Straylight in anterior segment disorders of the eye
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Chapter 5

QUALITY OF VISION IN PATIENTS WITH FUCHS’ ENDOTHELIAL DYSTROPHY AND AFTER DESCMEET STRIPPING ENDOTHELIAL KERATOPLASTY

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ABSTRACT

Objective
To evaluate the quality of vision (visual acuity and straylight) in patients with Fuchs’ dystrophy and the improvement in visual quality after Descemet stripping endothelial keratoplasty (DSEK).

Methods
There was an observational case series (Amsterdam group) and a prospective interventional case series (Mayo group). Corrected distance visual acuity (CDVA), straylight, and corneal thickness were measured in patients with phakic and pseudophakic eyes with Fuchs’ dystrophy recruited at the Academic Medical Center, Amsterdam, the Netherlands (99 eyes), and at Mayo Clinic, Rochester, MN, USA (48 eyes). The Mayo group was also examined at 1, 3, 6 and 12 months after DSEK; all these eyes were rendered pseudophakic during DSEK.

Results
Eyes with Fuchs’ dystrophy had decreased CDVA (mean [SD], 0.42 [0.26] logMAR; Snellen equivalent 20/53) and increased straylight (mean [SD], 1.54 [0.24] log(s)) compared with normal eyes. Younger patients were affected more by increased straylight than by decreased CDVA. CDVA ($r = 0.2; P = 0.003; n = 135$) and straylight ($r = 0.26; P = 0.003; n = 133$) were correlated with corneal thickness. CDVA and straylight improved at all postoperative examinations ($P < 0.001$), and improvement in straylight from before DSEK to 12 months after DSEK correlated with recipient age ($r = -0.43; P = 0.01; n = 33$). Improvement in straylight was more predictable than that of CDVA and was associated with preoperative straylight >1.33 log(s).

Conclusions
Quality of vision is severely impaired in patients with Fuchs’ dystrophy and improves significantly after DSEK. Straylight improves more in younger than in older eyes after DSEK. Preoperative straylight can be a useful clinical metric to predict postoperative improvement, especially in cases where preoperative visual acuity is close to 20/20.
INTRODUCTION

The more advanced stages of corneal endothelial dysfunction in Fuchs’ dystrophy are associated with decreased quality of vision.\(^1,2\) Even if visual acuity remains reasonable initially, corneal edema with disorganization of corneal stromal collagen fibrils\(^3\) and keratocytes\(^4\) will increase forward light-scatter and straylight. Straylight (disability glare) is a functional term that denotes scattered light falling on the retina as observed by the patient and is proportional to forward light-scatter. It causes symptoms of glare and halos,\(^1,2\) and is an objective physiologic measure of the large-angle domain of the retinal point-spread function, in contrast to visual acuity, which is degraded by the small angle domain of the retinal point-spread function.\(^5-9\) Because quality of vision is related to both domains of the point-spread function, visual acuity alone is not sufficient to assess all aspects of quality of vision, yet few studies have assessed straylight in Fuchs’ endothelial dystrophy.

The importance of straylight in Fuchs’ dystrophy relates to outcomes of the current surgical treatment of choice, which is Descemet stripping endothelial keratoplasty (DSEK).\(^10,11\) In comparison with penetrating keratoplasty (PK), DSEK is associated with lower postoperative astigmatism, better uncorrected visual acuity, and a more predictable refractive error,\(^10-12\) but quality of vision after DSEK remains diminished compared with otherwise normal pseudophakic eyes partly because of increased straylight induced by the residual host cornea.\(^10-12\) In a previous study, we found that straylight trended toward improvement after DSEK but we were unable to verify this statistically because of a small sample size.\(^10\) As a result, we were unable to determine the clinical utility of measuring straylight in patients with Fuchs’ dystrophy, and, specifically, if straylight could be an indicator of whether surgical intervention would be beneficial.

In this study, we determined the effect of Fuchs’ endothelial dystrophy on quality of vision, as assessed by visual acuity and straylight. We combined two groups of subjects with Fuchs’ dystrophy from two institutions to increase the number of subjects over a broad age range; both groups had standardized visual acuity and straylight measurements. In addition, we determined the improvement in quality of vision after DSEK in one of these groups, which was larger and had longer postoperative follow-up than previously reported,\(^10\) with the goal of assessing whether straylight could be a useful metric in the clinical evaluation of patients with Fuchs’ dystrophy.

