severity of corneal guttae.[23] We used a noncontact multifocal specular microscope (CEM 530; Nidek, Hiroishi, Japan) to examine the corneal endothelium at 1 spot centrally and at 8 points paracentrally over 5° of the visual angle for every 1.5 clock hours. The images were analyzed using MATLAB software (MathWorks, Inc, Natick, MA). The original images had different brightness levels of the pixels horizontally because the slit light in the specular microscope was tilted. Each pixel was homogenized by adding or subtracting the same vertical value so that the average vertical pixel values were equal in 1 image. The guttae were separated by a thresholding algorithm and were defined as bright areas under a fixed threshold. Nine images were analyzed for each eye, and the percentage of the pixels covered by guttae in the image (percentage of the guttae) was calculated for every specular microscopy image. The average of the ratio in 9 images was defined as the ARCG in the eyes (Fig 1).

The corrected distance visual acuity (CDVA), letter contrast sensitivity (LCS), and straylight expressed as an intraocular light scattering value were measured as parameters that reflect the QOV. The CDVA was expressed in logarithm of the minimum

Table 1. Comparison of Pseudophakic Eyes and Phakic Eyes

	Pseudophakic Eyes (n = 5)	Phakic Eyes (n = 18)	*P* Value
Age (yrs)	79.0±10.5	56.2±9.7	0.006
CDVA (logMAR)	−0.06±0.04	−0.11±0.09	0.03
LCS (log)	1.31±0.07	1.57 ±0.21	0.02
Straylight (log(s))	1.38±0.06	1.20±0.26	0.07
ARCG	0.62±0.26	0.36±0.32	0.15
CCT (μm)	606.0±44.0	591.0±55.0	0.74
HOAs (RMS, μm)	0.31±0.20	0.20±0.08	0.19

ARCG = area ratio of corneal guttae; CCT = central corneal thickness; CDVA = corrected distance visual acuity; HOAs = higher order aberrations; LCS = letter contrast sensitivity; logMAR = logarithm of the minimum angle of resolution; RMS = root mean square.
Data are average ± standard deviation unless otherwise indicated.

Table 2. Characteristics of 23 Study Eyes with Fuchs' Endothelial Corneal Dystrophy

Age (yrs)	61.2±13.6 (range, 47–89)
Men:women	4:19
CDVA (logMAR)	−0.08±0.11 (range, −0.18 to 0.10)
LCS (log)	1.51±0.22 (range, 1.20–1.90)
Straylight (log(s))	1.24±0.24 (range, 0.76–1.54)
ARCG	0.42±0.32 (range, 0.03–1.00)
CCT (μm)	595±52 (range, 502–666)
HOAs (RMS, μm)	0.22±0.12 (range, 0.09–0.66)

ARCG = area ratio of corneal guttae; CCT = central corneal thickness; CDVA = corrected distance visual acuity; HOAs = higher order aberrations; logMAR = logarithm of the minimum angle of resolution; LCS = letter contrast sensitivity; RMS = root mean square.
Data are average ± standard deviation unless otherwise indicated.

