Course of exfoliation and simplex glaucoma after primary trabeculectomy

Vladislav Popovic, Johan Sjöstrand

Abstract

**Aim**—To study the course of exfoliation and simplex glaucoma with respect to intraocular pressure (IOP) regulation and visual field survival after primary trabeculectomy.

**Methods**—Postoperative IOP regulation and complications were analysed prospectively in 95 patients. Mean follow up was 46 months. Visual field survival was studied by high pass resolution perimetry (HRP) in a subsample of 28 patients.

**Results**—Medical treatment was reinstated in 42% of exfoliation and in 36% of simplex glaucoma. In these patients, mean medicine free survival time, last untreated IOP, and mean IOP at the end of follow up were similar for both glaucoma types. Among patients with controlled postoperative IOP without added medication, mean IOP at the end of follow up was significantly lower in exfoliation glaucoma. Visual field deterioration and the pattern of complications were similar for both glaucoma types.

**Conclusion**—The effect of trabeculectomy on IOP regulation was good in both types of glaucoma, and somewhat better in exfoliation glaucoma. The magnitude of IOP lowering could not separate patients with continued visual field deterioration from those in whom visual fields remained stable. Visual field preservation was similar for both glaucoma types.

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was fashioned and a 0.3 mm thick limbus
based trapezoid or rectangular scleral flap was
raised. Paracentesis was done at the 9 o'clock
position; a little volume of the aqueous escaped
without visible shallowing of the anterior
chamber. In this way the risk for hasty IOP
decrease and flattening of the anterior chamber
during the next phase is minimised. The ante-
rior chamber was then penetrated under the
scleral flap and an approximately 1 x 3 mm
block of limbal tissue was excised. Basal iridec-
tomy was performed and the scleral flap was
reposed in two ways. In the first 60 operated
patients the scleral flap was secured with two to
four isolated 10-0 nylon sutures, and in the last
35 patients with two isolated and one
U-shaped releasable suture. In the first 48
operated patients the conjunctiva was sutured
with one single 10-0 nylon suture at each end
of the incision, while a continuous suture was
used to secure the conjunctival incision in the
last 47 patients. No antimetabolite therapy was
used. Postoperatively all patients were treated
with topical dexamethasone (Isopto-Maxidex)
three to four times daily for 5–6 weeks and
atropine (Isopto-Atropine) twice daily for
about 3 weeks. The first postoperative control
for all patients was on the first postoperative
day. If no serious complication was noted on
this visit, the next two visits were planned 1 and
3 weeks after operation for patients operated
on without releasable scleral flap sutures; for
patients in whom these sutures were used, one
extra control was planned on the fourth
postoperative day.

All patients were followed up prospectively.
Data were collected concerning patients’ age,
sex, glaucoma type, preoperative treatment as
well as IOP, best corrected monocular visual
acuity (VA) expressed as the minimum angle
of resolution (MAR), occurrence of cataract,
and results of visual field investigation before
operation. Postoperatively, IOP, visual acuity,
results of visual field investigation, and develop-
ment of early and late complications were
noted. Identification of the glaucoma type was
made clinically by preoperative slit lamp inves-
tigation in mydriasis and by gonioscopy. Exfo-
liation glaucoma was diagnosed if exfoliation
material was seen on the corneal endothelium,
iris surface, angle structures of the anterior
chamber, pupillary margin, or lens capsule. No
histopathological analysis of iris specimens was
done.

The term primary trabeculectomy designates
the first operation. Preoperative IOP refers to an
average of the last three preoperative
IOP measurements. IOP at last visit refers to
an average of the last three postoperative
measurements. An assessment of cataract
grade from an early stage (the margin of the
optic disc was clearly seen) to more advanced
stages was made clinically (by slit lamp investi-
gation and ophthalmoscopy with a dilated
pupil) and all but the early stage were excluded
from the visual field analysis.

Visual field was investigated by manual
Goldmann perimetry or one of the two
computerised perimetry techniques—namely,
high pass resolution perimetry (HRP) (High-
Tech vision SCI AB, Göteborg, Sweden) and
Competer (Bara Elektronik, Lund, Sweden).
Of the computerised methods we preferred
HRP perimetry and tried to use the same peri-
metry technique as long as possible during fol-
low up of every patient. However, patients with
extensive field defects and patients who did not
cooperate in any of the computerised methods
were tested with Goldmann perimetry. No
selection of different methods on the basis of
glaucoma type or for other reasons (e.g., age)
was made. Of all patients in the study,
visual field was investigated with HRP tech-
nique in 45%, Competer was used in 12%,
Goldmann perimetry in 32%, and in 11% the
perimetry technique at and after operation
was not uniform.