METHODS

Subjects

All subjects were patients who had corneal guttae with or without corneal edema, consistent with a diagnosis of Fuchs’ endothelial dystrophy. Two groups of patients were recruited at two sites. The first group had Fuchs’ dystrophy and was recruited at the Academic Medical Center (AMC), Amsterdam, the Netherlands; this group will be called the “Amsterdam group”. A second group
of patients, who had Fuchs’ dystrophy requiring DSEK, was recruited from the cornea service at Mayo Clinic, Rochester, Minnesota, USA; this group will be called the “Mayo group”. Patients were excluded from either group if they had other eminent ocular pathology, including decreased vision from any cause other than cataract. The study complied with the tenets of the Declaration of Helsinki, and all subjects gave informed consent to participate. Institutional Review Board approval was obtained at both sites.

DSEK procedure
Patients in the Mayo group were in a prospective study and were examined before and after DSEK. The surgical procedure has been described previously. Preoperatively, all eyes were either pseudophakic or had lenticular changes justifying cataract extraction, and postoperatively all eyes were pseudophakic. Postoperative follow-up was at least 6 months, and only 37 eyes were examined at 12 months because 1 patient had died, 2 patients had withdrawn from the study, 1 graft had failed after 6 months, and six eyes had not yet reached the 12-month examination.

Outcome measures
The severity of Fuchs’ dystrophy was assessed by measuring central corneal thickness with an ultrasonic pachymeter (DGH-1000; DGH technologies Inc, Frazer, Pennsylvania). High-contrast corrected distance visual acuity (CDVA) was measured in both groups by using the Early Treatment of Diabetic Retinopathy Study (ETDRS) protocol, and was reported as the logarithm of the minimum angle of resolution (logMAR).

Functional forward light-scatter was measured in both groups by using the Oculus C-Quant straylight meter (Oculus GmbH, Wetzlar, Germany, or Oculus, Lynwood, WA) and was reported as the logarithm of the straylight parameter \( \log(s) \). This measurement is based on the psychophysical “compensation comparison” technique and has been described in detail elsewhere. Briefly, the test consists of a computer-controlled 2-alternative forced-choice protocol. Straylight is a psychophysical measurement that is proportional to forward light-scatter; a higher value indicates more straylight (more sensitivity to glare). The test is repeatable, and the instrument supplies a reliability index, called the “estimated standard deviation” (ESD), for each measurement. The standard deviation of repeated \( \log(s) \) measurements has been approximately 0.07 log units when using the instrument’s reliability test. Straylight of phakic eyes with Fuchs’ endothelial dystrophy was compared with that of age-matched normal subjects. Normal data for straylight values as a function of age for healthy eyes were generated by measuring 3,182 eyes without comorbidity of a population of European drivers. Straylight of pseudophakic eyes with Fuchs’ endothelial dystrophy was compared with that of normal pseudophakic eyes, because the influence of the aging crystalline lens was absent in these
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eyes. A recent study of 56 normal pseudophakic eyes that had undergone uncomplicated cataract surgery showed that the age-related regression for straylight in pseudophakic eyes was log(s) = 0.003*age + 1.13, with subject age measured in years.23

Statistical analysis
All statistical analyses were performed in Excel (Microsoft Corp., Redmond, WA, USA) or SPSS version 16.0.2 (SPSS Inc., Chicago, IL, USA). Correlations were examined by using the bivariate Pearson method or when data were not normally distributed, the Spearman rho coefficient. A P-value of less than 0.05 was considered statistically significant, and unless otherwise stated, all tests were two-tailed. Straylight in patients was compared with straylight in age-adjusted normal subjects8,23 by using an unpaired t-test.

RESULTS
Subjects
Ninety-nine eyes of 66 patients with Fuchs’ endothelial dystrophy were included in the Amsterdam group; some fellow eyes were not included because they had had a previous PK or DSEK. Sixty-three eyes of 44 patients had mild to moderate cataract and 36 eyes of 30 patients were pseudophakic. Age of the phakic patients was 67 ± 11 years (mean ± SD; range, 44 to 84 years) and of the pseudophakic patients was 72 ± 12 years (range, 40 to 92 years; Table 5.1). Forty-eight eyes of 41 patients with Fuchs’ endothelial dystrophy were enrolled in the Mayo group and all underwent DSEK. Nine eyes were pseudophakic preoperatively, and 39 eyes had a cataract that justified extraction and was extracted at the same time as the DSEK procedure. Postoperatively, all eyes had posterior chamber lenses without posterior capsule opacification. Age at the time of surgery was 67 ± 10 years (range, 41 to 87 years; Table 5.1).