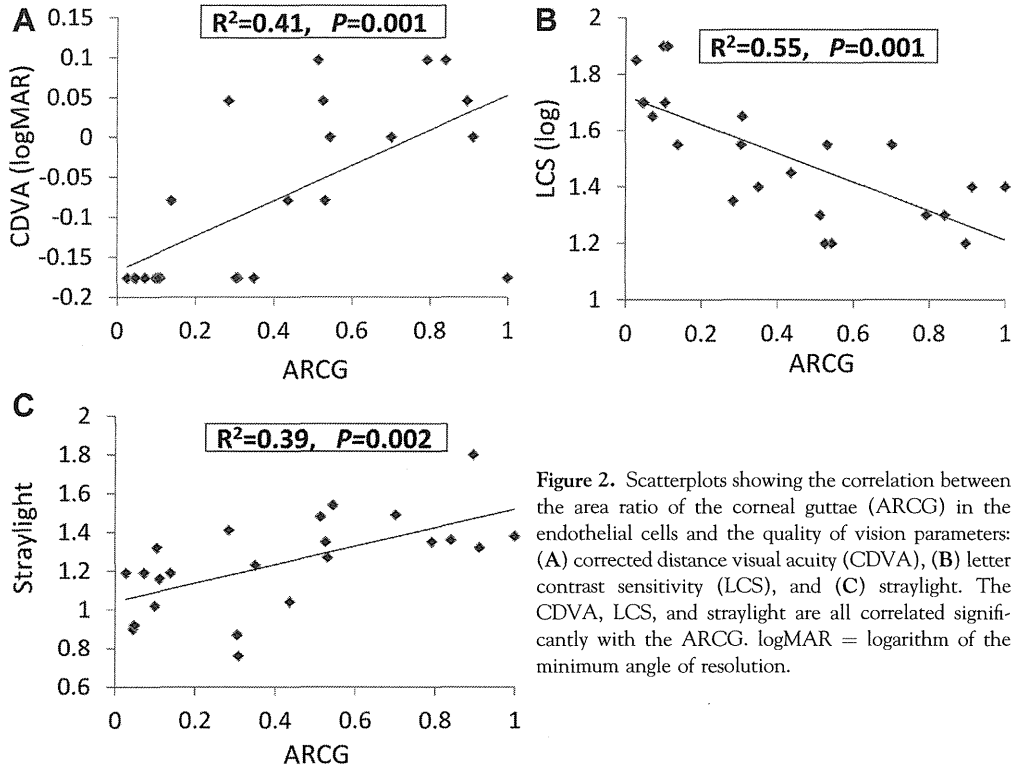

Figure 2. Scatterplots showing the correlation between the area ratio of the corneal guttae (ARCG) in the endothelial cells and the quality of vision parameters: (**A**) corrected distance visual acuity (CDVA), (**B**) letter contrast sensitivity (LCS), and (**C**) straylight. The CDVA, LCS, and straylight are all correlated significantly with the ARCG. logMAR = logarithm of the minimum angle of resolution.

angle of resolution (logMAR) units after the decimal visual acuity was measured. The LCS was measured using the CSV-1000RN letter chart (Vector Vision, Greenville, OH).[24] The CDVA and LCS are conventional QOV parameters. Straylight was examined using the C-Quant Straylight Meter (Oculus, Wetzlar, Germany), which quantifies the amount of intraocular forward light scatter by the compensation comparison method. During the straylight measurements, the refractive errors in all eyes were corrected with spectacles attached to the straylight meter. The examinations were performed in a dark room to avoid the effect of other straylight sources. The pupils were undilated because dilation increases straylight.[25,26] The straylight source in the C-Quant Straylight Meter is an annulus with a 5° to 10° radius in the visual field that corresponds to the areas of guttae that we measured.[27] Unreliable straylight measurements were detected by the reliability parameters, and data with low reliability parameters were excluded. Although there was no edema detectable by slit-lamp examination, to evaluate a correlation between subclinical corneal thickening and the QOV, the central corneal thickness (CCT) was measured using the Pentacam HR (Oculus). Higher-order aberrations (HOAs) also were examined using the Wave-Front Analyzer KR-1W (Topcon, Tokyo, Japan) because they can negatively affect the QOV in eyes with FECD. The HOAs were obtained in the central 4-mm diameter, and the root mean square values of the HOAs were calculated.

Linear regression models were used to analyze the relationship between the QOV parameters and the ARCG and between the straylight and conventional QOV parameters. The Wilcoxon signed-rank test was used to compare the results of pseudophakic

