Department of Ophthalmology
University of Helsinki
Head: Professor Tero Kivelä
Helsinki, Finland

Long-Term Outcome of Trabeculectomy in Primary Open-Angle Glaucoma and Exfoliation Glaucoma

by

Pia Ehrnrooth

ACADEMIC DISSERTATION

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SUPERVISED BY:
Professor Leila Laatikainen
Department of Ophthalmology
Helsinki University Central Hospital

Docent Päivi Puska
Department of Ophthalmology
Helsinki University Central Hospital

REVIEWED BY:
Professor Esko Aine
Department of Ophthalmology
Tampere University Hospital

Professor Jost Jonas
Universitäts-Augenklinik
Mannheim
Germany

DISCUSSED WITH:
Docent Marja-Liisa Vuori
Department of Ophthalmology
Turku University Central Hospital

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To my family

Contents

Abbreviations

AC	anterior chamber
AC IOL	anterior chamber intraocular lens
ALT	argon laser trabeculoplasty
BCVA	best corrected visual acuity
CME	cystoid macular edema
ECCE	extracapsular cataract extraction
EG	exfoliation glaucoma
F	female
ICCE	intracapsular cataract extraction
IOL	intraocular lens
IOP	intraocular pressure
LSL	laser suture lysis
M	male
OAG	open-angle glaucoma
PMMA	polymethylmethacrylate
POAG	primary open-angle glaucoma
SD	standard deviation
VA	visual acuity
VF	visual field

Original publications

This dissertation is based on the following original publications, which will be referred to by their Roman numerals I–IV:

I Ehrnrooth P, Lehto I, Puska P, Laatikainen L. Long-term outcome of trabeculectomy in terms of intraocular pressure. Acta Ophthalmol Scand 2002;80:267–271.

II Ehrnrooth P, Lehto I, Puska P, Laatikainen L. Effects of early postoperative complications and the location of trephined block on long-term intraocular pressure control after trabeculectomy. Graefe's Arch Clin Exp Ophthalmol 2003;241:803–808.

III Ehrnrooth P, Puska P, Lehto I, Laatikainen L. Progression of visual field defects and visual loss in trabeculectomized eyes. Graefe's Arch Clin Exp Ophthalmol 2005;243:741–747.

IV Ehrnrooth P, Lehto I, Puska P, Laatikainen L. Phacoemulsification in trabeculectomized eyes. Acta Ophthalmol Scand 2005;83:561–566.

Abstract

During this study, trabeculectomy has been the operation of choice for improving aqueous outflow to decrease intraocular pressure (IOP) in primary open-angle glaucoma (POAG) and exfoliation glaucoma (EG) at the Helsinki University Eye Hospital. This retrospective study was designed to examine long-term IOP control, further progression of visual field (VF) defects and visual impairment, and need for cataract surgery after trabeculectomy, and to evaluate possible factors related to these outcome measures in POAG and EG.

One hundred thirty-eight eyes of 138 consecutive patients over 40 years of age with POAG or EG undergoing trabeculectomies without the use of antimetabolites were studied. All surgeries were performed by one surgeon (I.L.) between November 1994 and August 1996. The mean age of the patients at trabeculectomy was 70.1 years. Of the 138 patients, 83 (60%) were females; 83 eyes (60%) had EG. Mean follow-up was 3.5 years (range 2-5 years). All patients were Caucasian.

Before trabeculectomy, the mean IOP was 24.6 (SD 5.8) mmHg in POAG and 28.0 (SD 11.2) mmHg in EG (p=0.044). At the last examination, the mean IOP in POAG was 16.6 (SD 4.2) mmHg and in EG 17.1 (SD 6.2) mmHg (p=0.95). Success rates for IOP control, without medication (complete success) or with one topical medication (qualified success) in the whole series, were 82% at 1 year, 70% at 2 years, 64% at 3 years, and 52% at 4 years. Rates for complete success were 63%, 54%, 45%, and 40%, respectively. Complete success was significantly more common in POAG than in EG (p=0.04), but when complete and qualified success were combined, the difference between POAG and EG became non-significant.

In EG, the patients were significantly older (p=0.03) and had higher preoperative IOP (p=0.044), and postoperative hyphema was more common (p=0.011), but none of these factors was an independent significant predictor of failure. Insufficient filtration (antiglaucomatous medication) at the end of the first postoperative month predicted long-term failure (p=0.0084).

Of the 83 eyes with comparable pre- and postoperative VF, the preoperative VF defect was considered severe in 33 eyes (40%). In 34 cases (41%), glaucomatous field defects progressed. Severe preoperative VF defect (p=0.0047), preoperative oral glaucoma medication (p=0.047), smaller initial IOP reduction from preoperative to 1-month follow-up (10.9 vs. 15.4 mmHg) (p=0.023), and smaller IOP reduction from preoperative to last postoperative examination (9.2 vs. 12.8 mmHg) (p=0.036) were significantly related to VF progression.

But the mean IOP at the last examination, 16.3 (SD 3.8) mmHg in eyes without progression and 17.6 (SD 7.4) mmHg in eyes with progression (p=0.58), or the mean number of topical antiglaucoma medicines did not differ. The high standard deviation of the mean last postoperative IOP indicates, however, that during follow-up, the IOP had been too high in some eyes that progressed. The prevalence of glaucoma-related low vision had increased from 6% to 7% and that of blindness from 4% to 10% in the operated eye.

During the follow-up of 2 to 5 years, 48 of the 138 eyes (35%) underwent a cataract operation performed 5.1 to 58.1 months (median 14.4 months) after trabeculectomy. Patients undergoing cataract surgery during the follow-up were significantly older (73.9 (SD 9.4) years) at the time of trabeculectomy than those without the operation (68.1 (SD 9.8) years) (p=0.001), and had worse visual acuity before trabeculectomy. At the last examination, the mean IOP 17.3 (SD 6.4) mmHg was not significantly higher than before cataract surgery (p=0.35), but the mean number of topical antiglaucoma medicines had increased significantly to 1.3 (SD 1.1) (p=0.0007). In 41% of the eyes, use of topical antiglaucoma medicines had increased after cataract surgery, although in an eye with good IOP control (complete success), a cataract operation improved the chances that the eye remained a complete success.

These results emphasize the importance of early postoperative control and therapy after trabeculectomy and the regular long-term follow-up of glaucoma patients including VF examinations also in cases with initially successful surgery. Earlier surgery might have improved the outcome. In eyes with good IOP control following trabeculectomy, cataract surgery may not worsen outcome.

1. Introduction

After critical appraisal of the glaucoma literature covering the years 1975 to 2002, the Finnish Glaucoma Guideline Team found ‘strong research-based evidence’ (Level A) for the statement that surgical treatment reduces intraocular pressure (IOP) more than does medical or laser treatment, but gave no strict guidelines based on scientific evidence concerning the type of surgery (Tuulonen et al. 2003).

Since the late 1960’s, trabeculectomy has been the operation of choice for improving aqueous outflow in glaucomatous eyes (Cairns 1968, Watson & Grierson 1981), and trabeculectomy is still regarded as the gold standard to which the newer operations are compared. The long-term successful control of IOP in eyes that have undergone primary trabeculectomy has ranged from 48 to 98%, depending on follow-up time and the criteria used to define successful outcome (Jerndal & Lundström 1979, D’Ermo et al. 1979, Mills 1981, Watson & Grierson 1981, Lamping et al. 1986, Akafo et al. 1992, Vesti 1993, Nouri-Mahdavi et al. 1995, Vesti & Raitta 1997, Jacobi et al. 1999). In most studies, complete success in terms of IOP has been described as an IOP of 21 mmHg or less, without medication. In 1993, Vesti reported a success rate of 74% without glaucoma medication after a mean follow-up period of 3 years in a selected group of Finnish patients. In her study, eyes with long-term miotic therapy and advanced exfoliation glaucoma (EG) were underrepresented.

Glaucoma is one of the main causes of visual impairment in older age groups, in patients aged over 65 years in Finland, it causes 10% of visual impairment (Ojamo 2003). The beneficial effect of reducing IOP by surgery, laser or medical treatment on visual fields (VF) has been shown in several studies (Jay & Murray 1988, Vogel et al. 1990, Mao et al. 1991, Migdal et al.1994, Suzuki et al. 1999, The AGIS Investigators 2000, Leske et al. 2003), but in some eyes the defects progress despite aggressive treatment (Watson et al. 1990, Brubaker 1996). Questions regarding risk indicators for VF defect progression and visual loss and the effect of trabeculectomy on these events in open-angle glaucoma (OAG) have been difficult to answer. Progression rates of VF defects after trabeculectomy have varied considerably, partly due to different criteria of VF loss, partly due to different length of follow-up; the probability of progressive field loss at 5 years’ follow-up has been reported in 27% (Parc et al. 2001), and at 11 to 15 years in 46% (Molteno et al. 1999).

In order to further improve and optimise glaucoma surgery success, the adjunctive use of antimetabolites (The Fluorouracil Filtering Surgery Study Group 1996, Bindlish et al. 2002), drainage device implantation (Wilson et al. 2000), and nonpenetrating glaucoma surgery techniques (Ambresin et al. 2002, Lüke et al. 2002, Carassa et al. 2003) have been investigated. One reason for the development of nonpenetrating surgery is the fairly common occurrence of postoperative complications after trabeculectomy, although effects of complications on the long-term outcome have rarely been reported. Further, the location of the trephined tissue block in the anterior chamber (AC) angle may influence the rate of postoperative complications and the long-term success of IOP control after trabeculectomy.

Numerous studies show that trabeculectomy expedites cataract formation (D'Ermo et al. 1979, Mills 1981, Watson & Grierson 1981, Törnqvist & Drolsum 1991, Akafo et al. 1992, Nouri-Mahdavi et al. 1995, Vesti & Raitta 1997, Popovic & Sjöstrand 1999, The AGIS Investigators 2001). Age, EG, postoperative hypotony, marked inflammation, and shallow or flat AC after trabeculectomy have been considered risk indicators for cataract progression (Mills 1981, Vesti 1993, The AGIS Investigators 2001). The effect of cataract surgery on IOP control in eyes that have undergone trabeculectomy varies because of patient selection and type of cataract surgery.

In the elderly Finnish population (70 years or older), the prevalence of exfoliation syndrome is more than 20% (Krause 1973, Peräsalo & Raitta 1992, Hirvelä et al. 1995), more than half the patients with exfoliation syndrome have glaucoma (Tarkkanen 1962), and about half the patients with OAG have exfoliation (Lindberg 1917, Hirvelä et al. 1995). Comparison of the outcome of trabeculectomy between eyes with primary open-angle glaucoma (POAG) and with EG therefore, warrants special attention.

