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The impact of corneal guttata on the results of cataract surgery

Andreas Viberg, MD, Per Liv, PhD, Anders Behndig, MD, PhD, Mats Lundström, MD, PhD, Berit Byström, MD, PhD

Purpose: To study the impact of corneal guttata on postoperative visual acuity and patients’ self-assessed visual function after cataract surgery.

Setting: Patient data from 49 Swedish cataract surgery units.

Design: Retrospective cross-sectional register-based study.

Methods: Data from patients who had cataract surgery from 2010 to 2017 and completed the Catquest-9SF questionnaire were obtained from the Swedish National Cataract Register. Logistic proportional odds regression was used to model the impact of corneal guttata on the visual acuity and self-assessed visual function. Adjustments were made for age, sex, ocular comorbidities, days to follow-up, preoperative corrected distance visual acuity (CDVA) and preoperative Rasch person score. The main outcome measures were postoperative CDVA and Rasch person score calculated from the Catquest-9SF questionnaire.

Results: The study comprised data from 33,741 patients. Cataract surgery greatly improved CDVA and self-assessed visual function in patients both with and without corneal guttata. Still, corneal guttata was significantly associated with a poorer visual acuity and a worse self-assessed visual function after cataract surgery. The negative effect of corneal guttata on visual acuity was most prominent during the first 3 weeks postoperatively, but it persisted at least 3 months postoperatively.

Conclusions: Patients with corneal guttata benefit substantially from cataract surgery but have an additional risk for inferior results compared with patients without corneal guttata. These findings could serve as valuable tools in clinical practice, in particular, when deciding to perform cataract surgery and how to inform the patient about surgical benefits and risks.

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A cataract extraction is the most common surgical procedure in Sweden today with over 115,000 operations yearly. The Swedish National Cataract Register (NCR) covers over 97% of all cataract surgeries performed in Sweden where phacoemulsification is the technique used in 99% of cases. Although the results are good and improving, and the complications are low and decreasing, some risks remain and must be taken into consideration.

For the patient-reported outcome measure, the NCR uses the Catquest-9SF questionnaire, which includes 9 questions (items) constructed with Rasch analysis (Figure 1). Rasch analysis assumes a probabilistic relationship between person ability (eg, patient ability) and item difficulty (eg, question difficulty). The Rasch-revised Catquest-9SF questionnaire has shown a very good responsiveness for measuring visual disability outcomes after cataract surgery.

The corneal endothelium is the innermost layer of the cornea and has a key function in keeping the cornea transparent by its pump function. Primary central corneal guttata is associated with abnormal excrescences of basement membrane and fibrillar collagens produced by distressed endothelial cells. The prevalence of corneal guttata in the population varies in studies from 4.1% to 11%. The variation might result from different populations’ classification criteria and that many elderly patients with corneal guttata might have been classed as normal for age. Age, female sex, thinner corneas, and smoking increase the risk for corneal guttata. Corneal guttata can lead to lower cell density and cell size variation, but...
Figure 1. The Catquest-9SF questionnaire.

A. Do you experience that your present vision is giving you difficulty in any way in your everyday life?

<table>
<thead>
<tr>
<th>Yes, very great difficulties</th>
<th>Yes, great difficulties</th>
<th>Yes, some difficulties</th>
<th>No, no difficulties</th>
<th>Cannot decide</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

B. Are you satisfied or dissatisfied with your present vision?

<table>
<thead>
<tr>
<th>Very dissatisfied</th>
<th>Rather dissatisfied</th>
<th>Fairly satisfied</th>
<th>Very satisfied</th>
<th>Cannot decide</th>
</tr>
</thead>
<tbody>
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<td></td>
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</tbody>
</table>

C. Do you have difficulty with the following activities because of your vision? If so, how much? In each row, mark only one cross, in the square you think agrees best with reality.

<table>
<thead>
<tr>
<th>Reading text in the daily paper</th>
<th>Recognise the faces of people you come across</th>
<th>See prices when shopping</th>
<th>Seeing to walk on uneven ground</th>
<th>See to do handwork, woodworking, etc.</th>
<th>Reading text on TV</th>
<th>See to carry on an activity/hobby you are interested in</th>
</tr>
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<tr>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

Many thanks for your help!