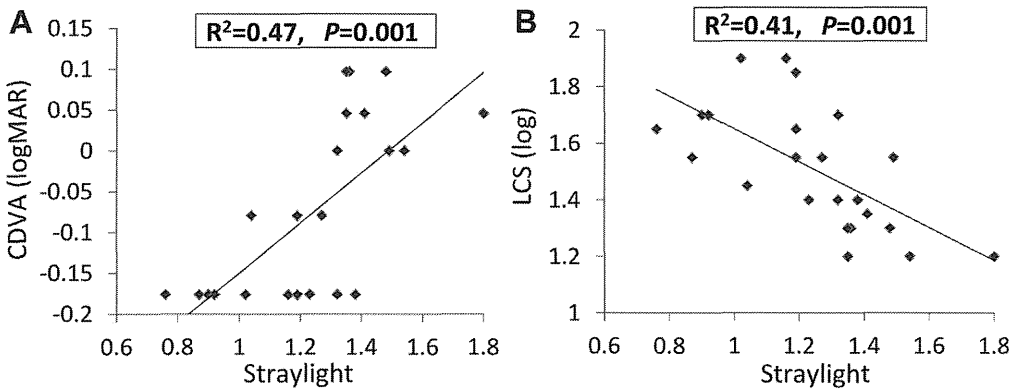

Figure 3. Scatterplots showing the correlation between straylight and (**A**) corrected distance visual acuity (CDVA) and (**B**) letter contrast sensitivity (LCS). Straylight is correlated significantly with CDVA and LCS. logMAR = logarithm of the minimum angle of resolution.

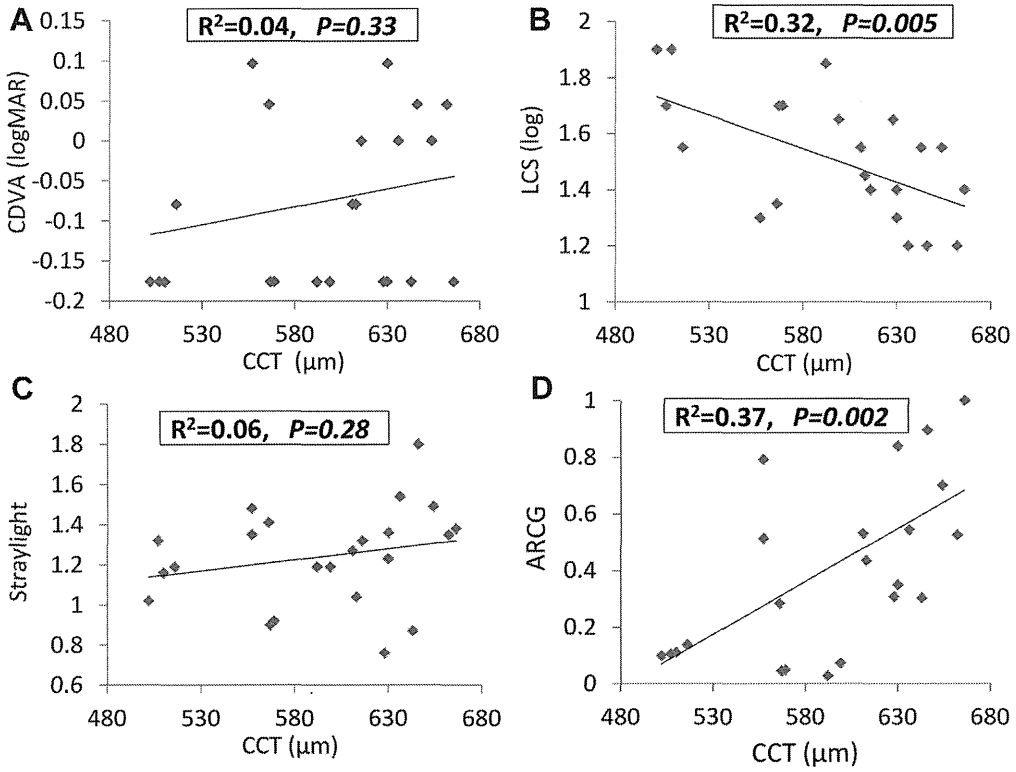

Figure 4. Scatterplots showing the correlation between the central corneal thickness (CCT) and (**D**) area ratio of the corneal guttae (ARCG) and the quality of vision parameters: (**A**) corrected distance visual acuity (CDVA), (**B**) letter contrast sensitivity (LCS), and (**C**) straylight. The CCT is correlated significantly with the ARCG and LCS. The CCT is not correlated significantly with CDVA and straylight. logMAR = logarithm of the minimum angle of resolution.

eyes and phakic eyes. All statistical analyses were performed using JMP Pro Software (SAS Inc, Cary, NC). *P* values less than 0.05 were considered statistically significant.