This study was designed to evaluate the outcome of trabeculectomy retrospectively in a series of consecutive cases of POAG and EG that had undergone primary surgery by a conventional technique without antimetabolites. Conventional trabeculectomy was the technique mainly used for refractory glaucoma at the Helsinki University Eye Hospital at the beginning of this study. Due to the well-known complications of trabeculectomy with antimetabolites (Kitazawa et al. 1991, Borisuth et al. 1999), use of these agents was limited to the high-risk cases, and nonpenetrating surgeries had not yet been introduced in this hospital. The aim was to obtain information on long-term IOP control, on further progression of VF defects and visual impairment, and on the need for cataract surgery after trabeculectomy, and to evaluate possible factors related to these outcome measures in POAG and EG.

2. Review of the literature

2.1 Indications and technique of trabeculectomy

In the literature, indications for glaucoma surgery have generally been failure of the maximal tolerated medication to control IOP or disease progression or both.

In 1961, Sugar described a case of 'experimental trabeculectomy', but for clinical use, trabeculectomy was accepted after the description of the technique by Cairns (1968). In the original technique, guarded by a half-thickness scleral flap, the intention was to excise a short length of the canal of Schlemm, with its trabecular adnexae anterior to the line of the scleral spur, leaving two cut ends opening directly into aqueous humor, with no trabecular tissue remaining as a barrier at that point. Originally, the aim was to relieve trabecular obstruction without intentionally creating external drainage. However, in a series of 80 cases, Cairns (1972) reported 67.5% controlled with a drainage bleb. Nowadays, this partial-thickness filtration operation is considered to reduce IOP via the establishment of a limbal fistula through which aqueous humor drains into the subconjunctival space, establishing a filtering bleb.

Since the original description of trabeculectomy, numerous modifications have been proposed, and some of these have been investigated in intervention studies, these involving more posterior location of the trabeculectomy (Watson 1970), site of surgery (Vesti & Raitta 1992, Sanders et al. 1993), limbus- versus fornix-based conjunctival flap (Shuster et al. 1984, Traverso et al. 1987), partial versus total tenonectomy (Miller et al. 1991), scleral flap size (Starita et al. 1984) and shape (rectangular versus triangular) (Kimbrough et al. 1982), high initial outflow vs standard technique (Batterbury & Wishart 1993), use of a trephine for dissection of trabecular meshwork (Fronimopoulos et al.1970), laser suture lysis to augment filtration when necessary (Hoskins & Migliazzo 1984, Savage & Simmons 1986), releasable sutures (Kolker et al. 1993, Raina & Tuli 1998), needling versus medical treatment in encapsulated blebs (Costa et al. 1997), scleral tunnel incision (Vuori & Viitanen 2001), and use of antimetabolites (5-fluorouracil and mitomycin) to inhibit postoperative fibrosis (The Fluorouracil Filtering Surgery Study Group 1989, The Fluorouracil Filtering Surgery Study Group 1996, Kitazawa et al. 1991, Bindlish et al. 2002). Postoperative steroids have been shown to be beneficial and limit the wound-healing process (Roth et al. 1991, Araujo et al. 1995).

2.2 Outcome of trabeculectomy

2.2.1 Definition of outcome

The aim of glaucoma surgery is to retard or halt glaucomatous VF loss. Interpretation of visual fields and detection of progression is, however, difficult (Werner et al. 1988, Katz et al. 1999, Salim et al. 2001). IOP has thus usually served as a measure of success. Since the presentation of the first trabeculectomy series by Cairns in 1968, the most common criterion for surgical success has been IOP <21 mmHg or ≤ 21 mmHg. In some studies, a proportionate criterion as a reduction in IOP of at least 20% or 33% from the presurgical level has served as an additional criterion for success (Nouri-Mahdavi et al. 1995, Chen et al. 1997, Edmunds et al. 2001), and some studies have used progression of visual field or optic disc defects or both as definition of failure (Törnqvist & Drolsum 1991). Success has been further defined as complete or qualified depending on whether the IOP was controlled without or with postoperative antiglaucoma medication, respectively (Mietz et al. 1999).

2.2.2 Outcome of trabeculectomy in open-angle glaucoma

In the literature, the outcome measures for trabeculectomy and the diagnoses of eyes operated on vary, making comparisons difficult. The definition 'long-term' has been used for follow-up times beginning from 1 year. In the early reports on trabeculectomy, the success rate in POAG ranged from 65% to 83% without medication (Table 1) and from 77% to 98% with the use of additional medical therapy or surgery or both after 1 to 2 years' follow-up (D'Ermo et al. 1979, Watson & Grierson 1981). Similar short-term IOP results (1-year follow-up) were obtained more recently in a large national survey in the United Kingdom carried out in 1996; the final IOP of less than 21 mmHg was achieved in 84% without medication and in 92% with antiglaucoma medication (Edmunds et al. 2001), and in a study with POAG patients over 46 years old the success rate was 79% at 1 year and 72% at 2 years without medication (Briggs & Jay 1999). Some studies have, however, reported less favourable results. Jerndal and Lundström (1977) reported success without medication in 58% of eyes after 1.5 to 3 years, Mietz et al. (1999) in 53% in eyes with stable VF and optic disc in 6 to 62 months, and Diestelhorst et al. (1999) in 48% after mean follow-up of 16.3 months.

In the early studies, the percentage of well-controlled eyes was believed to be substantially constant up to 5 years (D'Ermo et al. 1979). Later, the success rate has appeared to decrease with time (Popovic & Sjöstrand 1991, Briggs & Jay 1999). A decrease in success from 48% to 40% at 3 and 5 years, respectively, occurred when success was defined as IOP ≤ 20 mmHg and a reduction in IOP of at least 20% from the presurgical level (Nouri-Mahdavi et al. 1995).

Table 1. Success rates without medication in studies of primary open-angle glaucoma (POAG) eyes, with intraocular pressure (IOP) level of 21 mmHg as the limit for surgical success

	Follow-up			
Authors, Year	1–2 years	3–4 years	5 years	7years
D'Ermo et al. 1979	65%			
Jerndal & Lundstöm 1977*	58%			
Jerndal & Lundstöm 1980*			57%	
Watson & Grierson 1981	83%			
Kidd & O'Connor 1985			75%	
Akafo et al. 1992*				67%
Vesti 1993		77%		
Downes et al.1994	67%			
Mietz et al. 1999	53%			
Briggs & Jay 1999	72%	66%		
Diestelhorst et al. 1999	48%			

*open-angle glaucoma

2.2.3 Comparison of success in primary open-angle glaucoma and exfoliation glaucoma

Some studies comparing the results of trabeculectomy in POAG and EG are summarized in Table 2. Mills (1981) found a lower success rate (64%) in a small number of exfoliation eyes (n=14) than in POAG (73%) without medication. In contrast, better control without further therapy in EG than in POAG at 5 years has also been reported (Törnqvist & Drolsum 1991). In the latter study, however, EG eyes were operated on at an earlier stage. Most of the previous studies seem to show no significant difference in the outcome of trabeculectomy between POAG and EG (Mietz et al. 1999, Popovic & Sjöstrand 1999, Serguhn & Spiegel 1999, Edmunds et al. 2001). The proportionate reduction in IOP can, however, be significantly higher in EG because of initially higher IOP in EG (Edmunds et al. 2001).

Table 2. Success rates of intraocular pressure (IOP) control after trabeculectomy in eyes with primary open-angle glaucoma (POAG) and exfoliation glaucoma (EG)

Authors year	No. of eyes POAG/EG	Success criteria	Success without medication POAG (%)	EG (%)	Follow-up months
Mills 1981	220/14	<21 mmHg	73%	64%	not reported
Törnqvist &	84/160	without	56%	77%	24
Drolsum	56/107	defect	43%	64%	60
1991		progression*			
Mietz et al. 1999	209/117	≤21 mmHg*	53%	51%	6–62
Popovic & Sjöstrand 1999	42/53	without medication	64%	58%	46
Serguhn &	23/21	<21 mmHg+	78%**	81%**	12
Spiegel	17/21	≥20%	71%**	86%**	24
1999		decrease in IOP**			
Edmunds et al. 2001	1105/64	≥33% decrease in IOP	66%	70%	12

VF = visual field
* VF and optic disc required to be stable
** With or without medication

2.2.4 Preoperative factors related to poor postoperative IOP control

Various preoperative factors related to poor long-term IOP control have been suggested, such as the type and/or length of preoperative medication (Watson & Grierson 1981, Sherwood et al. 1989, Lavin et al. 1990, Broadway et al. 1994, Liesegang 1998), preoperative argon laser trabeculoplasty (ALT) (Schwartz et al. 1999), younger age, higher preoperative IOP, and diabetes (The AGIS Investigators 2002). Further, in POAG, early trabeculectomy has been reported to be more successful than delayed trabeculectomy (Lavin et al. 1990, Broadway et al. 1994).

2.2.5 Early postoperative complications

The occurrence of early postoperative complications in previous studies is summarized in Table 3. Some authors report no correlation between surgical complications and the long-term results of the operation (D'Ermo et al. 1979, Lavin et al. 1990, Watson et al. 1990). However, in the Advanced Glaucoma Intervention Study (The AGIS Investigators 2002), failure of trabeculectomy was associated with any postoperative complication; of the individual postoperative complications, elevated IOP and marked inflammation were statistically significant, but the effects of other specific complications were not reported separately.

Table 3. Early postoperative complications of trabeculectomy

Authors year	No. of eyes (patients)	Hyphema	Shallow AC*	Flat AC*	Choroidal detachment
D'Ermo et al. 1979	90(75)	9%		4%	4%
Mills 1981	435(349)	7%	9%	4%	5%
Watson & Grierson 1981	424(268)	15%	13%	3%	
Watson et al. 1990	239(177)		21%	3%	
Törnqvist & Drolsum 1991	277(239)	17%		16%	
Downes et al. 1994	203(203)	24%	10%	2%	
Popovic 1995	60(60)	25%	13%	3%	23%
Molteno et al. 1999	289(193)	9%	7%		11%
Picht et al. 2001	113(113)	5%	8%		19%
The AGIS Investigators 2002	509	11%	16%	9%	8%
Jampel et al. 2005	465(300)	10%	13% shallow or flat		11%

AC = anterior chamber
* definitions of shallow and flat AC vary

Low IOP (<17 mmHg) on the first postoperative day has been found to be an accurate predictor of a successful outcome (Downes et al. 1994). Results of the effect of early hypotony on the final outcome have been controversial, ranging from no effect of IOP ≤5 mmHg (Popovic 1995) to a statistically significant correlation between the lowest IOP in the early postoperative period and the 6-month and 12-month IOP (Schwenn et al. 2001) or to a greater chance of having higher final IOP in eyes with IOP <8 mmHg for more than 2 weeks in the immediate postoperative period (Migdal & Hitchings 1988).

The effect of laser suture lysis (LSL) is also controversial. Unexpectedly, the final mean IOP and the mean number of postoperative antiglaucoma medications have not differed significantly between the LSL and the non-LSL groups (Asamoto et al. 1995, Macken et al. 1996). It thus seems that LSL may not alter the fibrosis process of the filtering bleb.