The Catquest-9SF questionnaire.

PATIENTS AND METHODS

This retrospective cross-sectional study involves data from 49 Swedish cataract surgery units. The regional ethics committee and the Swedish Data Inspection Board approved the study, which was performed according to the tenets of the Declaration of Helsinki. In the NCR, an evaluation of the cataract surgery results including visual acuity and self-assessed visual function is performed every year in the month of March. In the present study, 34,074 patients who had cataract surgery from March 2010 through 2017 were initially included. Of these, 190 were excluded because of extensive missing data. Moreover, 143 patients had both eyes operated during this period. Because of the low number of repeated surgeries on the same patient, 1 eye of each of these patients was randomly selected to be included in the analysis, thereby obtaining unrelated samples. After these procedures, data from 33,741 patients remained for the analysis.

The variables available from the NCR are surgery clinic, personal identity number, age, sex, preoperative CDVA in the surgical eye, preoperative keratometry values, planned refraction, axial length, the intraocular lens formula used, preoperative CDVA in the fellow eye, ocular comorbidity, perioperative details and complications, and the preoperative Rasch person score (Table 1). The ocular comorbidity including presence of corneal guttata was reported by the operating surgeon by ticking yes or no in a form based on clinical examination. No information on the severity of the corneal guttata or presence of corneal edema was available. The follow-up was scheduled 1 month postoperatively, but with a range of 0 to 268 days after surgery. The variables available from the NCR from the follow-up visit are date, postoperative intraocular pressure, CDVA, refraction, and ocular comorbidity. The CDVA was converted into logarithm of the minimum angle of resolution (logMAR). As a patient-reported outcome measure, the self-assessed visual function was measured with Catquest-9SF questionnaire preoperatively and 3 months postoperatively. Rasch analysis was used to convert the ordinal raw data from the questionnaire into a Rasch person score, with an interval level measurement called logit unit. A logit is the natural log-odds of a respondent’s successful completion of an item versus unsuccessful completion. A positive logit score indicates that the level of ability is lower than the mean required level of difficulty for the items. If a logit score is negative, the perceived level of ability is higher than the average required level of difficulty. Preoperative and postoperative Rasch person scores were calculated for each patient.

Statistical Analyses

Descriptive data were analyzed using the Pearson chi-square test and the Mann-Whitney U test. Because the distributional form of both postoperative CDVA and the Rasch person score variables were markedly non-normal and no suitable transformation was found, a logistic proportional odds-regression model was used to model corneal guttata’s relationship to both variables, respectively. The postoperative CDVA was cut into intervals ranging from less than –0.2 to more than 2, in steps of 0.05 logMAR to form an ordered categorized dependent variable, with corneal guttata as the independent variable. The statistical model was adjusting for sex, glaucoma, age-related macular degeneration, diabetic retinopathy, time to follow-up, age, and preoperative CDVA, and data from the Swedish Cornea Register. The current study aimed to evaluate the impact of corneal guttata on the change in visual acuity and perceived visual function and satisfaction after cataract surgery with a great sample size enabled by the NCR. Simply put, the study sought to determine the risks and benefits for patients with corneal guttata undergoing cataract surgery.
where the latter 3 terms were modeled using cubic restricted splines with 5 knots at the 0.05, 0.275, 0.5, 0.725, and 0.95 quantile of their corresponding variable. Restricted cubic splines allow nonlinear effects on the dependent variable. The model includes the interaction between the variable corneal guttata and time to follow-up.

The postoperative Rasch person score was cut into intervals ranging from less than −6.4 to more than 4.1, in steps of 1. This variable was modeled as described for postoperative CDVA, except that it was not adjusted for time to follow-up and it was adjusted for the preoperative Rasch person score rather than preoperative visual acuity, also using restricted cubic splines. Logistic regression was used to model the relationship between guttata and a deteriorated result in visual acuity and Rasch person score. A difference between postoperative and preoperative status above 0 logMAR in CDVA and at least 1 logit in Rasch person score was considered a falling result.

The data were analyzed using SPSS Statistics for Mac software (version 24.0, IBM Corp.) and the computing environment R (R Development Core Team). Differences with a $P$ value less than 0.05 were considered statistically significant.