Twenty eight of the patients in the study
tested with HRP perimetry were chosen for
analysis of visual field survival after operation.
The inclusion criteria for visual field analysis
were as follows: visual field investigation with
HRP both at operation and during postoperative
follow up; minimum field follow up 12
months; and minimum of two postoperative
field investigations. Excluded from this study
were patients with age related macular degen-
eration and patients with cataract denser than
that of an early stage. However, cases which
underwent cataract operation after trabeculec-
tomy were again included in the follow up
analysis. Mean follow up of visual fields after
operation was 45.7 (SD 16.4) months (mini-
imum 16, maximum 82 months). Investigation
of visual field was performed on average 3.3
(range 2–6) times after operation.

Postoperative changes in global deviation
(GD) and neural capacity (NC) were studied.
GD is the mean deviation from the normal
threshold values over all tested points, and is an
indicator of severity of overall visual field deter-
riation. It is expressed in decibels (dB). NC is
based upon the linear relation between the
HRP thresholds expressed as MAR and retinal
ganglion cell separations.1 NC is expressed in
percentage of average normal.

Data are expressed as mean (SD) (Tables
1–4). The t test, Fisher’s exact test, $\chi^2$
test, multiple variable correlation, and Kaplan–
Meier analysis were used for statistical analysis.

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**Table 1 Patients’ characteristics at operation according to glaucoma type**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Exfoliation glaucoma</th>
<th>Simplex glaucoma</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (n):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21</td>
<td>24</td>
<td>0.102*</td>
</tr>
<tr>
<td>Female</td>
<td>32</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Age (years) (SD)</td>
<td>73.7 (8.3)</td>
<td>69.2 (9.1)</td>
<td>0.014†</td>
</tr>
<tr>
<td>IOP</td>
<td>28.8 (6.1)</td>
<td>24.4 (5.0)</td>
<td>0.000‡</td>
</tr>
<tr>
<td>No of drops</td>
<td>4.0 (1.6)</td>
<td>3.6 (1.3)</td>
<td>0.143‡</td>
</tr>
<tr>
<td>No of medicines</td>
<td>2.4 (0.7)</td>
<td>2.0 (0.9)</td>
<td>0.008‡</td>
</tr>
<tr>
<td>ALT (n):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>36</td>
<td>27</td>
<td>0.828*</td>
</tr>
<tr>
<td>No</td>
<td>17</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Duration to operation (years)</td>
<td>4.9 (3.5)</td>
<td>6.8 (4.5)</td>
<td>0.019†</td>
</tr>
<tr>
<td>LogMAR</td>
<td>0.4 (0.4)</td>
<td>0.3 (0.5)</td>
<td>0.657†</td>
</tr>
<tr>
<td>Cataract (n):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cataract</td>
<td>24</td>
<td>25</td>
<td>0.192‡</td>
</tr>
<tr>
<td>Early stage</td>
<td>28</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Hazy insight</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

p = significance level; IOP = intraocular pressure; ALT = argon laser trabeculoplasty; MAR = minimum angle of resolution; *Fisher’s exact test; †t test; ‡$\chi^2$ test.
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Results
Preoperative characteristics of all patients in the study according to glaucoma type are given in Table 1. Kaplan–Meier survival analysis of medical treatment free time after operation for both glaucoma types is shown in Figure 1. Mean medical treatment free survival time in exfoliation glaucoma was 31.7 (22.8) months, and in simplex glaucoma 32.7 (24.8) months (p=0.835). A reinstatement of medical treatment was done in 42% of patients with exfoliation and in 36% of patients with simplex glaucoma (p=0.673). Two patients with exfoliation and three patients with simplex glaucoma had, in addition, to be operated with new trabeculectomy. In all but three patients medical treatment was introduced owing to an unsatisfactory postoperative IOP level. Preoperative and postoperative characteristics in patients with added medication after operation are shown in Table 2. The IOP at operation, the untreated IOP, and the treated IOP at the end of follow up were similar for both glaucoma types. Among patients without postoperative medication the mean IOP at operation was 28.2 (5.4) mm Hg in exfoliation and 24.8 (3.4) in simplex glaucoma (p = 0.008), and at the end of follow up 14.3 (2.8) mm Hg and 17.0 (3.7) mm Hg (p = 0.002), respectively.