2.2.6 Location of trephined block and its effect on complications and long-term success

The location of trabeculectomy in the anterior chamber angle may influence the incidence of postoperative complications and the final success rate. In the anterior approach, a segment of the trabecular meshwork and the canal of Schlemm anterior of the scleral spur is removed (Cairns 1968), while in the more posterior approach, a segment of the scleral spur and the anterior longitudinal ciliary muscle is also dissected (Watson 1970). On comparing the complications of trabeculectomy by the anterior (115 eyes) and the posterior (101 eyes) approach, Watson and Grierson (1981) found that the average fall in IOP and progression of cataracts were significantly greater with the anterior approach, whereas hyphemas were significantly more common after the posterior approach. No statistically significant difference occurred in incidence of shallow anterior chambers.

Histological surveys of trabeculectomies have revealed no correlation between the anatomical location of the trephination (Duzanec & Kriegelstein 1981), or dissected block, (Taylor 1976, Konstas & Jay 1992) and postoperative success. The occurrence of postoperative complications has, however, varied. Taylor (1976) found no difference in the development of a postoperative flat anterior chamber or hyphema, Duzanec and Kriegelstein (1981) found that displacement of the trephination toward the sclera caused more postoperative choroidal detachments, and Konstas and Jay (1992) observed that the rate of hyphemas was significantly greater in eyes with posterior trabeculectomy fistulas.

2.2.7 Progression of visual field defects

VF deterioration may occur over the years despite effective IOP-lowering therapy (Kidd & O'Connor 1985, Watson et al. 1990, Rosetti et al. 1993, Brubaker 1996). In previous studies, progression rates of VF defects have varied considerably, partly due to different criteria of VF loss, partly due to different length of follow-up. The probability of progressive field loss at 4-5 years' follow-up has been reported in 18 to 27% (Kidd & O'Connor 1985, O'Brien et al. 1991, Parc et al. 2001), at 7 to 10 years in 27 to 76% (Hart & Becker 1982, Mikelberg et al. 1986, Chauhan & Drance 1992, Smith et al. 1996, Rasker et al. 2000, The AGIS Investigators 2002) and at 11 to 15 years in 46 to 68% (Molteno et al. 1999, Kwon et al. 2001). In trabeculectomy follow-ups based on survival methods, probability of progressive field loss at 5 years' follow-up has been reported in 27% (Parc et al. 2001), and at 11 to 15 years in 46% (Molteno et al. 1999).

2.2.8 Effect of IOP on progression of visual field defects

The beneficial effect of a lower IOP on VF progression has recently been documented in OAG in several randomised prospective studies. In the Advanced Glaucoma Intervention Study (The AGIS Investigators 2000), eyes with an average IOP greater than 17.5 mmHg over the first three 6-month follow-up visits had more VF progression than eyes with IOP less than 14 mmHg. In the associative analysis, in eyes with IOP less than 18 mmHg over the first 6 follow-up years, mean changes from baseline in VF defect score were close to zero during 6 or more years of follow-up. Even in this group, although mean IOP over the first 6 years of follow-up was 12.3 mmHg, about 14% of eyes experienced considerable field loss at 5 to 7 years despite having IOP less than 18 mmHg at all study visits. On the other hand, 18% in the same group showed VF improvements at 7 years. Larger IOP fluctuation (standard deviation of the IOP at all visits after the initial surgery) has also been associated with VF defect progression in eyes both with and without a history of cataract extraction in the Advanced Glaucoma Intervention Study (Nouri-Mahdavi et al. 2004). In the Collaborative Initial Glaucoma Treatment Study (CIGTS) (Lichter et al. 2001), minimal change in VF score was observed when aggressive treatment, either medical or surgical, was aimed at substantial reduction in IOP from baseline. Average IOP was, over the course of follow-up, 17 to 18 mmHg in the medicine group and 14 to 15 mmHg in the trabeculectomy group. The Early Manifest Glaucoma Trial (EMGT) (Leske et al. 2003) of early glaucoma showed that the progression risk decreased, with each mmHg of IOP reduction from baseline, by about 10%.

Several studies have tried to discover the level of a safe IOP. Mao et al. (1991) observed that in POAG and early glaucomatous damage, all the eyes with mean IOP higher than 21 mmHg during the follow-up period of 4 to 11 years had progressive glaucomatous changes, and conversely, eyes with mean IOP less than 17 mmHg remained stable, and Migdal et al. (1994) found no significant deterioration of VF in their trabeculectomy-treated group in which mean IOP at 5 years was 14.1 mmHg. Popovic and Sjöstrand (1999) reported a similar mean IOP (16.6 and 16.2 mmHg, respectively) and mean percentage of IOP reduction (39.5 and 41.7%, respectively) in eyes with unchanged/improved vs. deteriorated VF after trabeculectomy.

The progression rate in eyes treated with medical therapy or filtration surgery seems to be the same if the IOP outcome is similar (Stewart et al. 1996). Greater IOP reduction and better preservation of VF after surgical therapy have been reported (Jay & Murray 1988, Jay & Allan 1989, Migdal et al. 1994). In the CIGTS (Lichter et al. 2001), a clinically significant VF loss at some point during 5 years' follow-up was observed in 10.7% of medically and 13.5% of surgically treated patients, but after 5 years' follow-up, VF outcome was about the same in eyes having aggressive medical and in eyes with initial surgical therapy, although the IOP during the follow-up was 4 to 3 mmHg lower in the latter group.

2.2.9 Effect of other characteristics on progression of visual field defects

Several characteristics other than IOP indicate a greater potential for defect progression. In most studies, older age seems to be a risk factor (Mao et al. 1991, Stewart et al. 2000, Lichter et al. 2001, Leske et al. 2003, Jonas et al. 2004), and some have found baseline VF score (Lichter et al. 2001, Leske et al. 2003), or higher baseline IOP and exfoliation (Leske et al. 2003) also as risk factors for VF progression. Other possible risk factors presented are a larger cup-to-disk ratio, greater number of medications, and worse visual acuity (Stewart et al. 2000), or nonwhite race, diabetes, and time of study (Lichter et al. 2001), or bilateral disease, and frequent disc haemorrhages during follow-up (Leske et al. 2003), or small neuroretinal rim area and large beta zone of parapapillary atrophy (Jonas et al. 2004). In contrast, Mao et al. (1991) found that neither initial optic nerve appearance, initial VF findings, number of medicines, medical history, gender, nor race were significantly associated with stability or progression of glaucoma, but patients who remained stable were slightly younger.

Findings on the influence of initial VF status on rate of progression are contradictory. No significant correlation between the stage of glaucoma (i.e., starting field score) and subsequent change in field score has been reported (Migdal et al. 1994, Rasker et al. 2000, Kwon et al. 2001), but Grant and Burke (1982) reported that eyes with more damage at presentation are more likely to go blind. Baseline VF was shown to be more damaged in eyes with progressing VF defects in high-pass resolution perimetry (Martínez-Belló et al. 2000). It has also been evident that optic disc damage in eyes with advanced glaucomatous optic disc changes is more likely to progress despite IOP-lowering treatment, independent of IOP level (Tezel et al. 2001). In contrast, some studies have found VF with less baseline defect to be at increased risk for VF defect progression (O'Brien et al. 1991, The AGIS Investigators 2002).

2.2.10 Development of low vision and blindness

Glaucoma-related visual impairment is one of the main causes of visual impairment in elderly people. In the Finnish Register of Visual Impairment it comes second (10%) after age-related macular degeneration (58%) in people aged 65 years and older (Ojamo 2003). Various studies' prevalences of glaucoma-related visual impairment and blindness are difficult to compare, because the definition of blindness varies, and some studies do not separate glaucoma-related blindness from blindness due to other causes. Kwon et al. (2001) reported legal blindness (VA $\leq$20/200 and/or VF $\leq 20^{o}$ at its widest diameter) from glaucoma in POAG with standard therapy in 13% of eyes at a follow-up of 14 years. Chen (2003) reported in his retrospective analysis that at 15 years after diagnosis the Kaplan-Meier estimate for glaucoma-related blindness (VA ≤20/200 and/or VF ≤20º in all quadrants) in one eye was 14.6%, and in both eyes 6.4%. Hattenhauer et al. (1998) presented higher figures at 20 years' follow-up; they estimated the probability of glaucoma-related blindness (defined as VA ≤20/200 and/or VF ≤20º at its widest diameter) in newly diagnosed classic open-angle glaucoma treated with medical, laser or surgical therapy or a combination of these methods in at least one eye to be 54%, and 22% for both eyes. Most studies have not considered various treatment modalities (medicine, laser, filtration surgery) separately.

Few studies have examined the probability of becoming blind after filtration surgery. According to Molteno et al. (1999), the probability of losing useful vision (VA ≤20/400 or VF ≤5º radius) from any cause was 13%, 28%, and 40% at 5, 10, and 15 years, after trabeculectomy, but only one-third was due to progression of glaucoma. Parc et al. (2001) reported higher figures, but the criteria were less severe (VA ≤20/200 and/or VF ≤20º at its widest diameter); according to Kaplan-Meier analysis, the probability of legal blindness in patients with OAG who underwent filtration surgery was 22% at 5 years and 46% at 10 years. In the Advanced Glaucoma Intervention Study (The AGIS Investigators 2004), the 10-year cumulative incidence of unilateral first occurrence of VF impairment or visual acuity (VA) impairment (VA ≤0.2) or both in white patients in a trabeculectomy-ALT-trabeculectomy group was 30.4% from all causes.

Characteristics reported as risk factors for becoming blind because of glaucoma include more advanced field defects at the time of surgery (Grant & Burke 1982, Parc et al. 2001, Chen 2003), poor preoperative visual acuity (Molteno et al. 1999), advancing age (Hattenhauer et al. 1998), and noncompliance with the treatment regimen (Stewart et al. 1993, Chen 2003), as well as complete glaucomatous cupping of the optic disc, the mean IOP, variance of each patients' IOP measurements and history of ALT (Stewart et al. 1993). In most studies, postoperative IOP was unrelated to blindness (Watson et al. 1990, Parc et al. 2001, Chen 2003). The latest IOP was lower in blind eyes than in non-blind eyes, according to the findings of Parc et al. (2001). Acute loss of vision after surgery ('wipe-out') may also occur (Costa et al. 1993).

2.2.11 Progression of cataract after trabeculectomy

The progression of a cataract is generally considered a late complication of trabeculectomy (The AGIS Investigators 2001). In a prospective study, at our hospital, Vesti (1993) identified EG, age, hypotony (IOP ≤5 mmHg lasting ≥5 days), and early postoperative IOP rise >30 mmHg after trabeculectomy to be risk factors for cataract progression. The indicators for cataract progression in that study were not limited to need for cataract extraction, but also included were deterioration in VA by ≥2 Snellen lines, myopic change in refraction, and increase in lens opacity value, measured with a Lens Opacity Meter. Exfoliation syndrome has been suggested as a risk factor for progression of lens opacification also in nonglaucomatous eyes (Puska & Tarkkanen 2001). In the Advanced Glaucoma Intervention Study (The AGIS Investigators 2001), increased risk for cataract was associated with age, diabetes, and postoperative complications of trabeculectomy; of the individual postoperative complications, marked inflammation and flat AC were statistically significant.