**RESULTS**

**Postoperative Visual Acuity**

The study comprised data from 33,741 patients, of which 893 (2.6%) had corneal guttata. Patients with corneal guttata improved in CDVA after cataract surgery ($P < .001$) as did patients without corneal guttata who improved in CDVA after cataract surgery ($P < .001$) (Table 1). Corneal guttata was significantly associated with a higher logMAR category (ie, poorer visual acuity) after cataract surgery, with an adjusted odds ratio (OR) 1.74 (95% confidence interval [CI], 1.33-2.26; $P < .001$) at the median time to follow-up (33 days) (Figure 2). The adjusted cumulative probability distribution in Figure 3 shows the postoperative probability of being in each logMAR interval, adjusted to a patient with median values of covariates and mode values of factors (see Table 1).

In total, 1113 (3.3%) of all 33,741 patients had a worse CDVA after the cataract surgery than before. Fifty-two (5.8%) of the 893 patients in the group with corneal guttata had a worse CDVA after cataract surgery compared with 1051 (3.2%) of the 32,848 patients in the group without corneal guttata ($P < .001$). The adjusted OR for a patient with corneal guttata to have a deteriorated result in CDVA after the surgery was 2.09 (95% CI, 1.53-2.87; $P < .001$).

**Effect of Time to Follow-up on Visual Acuity**

The median time to the follow-up examination for patients with corneal guttata was 36 days, and for patients without guttata, 33 days ($P = .004$). Because the time to follow-up was modeled using nonlinear effects, its effect cannot be reported as an OR. Figure 4 shows the predicted probability of having a postoperative visual acuity worse than the median (logMAR > 0.05) as a function of time to follow-up for patients with or without corneal guttata. The difference in probability between the groups was greatest within the first three weeks, but a difference remained throughout the range of time to follow-up (Figure 4).

**Postoperative Self-Assessed Visual Function**

Patients with and without corneal guttata improved in the Rasch person score after cataract surgery ($P < .001$) (Table 1). Corneal guttata was significantly associated with inferior postoperative self-assessed visual function; that is, patients with corneal guttata had a higher postoperative Rasch person score, with an adjusted OR of 1.22 (95% CI, 1.08-1.37; $P = .001$) (Figure 5). Figure 6 shows the adjusted cumulative probability distribution for a patient to end up at least in a postoperative Rasch person score. Patients with corneal guttata had a lower probability to achieve results as good as patients without corneal guttata ($P = .001$).

In total, 1181 (3.5%) of the 33,741 patients had a worsening by at least 1 logit in self-reported visual function approximately 3 months after cataract surgery. Of the 893 patients in the group with corneal guttata, 42 patients (4.7%) had a worsening by at least 1 logit after cataract surgery, with no significant difference compared with the 1150 (3.5%) of the 32,848 patients in the group without corneal guttata ($P = .063$). There was a significant association between having corneal guttata and having an increased Rasch person score of more than 1 logit after the surgery, with an adjusted OR of 1.51 (95% CI, 1.09-2.08; $P = .025$).

**Other Associations With Corneal Guttata**

In female patients with corneal guttata, the median axial length was 23.25 mm compared with 23.36 mm in female patients without corneal guttata ($P = .004$) (Table 1). There was no statistically significant difference in axial length among men when comparing the group with corneal guttata with the group without ($P = .94$). The axial length data were available from year 2013 to 2017. The absolute biometry prediction error for patients with corneal guttata was 0.31 diopter (D) and 0.27 D for patients without corneal guttata ($P < .001$). The biometry prediction error with correct sign indicates the direction of the error (Table 1). The prevalence of glaucoma was slightly lower in the corneal guttata group compared with the group without corneal guttata, but the difference was not statistically significant ($P = .08$).

**DISCUSSION**

Cataract surgery affects the endothelial cells in both patients with and without corneal guttata with a risk for corneal edema, decompensation, and a decrease in visual acuity.11–22,26 Still, previous studies with smaller sample sizes show a modest effect on postoperative results and corneal parameters after cataract surgery when comparing patients with and without corneal guttata.11,18,19 This study aimed to examine the impact of corneal guttata on the results of cataract surgery with a greater sample size, addressing questions that clinicians struggle with in their everyday practice: Do the patients with corneal guttata improve in CDVA and self-assessed visual function after cataract surgery? Are patients with corneal guttata prone to have an
inferior result and what are the risks and benefits for patients with corneal guttata to undergo cataract surgery?