Results

Twenty-three eyes (5 pseudophakic eyes and 18 phakic eyes) of 14 patients were included. Table 1 shows the comparison of the results of pseudophakic eyes and phakic eyes. Statistical analysis showed that pseudophakic patients were significantly older and had significantly better CDVA and LCS than patients with mild cataract ($P = 0.006$, $P = 0.03$, and $P = 0.02$, respectively). Although there were significant differences in these parameters, the accuracy of the comparison is limited because of the smaller number and older age of the patients with pseudophakic eyes compared with the patients with phakic eyes. Therefore, we analyzed the 2 groups together. It was suggested that the cataracts in the phakic eyes were mild enough to be analyzed together with the pseudophakic eyes. Table 2 shows the characteristics of all the eyes. The patient ages ranged from 47 to 89 years; 83% were women. The mean CDVA was −0.08 logMAR (range, −0.18 to 0.10 logMAR), and 17 (74%) eyes had CDVA better than 0.00 logMAR. The mean ARCG was 0.42 (range, 0.03–1.00). The mean straylight value was 1.24 log(s) (range, 0.76–1.54 log(s)).

Correlation between Area Ratio of the Corneal Guttae and Quality-of-Vision Parameters

The ARCG was correlated significantly with the QOV parameters, that is, the CDVA, LCS, and straylight ($R^2 = 0.41$, $P = 0.001$; $R^2 = 0.55$, $P = 0.001$; and $R^2 = 0.39$, $P = 0.002$, respectively; Fig 2). The increase in ARCG negatively affected all QOV parameters.

Prediction of the Quality-of-Vision Parameters by Area Ratio of the Corneal Guttae Using a Linear Regression Formula

Because the ARCG was correlated significantly with the QOV parameters, each parameter could be predicted by the following formulas using linear regression models:

CDVA = −0.17 + 0.22 ARCG,
LCS = 1.72 − 0.51 ARCG, and
straylight = 1.04 + 0.48 ARCG.

Correlation between Straylight and Conventional Quality-of-Vision Parameters

The straylight was correlated significantly with the conventional QOV parameters, that is, the CDVA and LCS ($R^2 = 0.47$, $P = 0.001$; and $R^2 = 0.41$, $P = 0.001$, respectively; Fig 3). Patients with higher straylight had worse CDVA or LCS.

Correlation between Central Corneal Thickness and Area Ratio of the Corneal Guttae or Quality-of-Vision Parameters

The CCT was correlated significantly with the ARCG and patients with more guttae had thicker corneas ($R^2 = 0.37$, $P = 0.002$; Fig 4). The CCT was not correlated significantly with the CDVA