2.2.12 IOP control after cataract surgery

Phacoemulsification has an IOP-lowering effect both in healthy eyes and in unoperated glaucomatous eyes (Peräsalo 1997, Pohjalainen et al. 2001). Pohjalainen (2001) discovered that after phacoemulsification, 42% of POAG and 29% of EG eyes required less glaucoma medication at the last examination 1 to 3.7 years postoperatively than preoperatively. However, the effect of cataract surgery on IOP control in eyes that have undergone trabeculectomy seems to vary. Some studies show worsening of IOP control or greater number of antiglaucoma medications after phacoemulsification (Chen et al. 1998, Crichton & Kirker 2001, Halikiopoulos et al. 2001, Casson et al. 2002, Derbolav et al. 2002, Rebolleda & Muñoz-Negrete 2002, Shingleton et al. 2003), while others have noticed no negative effect of cataract surgery on IOP or on the number of glaucoma medicines overall (Park et al. 1997, Manoj et al. 2000, Mietz et al. 2001). The proportion of eyes with continuing good control of IOP without antiglaucoma medication after cataract surgery was reported to be 33% by Mietz et al. (2001), but when eyes with improved IOP control after cataract surgery are added, the corresponding figure was 42%. In some other studies, the percentage of eyes with good postoperative IOP control has been higher (Crichton & Kirker 2001, Halikiopoulos et al. 2001, Casson et al. 2002, Derbolav et al. 2002, Rebolleda & Muñoz-Negrete 2002), partly because of the higher percentage of eyes with good IOP control before cataract surgery (up to 100% by Rebolleda & Muñoz-Negrete 2002). In most of the latter studies, cataract surgery was performed only on selected cases with functioning bleb and good IOP control before surgery.

3. Aims of the present study

The purpose of the present study was to evaluate long-term outcome of trabeculectomy in POAG and EG.

The specific aims of the study were to evaluate:

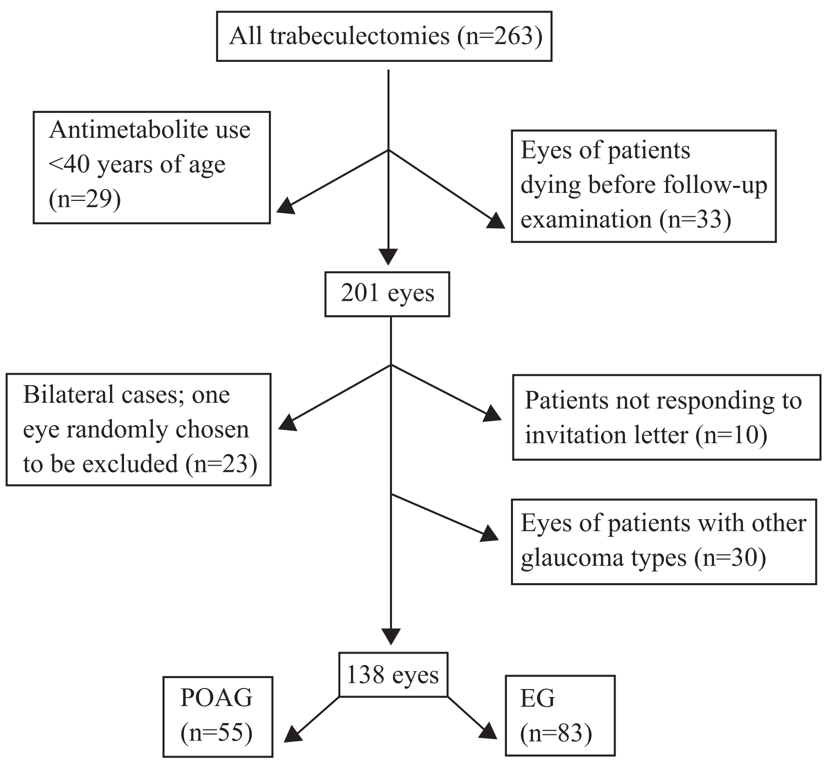
- preoperative characteristics of consecutive patients with POAG and EG who underwent primary trabeculectomy during the study period (I).
- long-term IOP control in POAG and EG after trabeculectomy with or without postoperative medication (I).
- complication rate immediately after trabeculectomy and effects of early complications on long-term IOP control (II).
- location of trephined block and its effect on complications and long-term success (II).
- degree of VF defect progression and development of low vision and blindness (III).
- risk indicators leading to cataract surgery after trabeculectomy and effect of phacoemulsification on IOP control, and to evaluate cataract surgery in POAG and EG (IV).

4. Patients and methods

4.1 Patients

All primary trabeculectomies performed by one surgeon (I.L.) at the Helsinki University Eye Hospital between November 1994 and August 1996 were studied retrospectively in 1998–1999 (263 eyes). Helsinki University Eye Hospital ethics committee approval was obtained for the study. Only eyes with POAG (not including normotensive glaucoma) or EG were included. Diagnoses of POAG and EG were based on preoperative definitions at the glaucoma unit. Patients under 40 years of age at the time of the operation and all the eyes operated on with the use of antimetabolites were excluded (29 eyes) (Fig.1). The 33 eyes of patients who died before the follow-up examination were also excluded. In 23 cases, both eyes of a patient had been operated on during the study period; only one eye of each of these patients was randomly chosen for the study. Ten patients did not answer the

Figure 1. Flowchart of the study patients



POAG = primary open-angle glaucoma, EG = exfoliation glaucoma letter of invitation. Thus 138 eyes comprised the study series. Of these, 102 patients were examined by the author at the end of the follow-up period in 1998–1999. In 36 cases, information for follow-up came from the patient's charts or from the referring physician.

From the analysis of VF progression (III), 55 of the 138 eyes were excluded because in 36 cases the preoperative fields (in 18 cases Octopus G1 and in 18 cases Goldmann VF) had been measured more than 3 months before the operation, in 6, patients had different kinds of fields pre- and postoperatively, and in 13 cases, the fields were unavailable for reasons such as dementia or loss of co-operation. Thus, at the last follow-up visit, comparable pre- and postoperative VF, measured by the same technique were available for 83 patients (60%), Octopus G1 fields for 40 eyes, and Goldmann fields for 43 eyes.

During the follow-up, of the 138 eyes, 48 (35%) underwent a cataract operation. One eye with endophthalmitis after trabeculectomy and one lacking information as to cataract surgery were excluded from further analysis of cataract surgery. The remaining 46 eyes are included in the study on cataract surgery (IV).

4.2 Methods

4.2.1 Clinical data recorded retrospectively

Clinical data on the patients were collected from the files of the Helsinki University Eye Hospital and from private ophthalmologists responsible for their referral and follow-up. Preoperative data collected included date of birth, gender, type of glaucoma, preoperative medication and its duration, dates of all surgical interventions including laser operations, best corrected visual acuity (BCVA) recorded as Snellen decimal notations, refraction, IOP, anterior segment status, posterior pole abnormalities, optic disc appearance, and results of visual field examinations. The preoperative IOP, was considered to be the value measured by Goldmann applanation tonometry at the visit immediately prior to trabeculectomy.

Intra- and postoperative complications of trabeculectomy (early postoperative IOP elevation >30 mmHg, hyphema, hypotony <5 mmHg ≥5 days, leakage of the filtering bleb, a shallow or flat AC, choroidal detachment, infection, cystoid macular oedema (CME), hypotony maculopathy, suprachoroidal haemorrhage, persistent uveitis and dellen formation) and any additional postoperative procedures were recorded (LSL, resuturation, reformation of the anterior chamber, or posterior sclerotomy).

Postoperative IOP values measured on the first postoperative day after trabeculectomy and one week and one month postoperatively were collected.

4.2.2 Data recorded at the follow-up examination

At the last follow-up visit, BCVA, refraction, IOP, anterior segment status including the lens, posterior pole status, and optic disc appearance were examined mostly by the author by standard clinical methods. Visual fields were examined with the same VF program as preoperatively. In addition, medications used and information concerning any additional operations (retrabeculectomy or cyclophotocoagulation) during the follow-up period were recorded. The date when glaucoma medication had been restarted came from the referring physician. In eyes having cataract surgery (IV) BCVA, IOP and medications used before the cataract operation, and details of cataract surgery including the technique and the incision used, and intraocular lens (IOL) type and placement, as well as intra- and postoperative complications were all recorded.

4.2.3 Indications and technique of trabeculectomy

Indications for trabeculectomy were uncontrolled IOP despite maximal tolerated medication or disease progression or both. All operations were performed by one senior surgeon (I.L.). The use of warfarin sodium or acetyl salicylic acid was discontinued 1 to 3 days before surgery. A limbus-based conjunctival flap was used, beginning about 5 mm posterior to the limbus. A rectangular 3 × 4 mm scleral flap extended into the clear cornea. Two 10–0 nylon sutures were preplaced in the corners of the flap. Trabeculectomy was performed with a 1.3 mm Geuder motor trephine. After peripheral iridectomy, the flap was closed with two to four sutures. Tenon and conjunctiva were reapproximated separately with 8–0 Vicryl sutures, and periocular injections of cefotaxime (Claforan®) and triamcinolone (Kenacort™) were given at the end of the operation. Postoperatively, topical atropine t.i.d., antibiotics q.i.d., and steroids q.i.d. were given for up to 1 month.

4.2.4 Definitions of complete success, qualified success, and failure (I–IV)

In terms of IOP, trabeculectomy was considered a complete success if IOP was 21 mmHg or lower without other therapy, a qualified success if IOP was 21 mmHg or lower with a single topical medication, and a failure if IOP was more than 21 mmHg or if an eye with lower IOP received more medications or had required further surgery, except laser suture lysis, because of glaucoma.

4.2.5 Examination of the trephined tissue block (II)

Of the 138 eyes, in 118 (86%), the trephined tissue block had been examined at the pathology laboratory of the Helsinki University Eye Hospital by one senior ophthalmologist (L.M.). The surgical specimen was fixed in 4% formalin, embedded in paraffin, cut, and stained with haematoxylin and eosin and with PAS stains. The cut sections were evaluated for the presence of identifiable landmarks, including Descemet's membrane, trabecular tissue, Schlemm's canal, and ciliary muscle. The location of a trabeculectomy was defined as anterior if any Descemet's membrane in addition to trabecular tissue was visible in the specimen. The specimens containing trabeculum only, with or without ciliary muscle but no Descemet's membrane, were defined as posterior.