Visual acuity
CDVA was similar between the Amsterdam and preoperative Mayo groups (Table 5.1). In Fuchs’ dystrophy, CDVA was correlated with age, with better CDVA being associated with younger patients (Amsterdam group: r = 0.24; P < 0.02; Mayo group: r = 0.49; P < 0.001); this trend was evident in both the phakic and pseudophakic eyes, but to a lesser extent in the pseudophakic group.

Mean (SD) preoperative CDVA of the phakic Mayo patients was 0.40 ± 0.21 logMAR (Snellen equivalent, 20/50) and of the pseudophakic patients was 0.56 ± 0.14 logMAR (Snellen equivalent, 20/73). At all postoperative examinations, CDVA was significantly better than it was before DSEK (P < 0.001, Table 5.2). Greater improvement in CDVA averaged over 3 to 12 months after DSEK was associated with worse preoperative CVDA (Figure 5.1).
### Table 5.1: Visual quality and corneal thickness in phakic and pseudophakic eyes with Fuchs’ endothelial dystrophy in the Amsterdam and Mayo groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of eyes</th>
<th>Age, years (range)</th>
<th>CDVA, log MAR (Snellen Equivalent)</th>
<th>Straylight, log(s)</th>
<th>Central Corneal Thickness, μm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Phakic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All eyes</td>
<td>102</td>
<td>66 ± 9 (41-84)</td>
<td>0.39 ± 0.23 (20/49)</td>
<td>1.55 ± 0.26</td>
<td>677 ± 62</td>
</tr>
<tr>
<td>Amsterdam</td>
<td>63</td>
<td>67 ± 11 (44-84)</td>
<td>0.39 ± 0.25 (20/49)</td>
<td>1.53 ± 0.25</td>
<td>696 ± 65</td>
</tr>
<tr>
<td>Mayo</td>
<td>39</td>
<td>64 ± 8 (41-83)</td>
<td>0.40 ± 0.21 (20/50)</td>
<td>1.57 ± 0.26</td>
<td>655 ± 51</td>
</tr>
<tr>
<td><strong>Pseudophakic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All eyes</td>
<td>45</td>
<td>73 ± 12 (40-92)</td>
<td>0.48 ± 0.26 (20/60)</td>
<td>1.51 ± 0.18</td>
<td>653 ± 64</td>
</tr>
<tr>
<td>Amsterdam</td>
<td>36</td>
<td>72 ± 12 (40-92)</td>
<td>0.45 ± 0.28 (20/56)</td>
<td>1.53 ± 0.19</td>
<td>650 ± 67</td>
</tr>
<tr>
<td>Mayo</td>
<td>9</td>
<td>78 ± 8 (58-87)</td>
<td>0.56 ± 0.14 (20/73)</td>
<td>1.42 ± 0.17</td>
<td>660 ± 51</td>
</tr>
</tbody>
</table>

Mean ± SD, all variables except number of eyes. CDVA, Corrected distance visual acuity; log MAR, logarithm of the minimum angle of resolution; log(s), logarithm of the straylight parameter. *n=35, †n=8 because straylight measurements were unreliable in 4 eyes and 1 eye, respectively.

### Table 5.2: Visual quality before and after Descemet stripping endothelial keratoplasty (DSEK) for Fuchs’ endothelial dystrophy. Only the Mayo group is shown in this table; patients in the Amsterdam group were not measured pre- and postoperatively.

<table>
<thead>
<tr>
<th>Before DSEK</th>
<th>Time after DSEK (months)</th>
<th>1</th>
<th>3</th>
<th>6</th>
<th>12</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>CDVA, log MAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD (Snellen Equivalent)</td>
</tr>
<tr>
<td>All eyes (48 eyes)</td>
</tr>
<tr>
<td>0.43 ± 0.21 (20/54)</td>
</tr>
<tr>
<td>0.35 ± 0.21 (20/45)</td>
</tr>
<tr>
<td>0.27 ± 0.20* (20/37)</td>
</tr>
<tr>
<td>0.23 ± 0.17* (20/34)</td>
</tr>
<tr>
<td>0.17 ± 0.16* (20/30)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Straylight, log(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD (Number of eyes) *</td>
</tr>
<tr>
<td>All eyes</td>
</tr>
<tr>
<td>1.55 ± 0.25 (43)</td>
</tr>
<tr>
<td>1.41 ± 0.16 (46)</td>
</tr>
<tr>
<td>1.36 ± 0.21* (48)</td>
</tr>
<tr>
<td>1.35 ± 0.21* (47)</td>
</tr>
<tr>
<td>1.35 ± 0.20* (37)</td>
</tr>
</tbody>
</table>