The major findings of the present study regarding cataract surgery and guttata are:

- Cataract surgery greatly improves CDVA and self-assessed visual function in the majority of patients both with and without corneal guttata.
- Still, corneal guttata is significantly associated with patients who have both inferior and worsened CDVA after cataract surgery in comparison to patients without corneal guttata.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Corneal Guttata</th>
<th>No Corneal Guttata</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex, n (%)</td>
<td>600 (67.2)</td>
<td>19 808 (60.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Median age, y (IQR)</td>
<td>76 (11)</td>
<td>75 (11)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Right eye, n (%)</td>
<td>476 (53.3)</td>
<td>16 834 (51.2)</td>
<td>.23</td>
</tr>
<tr>
<td>Diabetic retinopathy, n (%)</td>
<td>29 (3.2)</td>
<td>1328 (4.0)</td>
<td>.27</td>
</tr>
<tr>
<td>AMD, n (%)</td>
<td>153 (17.1)</td>
<td>5183 (15.8)</td>
<td>.30</td>
</tr>
<tr>
<td>Glaucoma, n (%)</td>
<td>65 (7.3)</td>
<td>2972 (9.0)</td>
<td>.08</td>
</tr>
<tr>
<td>Median preop CDVA logMAR (IQR)</td>
<td>0.40 (0.22)</td>
<td>0.30 (0.22)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Median postop CDVA logMAR (IQR)</td>
<td>0.10 (0.22)</td>
<td>0.00 (0.15)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Median preop Rasch person score (IQR)</td>
<td>−0.14 (2.52)</td>
<td>−0.18 (2.71)</td>
<td>.005</td>
</tr>
<tr>
<td>Median postop Rasch person score (IQR)</td>
<td>−3.16 (3.78)</td>
<td>−3.35 (3.17)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Median days to follow-up (IQR)</td>
<td>36 (40)</td>
<td>33 (36)</td>
<td>.004</td>
</tr>
<tr>
<td>Median axial length (mm) (IQR)*</td>
<td>23.47 (1.39)</td>
<td>23.58 (1.30)</td>
<td>.003</td>
</tr>
<tr>
<td>Female sex</td>
<td>23.25 (1.35)</td>
<td>23.36 (1.33)</td>
<td>.004</td>
</tr>
<tr>
<td>Male sex</td>
<td>23.85 (1.45)</td>
<td>23.87 (1.34)</td>
<td>.94</td>
</tr>
<tr>
<td>Median AbsBPE* (D) (IQR)</td>
<td>0.31 (0.49)</td>
<td>0.27 (0.40)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.32 (0.49)</td>
<td>0.27 (0.40)</td>
<td>.002</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.30 (0.48)</td>
<td>0.27 (0.40)</td>
<td>.03</td>
</tr>
<tr>
<td>Median BPESign* (D) (IQR)</td>
<td>+0.01 (0.62)</td>
<td>0 (0.54)</td>
<td>.16</td>
</tr>
<tr>
<td>Female sex</td>
<td>+0.01 (0.64)</td>
<td>0 (0.56)</td>
<td>.01</td>
</tr>
<tr>
<td>Male sex</td>
<td>+0.01 (0.59)</td>
<td>+0.03 (0.55)</td>
<td>.64</td>
</tr>
</tbody>
</table>

AbsBPE = absolute biometry prediction error; AMD = age-related macular degeneration; BPESign = biometry prediction error with correct sign; CDVA = corrected distance visual acuity; IQR = Interquartile range; logMAR = logarithm of the minimum angle of resolution.

*Data from year 2013 to 2017

- Corneal guttata is significantly associated with both inferior self-assessed visual function and a worsening in self-assessed visual function of at least 1 logit after cataract surgery.

**Figure 2.** Adjusted associations between patient factors and being in a higher postoperative logarithm of the minimum angle of resolution category. Corneal guttata was also adjusted for the median time to follow-up (33 days). The odds ratios for age and preop CDVA where calculated from the first and third quartile. Note that patients with corneal guttata were associated with a higher logMAR category (worse CDVA) after cataract surgery than patients without corneal guttata (AMD = age-related macular degeneration; CDVA = corrected distance visual acuity).