4.2.6 Evaluation of visual fields and progression of defects (III)

Preoperatively, VF had been examined by either automated static perimetry using the Octopus G1 program or by kinetic Goldmann perimetry, depending on the patient's capability to respond at the field examination. Degree of VF loss before surgery was scored as (1) mild to moderate or (2) severe by a modification of the classification originally described by Aulhorn (1978). The degree was severe if there was an extensive ring-shaped or half-ring-shaped absolute defect in the paracentral VF area extending up to 30º with or without a central island. In addition, all absolute scotomas within the central 5º, or a mean defect worse than –16 dB in the Octopus field (Heijl et al. 2002) was regarded as severe.

For progression of Octopus G1 VF defects, the criteria were those presented by the Glaucoma Laser Trial Research Group (Glaucoma Laser Trial Research Group 1995); progression is a change in each of two spots in the central 30 degrees of field showing any of the following characteristics: (1) threshold value 7 dB or more below the threshold value of an abnormal spot on the field of reference (deepening of an existing scotoma), (2) threshold value 9 dB or more below the threshold value of a normal spot adjacent to an abnormal point on the field of reference (enlargement of an existing scotoma), or (3) threshold value 11 dB or more below the threshold value of a normal spot on the field of reference (new scotoma). False-positive or false-negative rates greater than 20% indicated unreliability. Progressive loss of the Goldmann VF was defined as a definitive reduction in a field area or an extension toward fixation of a paracentral scotoma that was due to glaucoma (Molteno et al. 1999). The estimation of the progression of Goldmann VF was based on clinical judgement and agreement by two of the authors. In 68% of the cases (23 of 34 eyes), progression of the VF defect was confirmed by re-examination of VF, or by discovery of loss of fixation or concurrent optic disc changes. In 6 of the remaining 11 cases, high IOP at or above the preoperative level supported the conclusion of progression.

4.2.7 Visual acuity and definition of visual impairment (III)

BCVA was recorded as Snellen decimal notations. For comparison of pre- and postoperative values, the VAs were scored in four categories: ≥0.5, <0.5 to 0.3, <0.3 to 0.05, and <0.05. The two lower categories correspond to low vision (VA <0.3 to 0.05) and blindness (VA <0.05) according to the WHO definition (World Health Organization 1980). In addition, eyes with a VF constricted to less than 20˚ at its widest diameter without considering central VA were defined as blind. The cause of visual impairment was categorized as glaucoma-related if no other cause was discovered.

4.2.8 Indications and technique of cataract surgery (IV)

In a retrospective study, the indications for cataract surgery may have varied in individual cases. Cataract surgeries were performed by experienced surgeons, who in 45 of the 46 cases used the phacoemulsification technique. Of these cases, two were converted to extracapsular cataract extraction (ECCE) and one to intracapsular cataract extraction (ICCE) because of problems with phacoemulsification, and one additional ECCE was planned. The technique was roughly similar for all cases. A temporal 5.5-mm scleral tunnel incision was used in 40 eyes, and a clear corneal incision in 5. Thus, in uncomplicated cases, the area of trabeculectomy bleb located superiorly could be avoided. Sphincterotomies were cut in six eyes. An intraocular lens (IOL) was implanted in all eyes, in the capsular bag in 40 eyes: In 4 eyes a foldable lens and in 34 a polymethylmethacrylate (PMMA) lens was used, in 2 cases, information on lens type was lacking. In four eyes, a PMMA lens was implanted in the ciliary sulcus, and two eyes received an anterior chamber intraocular lens (AC IOL). In most uncomplicated cases, the incision was self-sealing. In 14 eyes, it was closed with a 10–0 nylon suture, and the conjunctiva with silk. Two eyes had anterior vitrectomy, and in one of them vitrectomy via pars plana and removal of a piece of nucleus were performed 6 days after phacoemulsification. Periocular cefotaxime and triamcinolone injections were given in 30 cases; in 7 cases cefuroxime 1 mg was injected into the anterior chamber, and 9 eyes received no intraocular or periocular injections. Postoperative medication included topical antibiotics and steroids or non-steroidal anti-inflammatory drugs q.i.d. for 4 weeks.

4.2.9 Statistical methods

Data were collected in Microsoft Excel 97 (Seattle,WA), and analysed by standard statistical methods, by GraphPad Prism™ 2.01. and the NCSS 2000 program from NCSS Statistical Software. Unpaired Student’s (two-sample) *t*-test or the Mann-Whitney test were used for comparison of the continuous variables between the groups. The chi-square test or Fisher's exact test were used to evaluate the significance of the differences between categorised data. Differences between pre-trabeculectomy IOP and last IOP, pre- and last post-cataract surgery IOP, and pre- and last post-cataract surgery topical medication within the POAG and EG groups were calculated with the paired t-test and Wilcoxon signed-rank test, as appropriate. Pearson's correlation was performed to detect the correlation between the lowest IOP within the first postoperative month after trabeculectomy and the last IOP. The success rates of IOP control in the different groups were analysed with Kaplan-Meier analysis. The significance level of the difference between the groups in the Kaplan-Meier survival curves was calculated with the log-rank test. Proportional hazards regression was used to detect multivariate influences on the success of trabeculectomy. Proportional hazards regression was also used to estimate risk indicators for cataract surgery. Logistic regression was performed to detect multivariate influences on progression of visual field defects. A p-value of 0.05 was considered significant.

5. Results

5.1 Preoperative patient characteristics (I)

Of the 138 patients included, 83 (60%) were females and 55 (40%) males. The mean age of the patients on trabeculectomy day was 70.1 years (range 41-90 years). All patients were Caucasian.

Fifty-five eyes (40%) had POAG, and 83 (60%) had EG (Table 4). The proportion of males was slightly but not significantly greater in the POAG group. Patients with POAG were significantly younger (p=0.03), but the duration of their glaucoma was slightly longer (p=0.06). Of both POAG and EG eyes, 98% were receiving topical medication, and 84% and 86% of them, respectively, were receiving two or more medications. The mean number of topical antiglaucoma medicines was 2.1 (SD 0.7) in both groups. In addition, more than half the patients were taking oral antiglaucoma medication. ALT had been performed in 28 eyes with POAG (51%) and in 47 eyes with EG (57%). Three eyes in the POAG group, and two in the EG group had undergone diode laser cyclophotocoagulation before trabeculectomy.

Table 4. Patient characteristics according to type of glaucoma

	POAG	EG	p
Number of eyes	55	83	
Age (mean, years) (SD)	67.8 (10.8)	71.6 (9.2)	0.03
range	40.6–88.6	50.4–90.2	
Gender M/F (%)	24/31 (44%/56%)	31/52 (37%/63%)	0.46
Duration of preoperative glaucoma medication			
(mean, years) (SD)	7.8 (5.6)	5.8 (6.3)	0.06
range	0–19.7	0–34.6	
Preoperative ALT (%)	28 (51%)	47 (57%)	0.51
Preoperative IOP			
(mean, mmHg) (SD)	24.6 (5.8)	28.0 (11.2)	0.044
range	13–37	14–70	
(95% Cl)	(23.1–26.2)	(25.5–30.4)	

POAG = primary open-angle glaucoma, EG = exfoliation glaucoma, ALT = argon laser trabeculoplasty, IOP = intraocular pressure

Before trabeculectomy, the mean IOP was 24.6 (SD 5.8) mmHg in the POAG group and 28.0 (SD 11.2) mmHg in the EG group (p=0.044). Of the 83 eyes in which comparison between pre- and postoperative VF could be made, the preoperative VF defect was considered severe in 33 eyes (40%) and mild to moderate in 50 (60%). Of the severe defects, 20 (61%) were discovered by Goldmann perimetry, 13 (39%) by Octopus perimetry.

5.2 Outcome of trabeculectomy in terms of intraocular pressure (I)

All patients were followed up for at least 2 years (mean 3.5 years, range 2–5). At the last examination, the mean IOP in the POAG group was 16.6 (SD 4.2) mmHg and in the EG group 17.1 (SD 6.2) mmHg (p=0.95) (Table 5). Mean reduction in IOP from the preoperative level was highly significant in both groups (p<0.0001). The final IOP was lower than the preoperative level in 84% of eyes. However, 45% of POAG eyes and 58% of EG eyes were on glaucoma medication, and 24% and 37% of them were receiving two or more medications (p=0.15). The mean number of topical antiglaucoma medicines was 0.8 (SD 1.0) in POAG and 1.1 (SD 1.1) (p=0.11) in EG. Of POAG eyes 11% and of EG eyes 13% (p=0.68) had undergone additional glaucoma surgery.

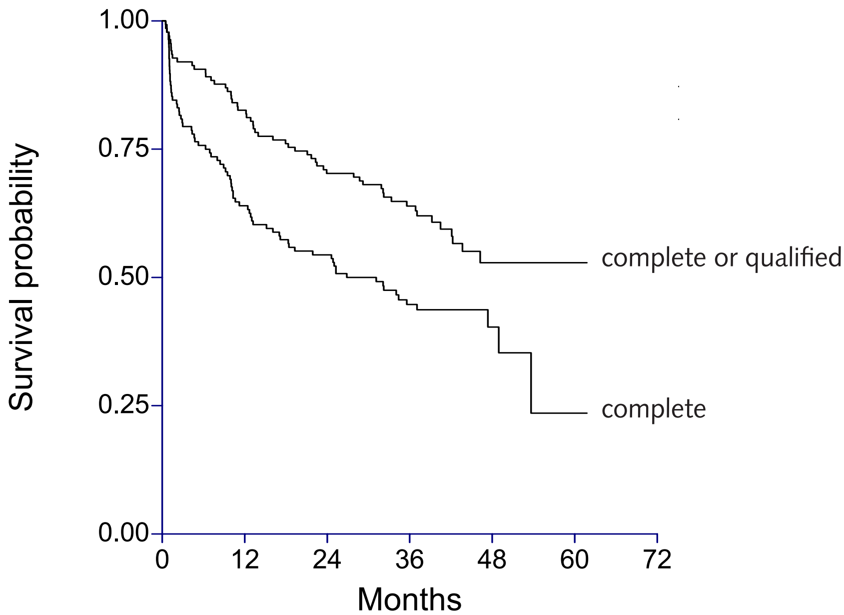
Table 5. Postoperative data according to type of glaucoma

	POAG	EG	p
Number of eyes	55	83	
Last postoperative IOP			
(mean, mmHg) (SD)	16.6 (4.2)	17.1 (6.2)	0.95
range	1–28	0–46	
(95% Cl)	(15.5–17.7)	(15.8–18.5)	
Absolute decrease in IOP			
(mean, mmHg) (SD)	8.0 (7.9)	10.8 (13.7)	0.35
(%)	(28%)	(30%)	
Number of eyes receiving topical medication (%)	25 (45%)	48 (58%)	0.15
Number of topical medication (mean, SD)	0.8 (1.0)	1.1 (1.1)	0.11
Follow-up after trabeculectomy (mean, months) (SD)	42.8 (8.1)	42.2 (8.2)	0.64

POAG = primary open-angle glaucoma, EG = exfoliation glaucoma, IOP = intraocular pressure

According to the Kaplan-Meier survival curve, success rates for the IOP control, including both complete and qualified success in the whole series, were 82% at 1 year, 70% at 2 years, 64% at 3 years, and 52% at 4 years. Rates for complete success were 63%, 54%, 45%, and 40% (Fig. 2). Complete success was significantly more common in eyes with POAG than in eyes with EG (p=0.04), but with qualified success included, the difference was not significant (p=0.1).