A correlation analysis between the last noted untreated IOP and the different preoperative characteristics (patients' age and IOP at operation, glaucoma type, sex, ALT, number of antiglaucoma eye drops and eye medicines, and length of time from glaucoma diagnosis to operation) was done by multivariate analysis. No significant correlation was found between the untreated IOP and any preoperative variable in patients with added medication after operation. In patients without any postoperative medication a significantly lower untreated IOP was found in exfoliation glaucoma (r = 400, p = 0.002).

The multivariate method was also used for analysis of correlation between the last untreated IOP regulation and the mode of conjunctival and scleral flap sutures. The two variables did not correlate significantly with untreated IOP regulation in any glaucoma type.

Mean age and mean IOP at operation as well as the distribution of glaucoma types were not significantly different between the patients included and patients excluded from visual field analysis. Fifty six per cent of the patients investigated with Goldmann perimetry had absolute central, paracentral, or peripheral scotoma for V-4 object involving central areas to 5 degree from the fixation point. Of these patients about 70% were patients with exfoliation glaucoma. Two patients with simplex glaucoma suffered from marked progress of field defects despite a satisfactory IOP decrease. In one of these patients magnetic resonance tomography showed a cerebral atrophy.

Preoperative characteristics of patients included in the HRP visual field analysis. Fifty six per cent of the patients investigated with Goldmann perimetry had absolute central, paracentral, or peripheral scotoma for V-4 object involving central areas to 5 degree from the fixation point. Of these patients about 70% were patients with exfoliation glaucoma.

Mean change in GD per year of postoperative follow up was 0.16 (0.4) dB for exfoliation and 0.08 (0.4) dB for simplex glaucoma (p = 0.560). At the last visit GD had deteriorated in 63% of patients with exfoliation and in 67% of patients with simplex glaucoma. Figure 2 shows a scatter plot of GD v postoperative follow up time in patients with deteriorating fields of both

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**Table 2** Characteristics of patients with added medication after operation (SD)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Exfoliation glaucoma</th>
<th>Simplex glaucoma</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At operation:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (n):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>10</td>
<td>10</td>
<td>0.175*</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>72.0 (7.8)</td>
<td>69.3 (7.7)</td>
<td>0.309†</td>
</tr>
<tr>
<td>IOP</td>
<td>29.0 (7.3)</td>
<td>29.3 (4.7)</td>
<td>0.877†</td>
</tr>
<tr>
<td>No of drops</td>
<td>4.3 (1.6)</td>
<td>4.3 (1.5)</td>
<td>0.697†</td>
</tr>
<tr>
<td>No of medicines</td>
<td>2.6 (0.6)</td>
<td>2.1 (0.7)</td>
<td>0.070†</td>
</tr>
<tr>
<td>ALT (n):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15</td>
<td>10</td>
<td>0.600*</td>
</tr>
<tr>
<td>No</td>
<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Duration to operation (years)</td>
<td>4.7 (3.2)</td>
<td>8.3 (3.3)</td>
<td>0.002†</td>
</tr>
<tr>
<td>After operation:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Untreated IOP</td>
<td>28.8 (7.3)</td>
<td>31.7 (7.6)</td>
<td>0.232†</td>
</tr>
<tr>
<td>Mean last IOP</td>
<td>18.7 (5.3)</td>
<td>19.3 (2.7)</td>
<td>0.720†</td>
</tr>
<tr>
<td>No of medicines</td>
<td>1.2 (0.9)</td>
<td>1.5 (0.9)</td>
<td>0.340†</td>
</tr>
</tbody>
</table>

p Value = significance level; IOP = intraocular pressure; ALT = argon laser trabeculoplasty; *Fisher’s exact test, †t test.

**Table 3** Characteristics at operation of patients included in the analysis of HRP visual field (SD)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Exfoliation glaucoma (n=16)</th>
<th>Simplex glaucoma (n=12)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>71.5 (7.7)</td>
<td>68.9 (7.7)</td>
<td>0.389</td>
</tr>
<tr>
<td>IOP</td>
<td>31.3 (5.5)</td>
<td>25.0 (2.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>No of medicines</td>
<td>2.7 (0.7)</td>
<td>2.2 (1.1)</td>
<td>0.198</td>
</tr>
<tr>
<td>Duration to operation</td>
<td>4.9 (4.0)</td>
<td>8.2 (5.4)</td>
<td>0.078</td>
</tr>
<tr>
<td>LogMAR</td>
<td>0.2 (0.3)</td>
<td>0.2 (0.3)</td>
<td>0.548</td>
</tr>
<tr>
<td>GD (dB)</td>
<td>3.6 (1.7)</td>
<td>2.9 (1.9)</td>
<td>0.272</td>
</tr>
<tr>
<td>NC (%)</td>
<td>29.5 (19.9)</td>
<td>35.5 (30.0)</td>
<td>0.530</td>
</tr>
</tbody>
</table>

p Value = significance level; IOP = intraocular pressure; MAR = minimum angle of resolution; GD = global deviation; NC = neural channels.