**Figure 3.** The adjusted cumulative probability distribution showing the probability of at least have the postoperative logMAR result in each interval of postoperative CDVA. The x-axis has an ordinal scale where intervals without data are not included in the graph. Note that patients with corneal guttata have a lower probability to achieve CDVA as good as patients without guttata (CDVA = corrected distance visual acuity; logMAR = logarithm of the minimum angle of resolution).
Corneal guttata has been reported to affect visual acuity negatively post-cataract surgery in comparison to patients without corneal guttata.

- The negative effect of corneal guttata on visual acuity is most prominent close to the surgery, diminishes during the first 3 weeks, but still persists at least 3 months after surgery.

The probability of an inferior result within the first 3 weeks in the guttata group supports that the decision for corneal transplantation should be postponed at least 3 weeks after the cataract surgery in these patients.

This study has several strengths, and the large number of patients with corneal guttata resulted in high statistical power in all analyses. The small group differences and effects were possible to detect, making it important to evaluate the effect size and its clinical value. The NCR receives data from the entire nation of Sweden and thereby comprises practically all cases operated in Sweden. This made the study less biased by local and regional variations. The present study measured the outcome in CDVA as well as the patients’ self-assessed visual function with Catquest-9SF questionnaire, a tool known to be good for evaluating the outcomes of cataract surgery.

A limitation in the current study is that corneal guttata is not a validated variable in the NCR. It is registered by the surgeon mainly based on the medical journal from a previous examination or at the day of the surgery. The frequency of corneal guttata is lower in this study (2.6%) compared with other studies, and can probably be explained by missed reporting of corneal guttata to the NCR. Errors in the reporting of corneal guttata can both underestimate its effect on cataract surgery by increased false-negative corneal guttata cases and overestimate the effect with a potential concentration of the most severe and most obvious form of corneal guttata and FECD as true positive.
Additional variables, such as a categorization of the severity of the corneal guttata, presence of cornea edema, preoperative and postoperative endothelial cell density and perioperative management (for example phacoemulsification time and the use of ophthalmic vicsosurgical devices) would have been desirable but was not available in the NCR for the present study.

The negative effect of corneal guttata on CDVA and self-assessed visual function is seen when adjusting for known confounders and preoperative function, which indicates that not only the preoperative corneal guttata per se affects the inferior results but also a deterioration of the corneal guttata associated with the cataract surgery. The impact of corneal guttata on the self-assessed visual function is statistically significant but mild, and its clinical value is uncertain. A 2.27 logit change in Rasch person score is considered a reliable clinical change in previous validation studies, but the minimum important difference is uncertain.

In conclusion, this present study shows that the majority of the patients with corneal guttata benefit from cataract surgery and might not require a corneal transplantation. With this in mind, it seems clinically reasonable to start with cataract surgery in most cases, which is already widely adopted. Still, some of the patients who undergo cataract surgery will later require corneal transplantation. Despite the findings of the present study, the extent to which corneal guttata in conjunction with cataract surgery affects the risk for future corneal transplantation is still unknown and further research is required to clarify this.

WHAT WAS KNOWN
- Corneal guttata has a small temporary, if any, effect on the result and on corneal status after cataract surgery.

WHAT THIS PAPER ADDS
- Knowledge from a large population study showing that:
  - Patients with corneal guttata benefit from cataract surgery.
  - However, corneal guttata is associated with inferior results in both visual acuity and patient self-assessed visual function in comparison to no corneal guttata.
  - Not only the preoperative corneal guttata per se affects the inferior results but also a deterioration of the corneal guttata associated with the cataract surgery.
  - The negative effect of corneal guttata on visual acuity is most prominent during the first 3 weeks after surgery and persists at least for 3 months.

REFERENCES


**OTHER CITED MATERIAL**


B. Byström B. Personal communication, August 23, 2018.

**Disclosures:** None of the authors has a financial or proprietary interest in any material or method mentioned.

**First author:** Andreas Viberg, MD

Department of Clinical Science/Ophthalmology, Umeå University, Umeå, Sweden