Figure 2. Kaplan-Meier survival analysis of complete and complete or qualified success rates of the intraocular pressure (IOP) control in the whole series



In POAG, 79% of eyes with complete success had received longstanding preoperative topical medication (>3 years), while in EG, the corresponding percentage was 43% (p=0.008). Thus it seems that the longstanding preoperative medication reduced chances of complete success in EG.

In multivariate analysis (proportional hazards regression) significant factors affecting complete success in the long term were the presence of EG (p=0.03) and an early postoperative peak of IOP over 30 mmHg (p=0.04), both worsening prognosis, whereas a cataract operation (p=0.02) improved the chances that an eye remained a complete success. When complete and qualified success were combined, no significant predictors of success could be found. The following characteristics were tested: age, gender, duration of glaucoma, number of preoperative medications, preoperative ALT, preoperative IOP, glaucoma diagnosis (POAG or EG), early postoperative peak of IOP over 30 mmHg, macroscopic hyphema during the first postoperative week, postoperative hypotonia defined as IOP less than 5mmHg lasting at least 5 days, and a cataract operation performed before an eye had to be considered a qualified success or a failure.

5.3 Complication rate immediately after trabeculectomy (II)

In the whole study group, the early postoperative complications included hyphema in 17%, marked hypotony (<5mmHg ≥5 days) in 25%, a shallow or flat AC in 15%, and choroidal detachment in 21%, with some of these complications occurring simultaneously.

Postoperative hyphema was the only complication that differed significantly between POAG and EG (p=0.011) (Table 6). Previous warfarin or acetyl salicylic acid medication did not affect the hyphema rate significantly in either group, and no difference existed in preoperative IOP between eyes with or without hyphema. In the EG group, the number of preoperative drops was significantly higher in the hyphema cases (p=0.01), but otherwise the eyes with hyphema did not differ from those without. Two hyphema cases resulted directly from LSL (2.9% of eyes with LSL).

Table 6. Early postoperative complications within one month after trabeculectomy in patients with POAG and EG

Complication	POAG Number of eyes (%) 55	EG 83	All eyes Number (%) 138
Hyphema	4 (7%)*	20 (24%)*	24 (17%)
Early postoperative IOP elevation >30 mmHg	8 (15%)	17 (20%)	25(18%)
Hypotony <5mmHg ≥5days	13 (24%)	21 (25%)	34 (25%)
Leakage of filtering bleb	2 (4%)	6 (7%)	8 (6%)
Shallow or flat AC	7 (13%)	14 (17%)	21 (15%)
Choroidal detachment	11 (20%)	18 (22%)	29 (21%)
Endophthalmitis	1 (1.8%)	0 (0%)	1 (0.7%)
Bacterial conjunctivitis	0 (0%)	2 (2.4%)	2 (1.4%)
Fibrinous reaction in AC	1 (1.8%)	1 (1.2%)	2 (1.4%)

POAG = primary open-angle glaucoma, EG = exfoliation glaucoma, IOP = intraocular pressure, AC = anterior chamber
* p=0.011

Early postoperative IOP elevation (IOP >30 mmHg) was equally common in POAG (15%) and EG (20%). Altogether 70 eyes (51%) received LSL, and 22 eyes (16%) were put on pressure-lowering medication at the end of the first month because of insufficient filtration (despite LSL in 13 of them). Of these eyes, 6 (27%) had POAG and 16 (73%) EG. Four of these patients were found to be steroid responders; in these eyes, glaucoma medication could be reduced during the first 6 postoperative months. One eye had insufficient filtration following postoperative endophthalmitis. Insufficient filtration (antiglaucomatous medication) at the end of the first postoperative month predicted long-term failure (p=0.0084), but failure did not correlate with any of the other early complications or LSL.

One or more complications related to excessive filtration occurred in 45 eyes (33%); in 30 of them, several complications. A shallow anterior chamber was recorded in 21 eyes (15%), with iridocorneal contact in 8 eyes. Reformation of the anterior chamber with or without posterior sclerotomy was indicated in seven eyes, in four of which the scleral flap was resutured. No significant correlation appeared between the lowest IOP within the first postoperative month and the latest IOP, nor was there any correlation between lowest postoperative pressure and success (complete or qualified).

Of 70 eyes, in 6 (9%), LSL was followed by excessive filtration, and 5 of these eyes had several complications. Two iris incarcerations into two trabeculectomy fistulas, and two cases of hyphema resulted directly from LSL. Except for the two iris incarcerations, which were treated with the YAG laser, all the other complications related to LSL resolved with conservative treatment.

5.4 Effect of position of trephined block in the anterior chamber angle (II)

In 60 eyes, trabeculectomy was defined as anterior, and in 53 eyes as posterior. Patient characteristics did not differ significantly between those patients with eyes having anterior and those having posterior trabeculectomy among POAG or EG patients. Postoperative hyphemas were equally common in the anterior and posterior trabeculectomy group. Hypotony of <5 mmHg for at least 5 days, a flat or shallow AC, and choroidal detachment were more common, although not significantly so, in the anterior group.

The long-term success rates for both complete success and qualified success did not significantly differ between the anterior and the posterior groups in the Kaplan-Meier survival analysis, but a tendency appeared for the posterior location to survive better in the EG group.

5.5 Progression of visual field defects after trabeculectomy (III)

Of the 83 eyes for which a comparison between pre- and postoperative VF could be made, the VF remained stable in 37 eyes (45%). In 34 cases (41%), progression of glaucomatous field defects was classified as undisputable, and in 6 (7%), progression of defects was suspected, but some of these fields were unreliable, or progression may have been due to changes in the macula. Six eyes (7%) had other causes for progression of field defects (in one each, neovascular glaucoma, cerebral infarction, cataract, endophthalmitis; two had central retinal vein occlusion).

The preoperative VF defect was considered severe in 33 eyes (40%) and mild to moderate in 50 (60%). Of the 33 severe defects, 20 (61%) showed undisputable progression compared to 14 of 50 cases (28%) of mild to moderate defects. Thus, of the 34 fields that showed progression of defects, 20 (59%) were preoperatively classified as severe (with 8 cases of Octopus G1) and 14 (41%) as mild or moderate (with 8 cases of Octopus G1).

5.6 Risk indicators for progression of visual field defects (III)

VF progression was slightly but not significantly more common in EG (52%) than in POAG (40%) (p=0.33). In logistic regression analysis only severe preoperative VF defect (p=0.0047) and preoperative oral glaucoma medication (p=0.047) were significantly related to VF progression.

In univariate analysis, initial IOP reduction from preoperative to 1-month follow-up (15.4 vs. 10.9 mmHg) and IOP reduction from preoperative to last postoperative examination (12.8 vs. 9.2 mmHg) were significantly smaller in eyes with VF defect progression, (p=0.023, p=0.036, respectively). But the mean IOP at the last examination, 16.3 (SD 3.8) mmHg in eyes without progression and 17.6 (SD 7.4) mmHg in eyes with progression (p=0.58), or the mean number of topical antiglaucoma medicines, 0.76 (SD 0.95) and 1.03 (SD 0.97), respectively (p=0.2), did not differ. Nor was the difference in mean percentage IOP reduction (39.4 vs. 26.4%) from the preoperative to the last examination significant (p=0.095).

Progression of VF loss did not correlate significantly with success rate when an IOP level 21 mmHg or lower (without or with a single medication) or an IOP level less than 18 mmHg (without medication or additional surgery) at the last follow-up visit served as the marker. Nine eyes had an IOP of less than 13 mmHg at the last examination without medication or additional glaucoma surgery during the follow-up period, but despite the low IOP, in three of these eyes, VF defects progressed.

5.7 Development of low vision and blindness after trabeculectomy (III)

Preoperatively, 13 (9%) of the 138 eyes had low vision, and one eye (0.7%) was blind based on visual acuity and 5 eyes due to restriction of VF (Table 7). One patient was bilaterally blind. At the last follow-up visit, 19 eyes (14%) had low vision, and 7 (5%) were blind by VA criteria and 10 (7%) due to constriction of the VF. Of the 26 eyes with visual impairment by VA criteria, 15 were considered glaucoma-related, and 11 were due to other causes (cataract in 5, cellophane maculopathy or pucker in 2, and in 1 each, endophthalmitis, central retinal vein occlusion, and neovascular glaucoma; for 1 eye postoperative VF was unavailable). During the mean follow-up of 3.5 years, the prevalence of glaucoma-related low vision had increased from 6% to 7% and that of blindness from 4% to 10% in the operated eye. Two patients were bilaterally blind.

Table 7. Prevalence of low vision (VA <0.3–0.05) and blindness (VA <0.05 or VF constricted to less than 20º at its widest diameter) in the operated eye preoperatively and at the last follow-up examination

	All causes		Glaucoma-related	
		Number of eyes (%)		
	Preoperative	Last	Preoperative	Last
Low vision				
VA criteria	13 (9.4%)	19 (13.8%)	8 (5.8%)	10 (7.2%)
Blindness				
VA criteria	1 (0.7%)	7* (5.1%)	1 (0.7%)	5** (3.6%)
VF criteria only	5 (3.6%)	10 (7.2%)	5 (3.6%)	9 (6.5%)
All blindness	6 (4.3%)	17 (12.3%)	6 (4.3%)	14 (10.1%)

VA = visual acuity, VF = visual field

* 2 eyes fulfilled also VF criteria for blindness, ** 1 eye fulfilled also VF criteria for blindness

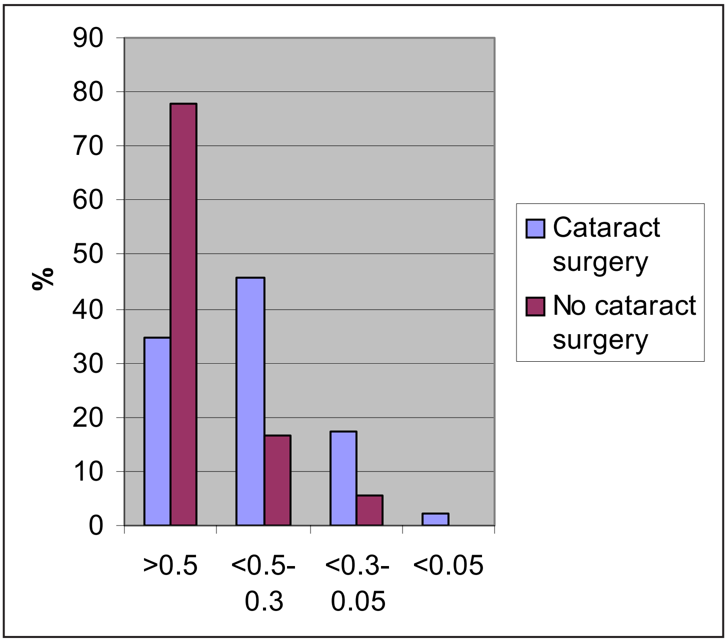
Visual impairment (low vision and blindness) at the last visit correlated significantly ($p=0.008$) with severe VF defect preoperatively.