*P<0.0001

CDVA, Corrected distance visual acuity; log MAR, logarithm of the minimum angle of resolution; log(s), logarithm of the straylight parameter.

* For straylight, unless otherwise indicated, data were unreliable in some eyes, reducing the number of eyes available for analysis.
Straylight was remarkably similar between the Amsterdam and Mayo groups (Figures 5.2 and 5.3). In both phakic and pseudophakic eyes with Fuchs’ dystrophy, straylight was increased compared with age-matched normal eyes ($P < 0.01$, Figures 5.2 and 5.3). Straylight in younger subjects with Fuchs’ dystrophy was higher than that of age-matched normal subjects ($P< 0.01$), whereas straylight in older subjects with Fuchs’ dystrophy approached that of age-matched normal subjects (Figures 5.2 and 5.3).

Preoperatively, mean (SD) straylight of the phakic eyes in the Mayo group was $1.57 \pm 0.26$ log($s$) and of the pseudophakic eyes in the Mayo group was $1.42 \pm 0.17$ log($s$). At all postoperative examinations, straylight was significantly improved compared with straylight before DSEK ($P < 0.001$, Table 5.2). The improvement in straylight from before DSEK to 12 months after DSEK correlated with recipient age ($r = -0.43; P = 0.01; n = 33$, Figure 5.4). Greater improvement in straylight averaged over 3 to 12 months after DSEK was associated with higher preoperative straylight (Figure 5.5). The improvement in straylight was more predictable than the improvement before DSEK.
Figure 5.2 Straylight as a function of age for the Amsterdam (open circles) and Mayo (open triangles) patients with phakic eyes and Fuchs' endothelial dystrophy. Straylight was increased compared with normal eyes of the same age ($P < 0.01$), especially in younger patients. The central black line represents average straylight in healthy phakic eyes. The two dotted lines represent ± 0.2 log intervals.

Figure 5.3 Straylight as a function of age for the Amsterdam (open circles) and Mayo (open triangles) patients with pseudophakic eyes and Fuchs' endothelial dystrophy. Straylight was increased compared with normal eyes in patients of the same age ($P < 0.01$), especially in younger patients. The central black line represents average straylight in healthy pseudophakic eyes. The two dotted lines represent ± 0.2 log intervals.
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**Figure 5.4** Postoperative improvement in straylight as a function of recipient age. The improvement in straylight from before to 12 months after DSEK correlated with recipient age ($r = -0.43; P < 0.01; n = 33$).

**Figure 5.5** Postoperative improvement in straylight as a function of preoperative straylight values. After Descemet stripping endothelial keratoplasty (DSEK), straylight improved to approximately $1.35 \log(s)$, regardless of preoperative straylight. As a consequence, postoperative improvement in straylight was correlated with preoperative straylight. The regression line ($y = 0.931x - 1.2423$, where $y$ is the postoperative improvement and $x$ is preoperative straylight) highlights that eyes with preoperative straylight higher than $1.33 \log(s)$ ($1.24/0.93$) can be expected to improve after DSEK. Zero improvement is denoted (- - -).
in CDVA. From the regression line in Figure 5.5 (y = 0.93x – 1.24), the preoperative straylight for which there was no average improvement in postoperative straylight was 1.33 log(s) (1.24/0.93).

Corneal Pachymetry
The distribution of central corneal thickness was remarkably similar between the Amsterdam and Mayo groups. Central corneal thickness in the Amsterdam group was 683 ± 105 µm (range, 549 – 837 µm) and in the preoperative Mayo group was 662 ± 46 µm (range, 572 – 779 µm). Although corneas appeared slightly thicker in younger patients, the difference was not statistically significant. Preoperative straylight (r = 0.26; P = 0.003; n = 133) and CDVA (r = 0.26; P = 0.003; n = 135) were correlated with central corneal thickness (Figure 5.6).