**Table 4** Characteristics at last visit of patients included in the analysis of HRP visual field (SD)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Exfoliation glaucoma (n=16)</th>
<th>Simplex glaucoma (n=12)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow up (months)</td>
<td>46.2 (16.4)</td>
<td>45.0 (17.1)</td>
<td>0.854</td>
</tr>
<tr>
<td>IOP</td>
<td>15.3 (5.1)</td>
<td>17.7 (3.2)</td>
<td>0.166</td>
</tr>
<tr>
<td>IOP reduction (%)</td>
<td>−50.0 (17.0)</td>
<td>−28.7 (13.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Change in GD* (dB)</td>
<td>+0.4 (1.2)</td>
<td>+0.3 (1.5)</td>
<td>0.854</td>
</tr>
<tr>
<td>Change in NC† (%)</td>
<td>+1.6 (13.1)</td>
<td>+3.9 (12.8)</td>
<td>0.638</td>
</tr>
<tr>
<td>Change in logMAR‡</td>
<td>+0.1 (0.3)</td>
<td>0.0 (0.2)</td>
<td>0.181</td>
</tr>
</tbody>
</table>

*Mean postoperative GD = GD at operation; †mean postoperative NC = NC at operation; ‡logMAR at last visit − logMAR at operation.

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Figure 1  Medicine free time after trabeculectomy. Thick line = exfoliation glaucoma, thin line = simplex glaucoma.
glaucoma types. Starting from different levels at base line, the least square fit for the two groups showed a decay with time of a similar magnitude. The linear trend was not significant for any glaucoma type (slope 0.02, p = 0.166 for exfoliation and slope 0.013, p = 0.457 for simplex glaucoma), nor was there significant difference between the trend of the two lines (p = 0.729).

Mean change in postoperative GD per year of follow up v IOP at last visit for all 28 patients is given in Figure 3. Mean IOP at last visit in patients with improved GD was 16.6 (2.1) mm Hg and in patients with deteriorated GD 16.2 (5.4) mm Hg (p = 0.801). Mean percentage of IOP reduction in patients with unchanged/improved and deteriorated GD after operation was 39.5% (13.2%) and 41.7% (21.4%) (p = 0.775), respectively.

Among those with deterioration of GD (n=18) the mean change of NC per year was −1.5% (3.0%) in exfoliation and −0.3% (2.5%) in simplex glaucoma (p = 0.392). Two cases of both glaucoma types showed an anomalous pattern with an improvement of NC (2-3%) in spite of deterioration of GD of in average 0.25 dB.

The pattern of complications was similar in both glaucoma types. The most common complication was cataract progression (60% in exfoliation and 48% in simplex glaucoma, \( \chi^2 = 3.7, p = 0.298 \)). Thirty two per cent of patients with exfoliation glaucoma and 19% of patients with simplex glaucoma were operated for cataract following trabeculectomy. Fisher’s exact test reveals no significant dependence between cataract surgery and glaucoma types (p=0.164). In relation to sex, cataract surgery was performed in 29% of males and in 24% of females (p = 0.820).

**Discussion**

The rates of exfoliation (56%) and simplex glaucoma (44%) in the present study are similar to the rates of these glaucoma types in a previous study from Scandinavia.\(^1^1\) The higher rates of exfoliation glaucoma in these two Scandinavian studies in comparison with the study of Konstas et al\(^1^2\) may indicate regional differences in prevalence of the two glaucoma types.

In comparison with simplex glaucoma (Table 1), patients with exfoliation glaucoma were older and suffered from more aggressive glaucoma before the operation. The aggressiveness of exfoliation glaucoma is reflected by a higher IOP, more topical antiglaucoma drugs, and a shorter duration to operation. The shorter duration to operation in exfoliation glaucoma was again demonstrated in patients with added medication after operation (Table 2) and the higher preoperative IOP in the subsample of patients who underwent visual field analysis (Table 3).

Concerning IOP regulation after operation, two groups of patients were identified. The first group consists of patients with need for addition of medication after operation to achieve satisfactory IOP regulation. In these patients the mean IOP at operation, the last noted postoperative untreated IOP, and the mean IOP at the end of follow up were similar for both glaucoma types. The second group consists of patients in whom the IOP was controlled during the whole postoperative follow up without any added treatment. Among these patients the mean IOP in exfoliation glaucoma was significantly higher at operation and significantly lower at the end of follow up.