5.8 Risk indicators for cataract surgery (IV)

During the follow-up period, 48 eyes (35%) underwent cataract surgery. Of these, 46 were analysed in detail. One eye with endophthalmitis after trabeculectomy and one lacking information as to cataract surgery were excluded. The 46 cataract operations were performed 5.1 to 58.1 months (median 14.4) after trabeculectomy. Mean follow-up after cataract surgery was 25.3 (SD 12.9) months (median 24.8).

Patients undergoing cataract surgery during the follow-up were significantly older (73.9 (SD 9.4) years) at the time of trabeculectomy than those without the operation (68.1 (SD 9.8) years) (p=0.001), and eyes with a cataract operation had worse initial BCVA before trabeculectomy than did eyes without cataract surgery (Fig. 3). The following characteristics: gender, type of glaucoma, duration of glaucoma, number of preoperative medications, ALT before trabeculectomy, pre-trabeculectomy IOP, early postoperative peak of IOP >30 mmHg after trabeculectomy, macroscopic hyphema during the first postoperative week, hypotony defined as IOP <5 mmHg lasting at least 5 days after trabeculectomy, or shallow or flat AC, did not differ between eyes with cataract operation and those without (proportional hazards regression).

Figure 3. Visual acuity before trabeculectomy in eyes with and without cataract surgery



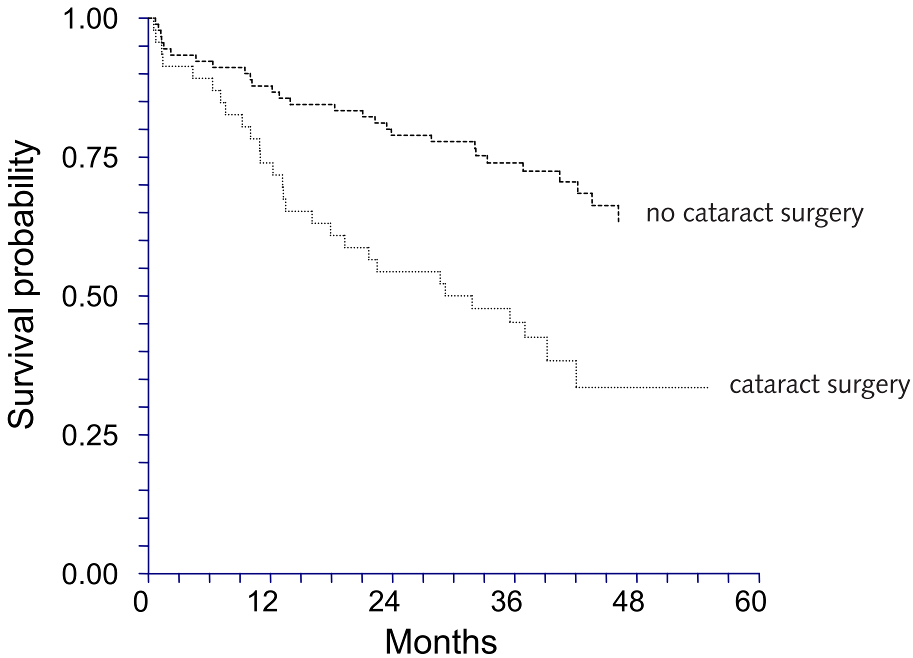
5.9 Effect of phacoemulsification on intraocular pressure (IV)

Before cataract surgery, the mean IOP was 16.2 (SD 4.9) mmHg and the mean number of topical antiglaucoma medicines was 0.8 (SD 1.0). One patient took oral antiglaucoma medication. At the last examination, the mean IOP 17.3 (SD 6.4) mmHg was not significantly higher than before cataract surgery (p=0.35), but the mean number of topical antiglaucoma medicines had increased significantly to 1.3 (SD 1.1) (p=0.0007). In addition, 3 patients required oral antiglaucoma medication.

Prior to cataract surgery, 22 of the 46 eyes (48%) were categorized as complete success, 10 eyes (22%) as qualified success, and 14 eyes (30%) as failures. Of the 14 failures, 11 (79%) had an IOP of 21 mmHg or lower but required two or three medicines or had undergone cyclophotocoagulation (4 eyes) before cataract surgery.

Of the 22 eyes categorized as a complete success prior to cataract surgery, 13 (59%) had remained so, one eye had become a qualified success (requiring one topical medicine), and 8 eyes (36%) were failures at the last examination. Altogether, the number of failures in these eyes had increased from 14 (30%) before surgery to 28 (61%) after cataract surgery. Of the 14 new failures, 7 had IOP <21 mmHg but required two topical medicines. The proportion of failures in the cataract surgery group was twice as high as in eyes with no cataract surgery (61% vs. 31%, p=0.0016) (Fig. 4). Of the nine eyes with complicated cataract surgery, six were failures at the last examination.

Figure 4. Kaplan-Meier survival analysis of complete or qualified success rates of intraocular pressure (IOP) control in eyes with and without cataract surgery



In 19 of the 46 eyes (41%), use of topical antiglaucoma medicines had increased after cataract surgery. At the last examination, 70% of eyes with cataract surgery and 44% of eyes with no cataract surgery (p=0.006) were on glaucoma medication, and 52% and 24% of them, respectively (p=0.001), were receiving two or more medications. In the cataract group, one eye had undergone retrabeculectomy and cyclophotocoagulation, and four eyes cyclophotocoagulation before cataract surgery, and four eyes had cyclophotocoagulation after cataract surgery (a total of 9 eyes). In eyes with no cataract surgery, one eye had undergone retrabeculectomy and 6 eyes cyclophotocoagulation during the follow-up (a total of 7).

5.10 Cataract surgery in primary open-angle glaucoma and exfoliation glaucoma (IV)

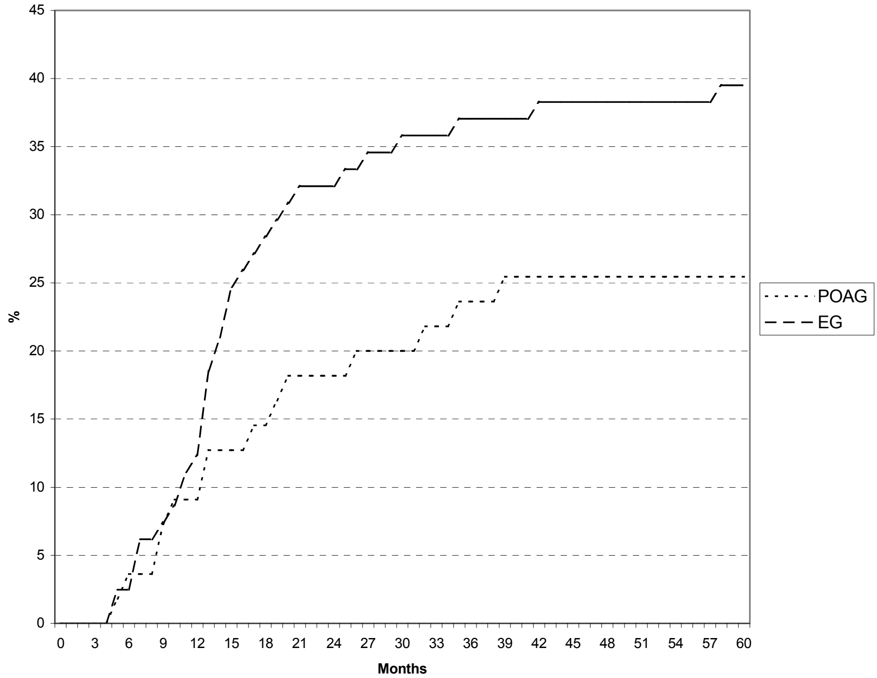
Of the 46 eyes with cataract surgery, 14 eyes (30%) had POAG, and 32 (70%) had EG. Cataract surgery was, however, not significantly more common in eyes with EG than in those with POAG (p=0.09). The other parameters in Table 8 also did not differ significantly between these groups. Cumulative probability of cataract surgery in POAG and EG was similar during the first year of follow-up, but after that, the probability increased in EG to 40% and in POAG to 26% (Fig. 5).

Table 8. Patient characteristics in cataract surgery group according to type of glaucoma

	POAG	EG	p
Number of cataract operations (%)	14/55 (25.5%)	32/81 (39.5%)	0.09
Age on trabeculectomy day			
(mean, years) (SD)	71.2 (11.6)	75.1 (8.1)	0.21
Time from trabeculectomy to cataract surgery			
(mean, months) (SD)	18.6 (11.0)	17.6 (11.2)	0.9
median	15.4	14.4	
Follow-up after cataract surgery			
(mean, months) (SD)	24.3 (13.2)	25.7 (12.9)	0.7
IOP before cataract surgery			
(mean, mmHg) (SD)	15.7 (5.5)	16.3 (4.7)	0.9
IOP at last visit			
(mean, mmHg) (SD)	16.2 (6.1)	17.8 (6.5)	0.9
Topical medication before			
cataract surgery (n)	0.7 (1.0)	0.9 (1.0)	0.5
Topical medication			
at last visit (n)	1.3 (1.2)	1.4 (1.1)	0.8

POAG = primary open-angle glaucoma, EG = exfoliation glaucoma, IOP = intraocular pressure

Figure 5. Cumulative probability of cataract surgery in primary open-angle glaucoma (POAG) and exfoliation glaucoma (EG)



6. Discussion

6.1 Selection of patients

The principal aim of this study was to determine in OAG eyes the success rate for long-term IOP control after primary conventional trabeculectomy and the need for further antiglaucomatous treatment either medical or surgical. Based on clinical experience and on the literature, in the high-risk cases including young patients, black patients, eyes with previous ocular surgery (failed trabeculectomy), trauma, aphakia, active uveitis or neovascular glaucoma, the routine filtration surgery often will fail (Broadway & Chang 2001). In these high-risk eyes, antimetabolites together with conventional filtering surgery or drainage-device implantation is often indicated. This study excluded the high-risk cases. In addition, eyes with normotensive glaucoma were excluded, because the criteria for successful postoperative IOP level are different from POAG or EG. Thus the study group consisted of a consecutive series of primary trabeculectomies performed by one experienced surgeon on eyes with POAG and EG. For statistical reasons, only one eye per patient was included. When the 33 patients of the whole series who had died before the follow-up examination were also excluded, data were available for 138 (93%) eyes.