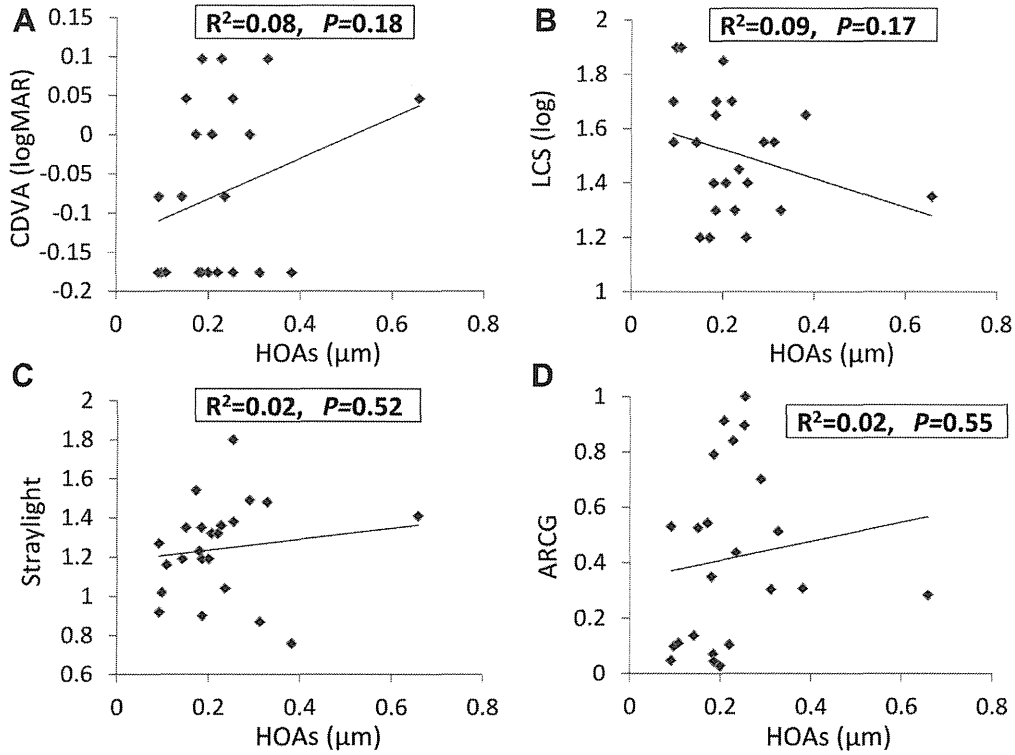

Figure 5. Scatterplots showing the correlation between higher-order aberrations (HOAs) and (**D**) area ratio of the corneal guttae (ARCG) and the quality of vision parameters: (**A**) corrected distance visual acuity (CDVA), (**B**) letter contrast sensitivity (LCS), and (**C**) straylight. The HOAs were obtained in the central 4-mm diameter, and the root mean square values of the HOAs were calculated. The HOAs were not correlated significantly with CDVA, LCS, straylight, or ARCG. logMAR = logarithm of the minimum angle of resolution.

and straylight ($R^2 = 0.04$, $P = 0.33$; and $R^2 = 0.06$, $P = 0.28$, respectively), whereas the LCS was correlated significantly with the CCT ($R^2 = 0.32$, $P = 0.005$; Fig 4).

Correlation between Higher-Order Aberrations and Area Ratio of the Corneal Guttae or Quality-of-Vision Parameters

The HOAs were not correlated significantly with the CDVA, LCS, straylight, or ARCG ($R^2 = 0.08$, $P = 0.18$; $R^2 = 0.09$, $P = 0.17$; $R^2 = 0.02$, $P = 0.52$; and $R^2 = 0.02$, $P = 0.55$, respectively; Fig 5).

Discussion

The current study showed the correlation between corneal guttae and deterioration of the QOV parameters, i.e., CDVA, LCS, and straylight, even without corneal edema seen on slit-lamp examination. It is assumed that as the corneal guttae enlarge, the irregularity and opacity of the posterior cornea cause more forward light scatter (Fig 6). The straylight also was significantly negatively correlated with the CDVA and LCS. Therefore, the current study confirmed that corneal guttae increase intraocular forward light scatter in eyes with FECD and result in visual deterioration.

However, thick corneas were correlated with severe guttae and impaired LCS, but not poor CDVA or increased straylight. Although the LCS can be affected by the CCT, the CDVA and straylight are not thought to be affected by the CCT. Therefore, the effect of subclinical corneal thickening on the QOV parameters is considered limited in eyes with mild FECD.

Although FECD is classified according to the severity of the edema or the extent of confluent guttae by semi-quantitative slit-lamp examination, there is no objective method based on the ARCG to assess the severity of the FECD in mild cases without significant edema.[4,6,7,28] The current study showed that the severity of the guttae was