DISCUSSION
In this study, we found that quality of vision was decreased in subjects with Fuchs’ endothelial dystrophy, with older subjects being affected by decreased visual acuity more than younger
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subjects, and younger subjects being affected by increased straylight compared with older subjects. After DSEK, mean visual acuity and straylight improved, but the improvement in straylight was greater in younger subjects than in older subjects. This study is important because it corroborates anecdotal clinical experiences that some younger patients with Fuchs’ dystrophy can have symptoms of increased straylight despite having good visual acuity and that endothelial keratoplasty can be a reasonable treatment to improve straylight.

Quality of vision (CDVA and straylight) of the subjects with Fuchs’ endothelial dystrophy was similar between the Amsterdam and Mayo groups (Table 5.1). Younger subjects with Fuchs’ dystrophy with decreased quality of vision often maintained good CDVA but suffered from increased straylight compared with that of age-matched normal subjects. Although increased straylight has typically been associated with scattered light induced by lenticular changes and cataract,7,8,24 these changes are typically not advanced in younger subjects. In Fuchs’ dystrophy, because the anterior and posterior cornea are a significant source of scattered light,10 increased straylight in the younger subjects probably resulted from the abnormal cornea, explaining why these subjects might be bothered by symptoms of poor contrast and glare. In contrast, our results indicated that quality of vision in the older subjects with Fuchs’ dystrophy was impaired by decreased visual acuity because straylight was similar to that of age-matched normal subjects. However, because many of the older subjects in this study had cataracts sufficient to degrade visual acuity and straylight,5,7,8 separating the visual degradation caused by cataract versus Fuchs’ dystrophy in these eyes was not possible. Nevertheless, that straylight in the pseudophakic eyes with Fuchs’ dystrophy in our study was higher than that of otherwise normal pseudophakic eyes8 (Figure 5.3) is further evidence that increased straylight can at least partly be attributed to the cornea in Fuchs’ dystrophy.

Straylight and CDVA significantly improved after DSEK, and the improvement was greater in patients with poorer preoperative straylight and visual acuity. Visual recovery after DSEK is limited in part by the surgical lamellar interface and chronic host corneal changes associated with longstanding endothelial dysfunction.10-12 Of interest, the improvement in straylight from before DSEK to 12 months after DSEK was greater with younger recipient age (Figure 5.4), further indicating the importance of straylight in younger subjects with Fuchs’ dystrophy and suggesting that repair of the host stroma after DSEK is quicker in younger corneas.9,10 In addition, we found that postoperative straylight was likely to improve when preoperative straylight was higher than 1.33 log(\(s\)), regardless of the preoperative lenticular status. Thus, straylight is a useful clinical metric to help determine the timing of surgical intervention and can be especially helpful in younger symptomatic subjects with Fuchs’ dystrophy whose CDVA is close to 20/20. Straylight can be measured easily and quickly in clinical practice, and the data were remarkably similar at
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the two different institutions in this study, indicating the reproducibility of the measurement and applicability to clinical practice or even multicenter studies. The relationship between postoperative improvement in straylight and preoperative straylight was more predictable than that for CDVA; while CDVA remains an important determinant of when to offer surgical intervention for Fuchs’ dystrophy, straylight can be a useful additional test in many cases.

The distribution of corneal thickness was similar between the Amsterdam and Mayo groups. Although there were significant correlations between central corneal thickness and CDVA in both groups, the predictive value ($r^2 = 0.07$) was low, indicating that quality of vision cannot be judged from central corneal thickness. Seitzman et al. also found that decreased CDVA was associated with increased corneal thickness in patients with Fuchs’ dystrophy, with particular deterioration of CDVA when corneal thickness exceeded 640 µm.

In summary, the subjects with Fuchs’ endothelial dystrophy in the Amsterdam and Mayo groups experienced remarkably similar quality of vision. CDVA, straylight and central corneal thickness were all comparable between these two groups. Consequently, the conclusions drawn for the postoperative Mayo subjects may also be valid for the Amsterdam subjects. Straylight symptoms dominate visual impairment in younger patients with Fuchs’ dystrophy, even in the presence of acceptable visual acuity. Because straylight and CDVA are two separate aspects of visual function, straylight is a useful independent measurement of visual function and easily measured in the clinic.
REFERENCES
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