In previously published studies on different glaucoma types, the rate of long term IOP control after primary trabeculectomy without antiglaucoma medications, and duration to operation.\(^1^6\) Among other factors, the efficacy of trabeculectomy on IOP regulation in chronic open angle glaucoma may be influenced by patient age, glaucoma types, number of antiglaucoma medications, and duration to operation.\(^1^6\)

There are very few studies in which the effect of trabeculectomy in exfoliation and simplex glaucoma is compared. In the study by Konstas et al\(^1^5\) the untreated IOP was significantly lower in exfoliation than in simplex glaucoma 6 months after operation. Our findings on medicare free time after operation in all patients in the study and untreated IOP regulation among patients with added postoperative medication,
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after on average 46.2 months of follow up, indicate that the effect of trabeculectomy alone is similar for both glaucoma types (Table 2, Fig 1). However, the IOP regulation in patients without any medication postoperatively was in agreement with the results in the above cited study.12

Visual field examination has an essential role in diagnosis and follow up of glaucoma. Results are influenced by many factors—for example, patient age, media opacities, visual acuity, perimeter technique, patient reliability, and selection of subsample. In the subsample of patients who underwent visual field analysis in the present study, perimeter was performed by HRP; a technique found to be comparable with Humphrey perimetry in detection and follow up of glaucomatous visual field defects.19 20 To minimise the influence of cataract on visual field results we excluded from the analysis all visual fields of patients with cataract denser than early stage opacities. Other factors that may affect the calculation of the deterioration during follow up may be the effect of training or the effect of aging as described by Martin and Wanger21 using the same perimetric methodology. The effect of age, however, is adjusted in the calculation of GD.22 About two thirds of the cases showed visual field deterioration in both types of glaucoma. The magnitude of GD deterioration per year was higher (eight times in exfoliation and four times in simplex glaucoma) than the expected age related deterioration. In a 5 year follow up of cases on medical antiglaucoma treatment, Martin and Wanger21 found that 45% deteriorated and that the visual field deterioration was on average 0.41 db per year—that is, more than 20 times the expected age related deterioration.

The lower rates of field deterioration in our study cannot be explained by more efficacious IOP lowering in comparison with the above cited study. The findings that the average IOP was at the same level (about 16 mm Hg) in the group with and without visual field deterioration, and that GD change per year was unrelated to IOP level or IOP reduction, indicate that factors other than IOP affect visual field decay.

Martin and Wanger21 found that the visual field deterioration was preceded by a transient improvement during the first 2 years after the initiation of antiglaucoma treatment. This effect was rare in our study and was noted only at the first postoperative investigation in a few patients with continued field loss. This may be explained by the fact that none of our patients had newly diagnosed glaucoma, and all were used to visual field investigation from the time before trabeculectomy.

In HRP NC generally increases when the GD level decreases and vice versa. GD is an index that reflects the state of the whole field inside 30 degrees, both within its central and peripheral part. NC accounts for changes mostly in the central part of the visual field owing to the fact that most of the neural channels are located centrally.13 The difference between the two indices may explain the finding of obvious deterioration of GD associated with improvement of NC in some patients. In these patients the most central part of the visual field remained stable while the peripheral part deteriorated.

In our study the treated IOP at last visit was better controlled in exfoliation than in simplex glaucoma. However, the untreated IOP and visual field survival were similar for both types of glaucoma. Therefore, the present study does not support the findings in the study of Törnqvist and Drolsum,11 in which the trend for progression of visual field decay and optic disc changes after operation was significantly lower in patients with exfoliation than in patients with simplex glaucoma. However, the results in these two studies may not be fully comparable owing to difference in outcome measures.

Cataract progression was found to be the most common late complication after trabeculectomy, in agreement with previous reports.23 24 In the study of Vesti25 cataract was more accelerated in exfoliation than in primary open angle glaucoma. The criteria for acceleration of cataract in the above cited study26 were the number of cases with cataract extraction, the shift of refraction to myopia, and increase in the lens opacity value measured with a Lens Opacity Meter 701. In the present study cataract progression was assessed by slit lamp investigation and ophthalmoscopy with a dilated pupil and the rates for progression were not significantly different between the two glaucoma types.

In summary, patients with exfoliation glaucoma were older and suffered from more aggressive glaucoma before operation compared to patients with simplex glaucoma. The IOP lowering effect of trabeculectomy alone was similar for both types of glaucoma. A good IOP regulation did not always imply a successful operation with respect to visual field survival. The visual field survival was similar for both glaucoma types.

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