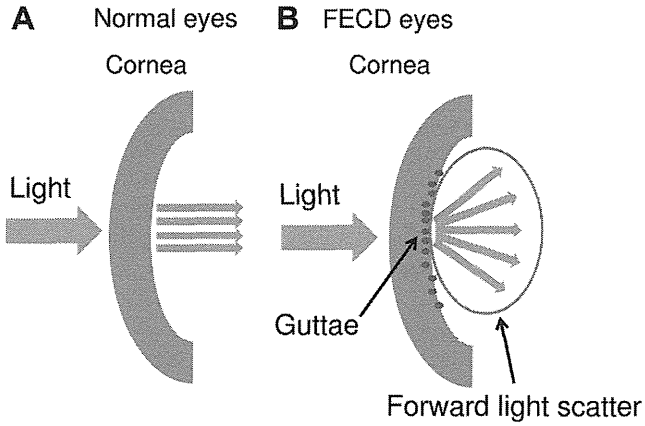

Figure 6. Illustrations showing forward light scatter resulting from corneal guttae. **A**, No significant forward light scatter is generated in normal eyes without corneal guttae. **B**, Forward light scatter increases because of corneal guttae in eyes with Fuchs' endothelial corneal dystrophy (FECD).

useful clinically to evaluate the severity of the visual impairment in eyes with mild FECD.

Corneal guttae in eyes with FECD appear first in the central cornea and expand to the periphery.[29] Repp et al[8] reported that corneal thickening in eyes with early-stage FECD was significant in the central cornea compared with the periphery. Because such corneal irregularity can increase HOAs and cause visual impairment in eyes with mild FECD, we assessed the effect of HOAs on QOV. However, no significant correlations were seen between the HOAs and ARCG or the QOV parameters. Progressive enlargement of the size of the guttae did not increase the HOAs, which are not the primary cause of visual impairment. Thus, straylight resulting from guttae may be the main cause of deterioration of the conventional QOV parameters, that is, the CDVA and LCS in eyes with mild FECD.

Price and Price[20] reported that guttae should be removed during endothelial keratoplasty to obtain optimal postoperative vision, because guttae can cause intraocular light scatter. The current results support that opinion, and the negative effect of guttae on the QOV should be considered when endothelial keratoplasty is performed. Descemet membrane endothelial keratoplasty techniques have been evolving dramatically, and the indications for the surgery have been expanding.[30–37] In addition, endothelial keratoplasty is challenging in cases with severe corneal edema. Therefore, early endothelial keratoplasty for patients with mild FECD without severe edema should be considered to remove corneal guttae that affect the QOV parameters.

As the current study showed, quantitative measurements of the ARCG were predictive of the CDVA, LCS, and straylight if the patient had minimal lens opacity, indicating that quantification of corneal guttae can be useful for evaluating the QOV objectively in eyes with FECD even with other ocular disorders, including cataract. If a patient's parameters are worse than the predicted QOV parameters using the ARCG, the difference is probably caused by ocular diseases other than FECD. It is sometimes controversial whether simultaneous endothelial keratoplasty should be performed with cataract surgery for patients with mild FECD. Thus, if measurement of the ARCG becomes much more accessible for most clinicians because of the development of equipment and software, quantification of the ARCG may be helpful to determine whether simultaneous endothelial keratoplasty should be performed at the time of cataract surgery in the future.

In conclusion, in eyes with mild FECD without severe corneal edema, corneal guttae increase forward light scatter that negatively affects the QOV. Quantification of corneal guttae would be useful to determine the surgical indications for eyes with mild FECD.

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Footnotes and Financial Disclosures

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Author Contributions:

Conception and design: Watanabe, Oie, Fujimoto, Maeda, Nishida

Analysis and interpretation: Watanabe, Oie, Fujimoto, Maeda

Data collection: Watanabe, Oie, Fujimoto, Soma, Koh, Tsujikawa, Maeda

Obtained funding: Nishida

Overall responsibility: Watanabe, Oie, Fujimoto, Maeda, Nishida

Abbreviations and Acronyms:
ARCG = area ratio of the corneal guttae; **CCT** = central corneal thickness; **CDVA** = corrected distance visual acuity; **FECD** = Fuchs' endothelial corneal dystrophy; **HOA** = higher-order aberration; **LCS** = letter contrast sensitivity; **logMAR** = logarithm of the minimum angle of resolution; **QOV** = quality of vision.

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Markers for Distinguishing Cultured Human Corneal Endothelial Cells from Corneal Stromal Myofibroblasts

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