Due to the common occurrence of exfoliation syndrome in Finland (Lindberg 1917, Tarkkanen 1962, Krause 1973, Peräsalo & Raitta 1992, Hirvelä et al. 1995) and the poorer response of EG to medical treatment, the proportion of EG in this series was high (60%), in contrast to most previous studies'. High percentages of EG have also been reported in other Nordic studies; 64% (Törnqvist & Drolsum 1991) and 56% (Popovic & Sjöstrand 1999) of all patients in each study.

6.2 Choice of methods

This study is a retrospective single-surgeon series of consecutive primary trabeculectomies. By primary trabeculectomy, we mean the first filtrating surgery performed on an eye. The main indications for surgery were uncontrolled IOP or progression of VF or optic disc defects despite maximal tolerated medication. During the period of surgery (November 1994 to August 1996), the technique of trabeculectomy remained fairly unchanged.

Patients were examined by standard clinical methods. The final clinical examination was performed by the author in 102 (74%) of the cases and by one of the coauthors in another 17 cases (12%). Thus, the clinical examinations of the patients were comparable. The patients were followed up for 2 to 5 years (mean 3.5 years).

The retrospective nature of the study caused some problems, particularly in the evaluation of the VF changes. In 36 cases, the preoperative VF had been performed more than 3 months before trabeculectomy, and 6 patients had different kinds of VF examination methods pre- and postoperatively. These cases were excluded from the VF comparison, and in 13 cases fields were unavailable for reasons like dementia or loss of cooperation. Thus, VF defect progression could not be estimated in every case. In the clinical routine, the goal of many prospective glaucoma studies, to examine automated perimetry repeatedly to exclude variation between examinations (Heijl et al. 1989, The AGIS Investigators 1994), could not be fulfilled in every case. In this unselected series, because many of the patients were not capable of performing automated perimetry reliably, kinetic perimetry was used in more than half the cases (52%) reflecting the difficulty of the perimetry and the severity of the cases.

In a retrospective study, the indications for cataract surgery may have varied in individual cases. Cataract surgery was performed by experienced surgeons using the phacoemulsification technique whenever possible.

6.3 Outcome of trabeculectomy in terms of IOP

No standard definition exists for the success of glaucoma surgery with regard to IOP, because no single target pressure can be regarded as a safe limit for disease control in all individual eyes (Kidd & O'Connor 1985, Popovic & Sjöstrand 1991, Singh et al. 2000, Palmberg 2002). We used the limit of 21 mmHg because it makes this study comparable with most of the other studies on the same topic. In some studies, a reduction in IOP of at least 20% or 33% from the presurgical level has served as an additional criterion for success (Nouri-Mahdavi et al. 1995, Chen et al. 1997, Edmunds et al. 2001), and some have used progression of VF defects as a definition of failure (Törnqvist & Drolsum 1991).

With an IOP level of 21 mmHg as the definition of success, the success rate in previous studies has ranged between 48% and 98% depending on follow-up time. The success rate has been shown to decrease with time (Popovic & Sjöstrand 1991, Chen et al. 1997, Briggs & Jay 1999, Molteno et al. 1999). In the present study, the one-year success rate, defined as an IOP of 21mmHg or lower without medication or with a single medicine, was 82%, corresponding to the best previous results without medication in OAG (Watson & Grierson 1981, Briggs & Jay 1999, Edmunds et al. 2001), but it gradually decreased to 52% at 4 years. Similar long-term figures using different criteria have been presented (Jerndal & Lundström 1980, Törnquist & Drolsum 1991, Nouri-Mahdavi et al. 1995). At the last examination, 53% of the eyes were on antiglaucomatous medication, and 12% had had further glaucoma surgery during the follow-up period, indicating the importance of regular long-term follow-up after trabeculectomy.

In the present study, complete success was significantly more common in eyes with POAG than in eyes with EG. A lower success rate without medication in exfoliation eyes has been observed (Mills 1981), but in most of the previous studies the outcome of trabeculectomy between POAG and EG has not significantly differed (Mietz et al. 1999, Popovic & Sjöstrand 1999, Serguhn & Spiegel 1999, Edmunds et al. 2001). The proportionate reduction in IOP can, however, be significantly higher in EG because of initially higher IOP in EG (Edmunds et al. 2001). Better control without further therapy in the EG group has also been reported (Törnqvist & Drolsum 1991, Konstas et al. 1993), but in these studies, the length of use of the preoperative medication in EG was considerably shorter than in our series.

In the present study, the only factors related to losing long-term IOP control in complete-success cases in multivariate analysis were the presence of EG and an early postoperative peak of IOP over 30 mmHg. When complete and qualified success were combined, the difference between POAG and EG became non-significant, with no independent factors worsening the prognosis. Reasons for the less favourable outcome in EG eyes in this study are not clear. In the EG group, the patients were significantly older, the preoperative IOP was significantly higher, and postoperative hyphema was significantly more common than in the POAG group, but none of these factors proved to be an independent significant predictor of failure in the statistical analysis (proportional hazards regression). In our EG group, qualified success and failure eyes had a longer duration of preoperative glaucoma medication than did eyes with complete success ($p=0.06$). This may in part explain the results, because long-term use of topical antiglaucoma medications have been shown to affect the results of trabeculectomy adversely (Sherwood et al. 1989, Lavin et al. 1990).

In this study, early postoperative complications after trabeculectomy were common, but the only complication associated with failure was elevated IOP at the end of the first postoperative month resulting from insufficient filtration. Early hypotony (<5 mmHg lasting 5 days or longer), observed in 25% of the eyes, did not predict long-term success or failure, as was also reported by Popovic (1995), but which is in contrast with the findings of Migdal and Hitchings (1988), who noticed higher final IOP in eyes with low postoperative pressures. On the other hand, Schwenn et al. (2001) reported a positive correlation between the lowest postoperative pressure and later follow-up pressures. In this series, final success (complete or qualified success) did not correlate with lowest postoperative IOP. Reasons for these differences are difficult to explain. Possibly they reflect differences in the management of the postoperative complications.

Studies comparing complication rates between POAG and EG are few. Popovic & Sjöstrand (1999) found a similar pattern of complications in POAG and EG; specific complications were not reported separately. In the present series, postoperative hyphema, found in 17% of the eyes, was the only complication that differed significantly between POAG (7%) and EG (24%). Törnqvist and Drolsum (1991) reported hyphema rates of 14% in POAG and 19% in EG. Increased risk for postoperative hyphema may be explained by the common occurrence of vasculopathy in the iris of exfoliative eyes (Vannas 1969, Naumann et al. 1998).

Concerning the effect of the location of trabeculectomy on IOP and occurrence of complications, results are somewhat controversial. One might expect that the posterior location results in lower IOP due to increased uveal outflow or a cyclodialysis type of effect. This has not, however, been the case; some studies have shown better results with an anterior approach (Watson & Grierson 1981) or have reported no correlation with outcome (Taylor 1976, Duzanec & Kriegelstein 1981, Konstas & Jay 1992). For the same reason, the risk of complications, particularly hypotony (Duzanec & Kriegelstein 1981) and bleeding (Watson & Grierson 1981, Konstas & Jay 1992), may be increased by the posterior approach, as was also observed in some studies, but not in others (Taylor 1976). In the present study, location of the trephined block in the AC angle did not influence the final success rate of IOP control or the complication rate significantly, despite a tendency for the posterior location to survive better in the EG. In contrast, early hypotony was slightly but not significantly more common in the anterior group. In this series, the difference between anterior and posterior location observed in histological preparations was probably not marked, because during surgery different locations were not the aim.

Elevated IOP at the end of the first postoperative month resulting from insufficient filtration was the only complication associated with failure. This highlights the importance of the early postoperative follow-up visits after trabeculectomy and the chance to save some of the filtering blebs from scarring during the first postoperative month. Proper timing of LSL within 7 to 14 days after surgery (Savage et al. 1988, Liebmann & Ritch 1996) and recognizing clinical signs possibly associated with poor development of the filtering bleb and adjusting the postoperative anti-inflammatory medication in these eyes might enhance long-term bleb function (Stewart et al. 1991, Stewart & Pitts 1993, Shingleton 1996, Marquardt et al. 2004).

6.4 Progression of visual field defects

The present study confirms earlier findings that VF deterioration may occur over the years despite effective IOP-lowering therapy (Kidd & O'Connor 1985, Watson et al. 1990, Rosetti et al. 1993, Brubaker 1996). Progression of glaucomatous VF defects occurred in (41%) eyes during the follow-up of 2 to 5 years (mean 3.5) after trabeculectomy.

Most of the fields that had progressed were preoperatively classified as severe (20 severe vs. 14 mild or moderate). Progression of defects in Goldmann and Octopus fields was equally common (18/43 vs. 16/40 cases). The fairly high progression rate in this series may be explained in part methodologically; the ten patients with early trabeculectomy had only one preoperative VF, and in only two-thirds of the cases with VF progression was the decision concerning defect progression confirmed by re-examination of VF or by discovery of concurrent optic disc changes or loss of fixation. It is possible that the inter-test variation played some role (Heijl et al. 1989, The AGIS Investigators 1994). Misinterpretation of the defect progression particularly in cases with severe defects (40% of preoperative VFs), of which 61% were examined by Goldmann perimetry, is possible. The progression of VF defects by Octopus perimetry was interpreted by the criteria presented by the Glaucoma Laser Trial Research Group (1995). For severe defects, these criteria for progression might have been too loose.

One explanation for the high progression rate is postoperative IOP level. The initial IOP reduction and the absolute IOP reduction from preoperative to last examination was significantly smaller in eyes with VF defect progression. In eyes without progression and in eyes with progression, the mean last postoperative IOP did not, however, differ significantly, nor did the percentage reduction reach statistical significance, corresponding to the results of Popovic & Sjöstrand (1999) in eyes with unchanged/improved vs. deteriorated VF after trabeculectomy. The high standard deviation in mean postoperative IOP in the present study indicates, however, that during follow-up, the IOP had been too high in some eyes, particularly in eyes that progressed. And it is possible that the single IOP measurements did not discover diurnal peaks, although these may be less common following filtration surgery than in unoperated glaucomatous eyes (Migdal et al. 1986, Wilensky 2004). In newly diagnosed glaucoma with mild VF defects, IOP levels 15 to 17 mmHg are probably safe, as shown in the Collaborative Initial Glaucoma Treatment Study (CIGTS) (Lichter et al. 2001), but in eyes with advanced defects, IOP should be kept as low as the 12 mmHg shown to be safe in associative analysis in the Advanced Glaucoma Intervention Study (The AGIS Investigators 2000). VF of eyes even with this low pressures have been shown to progress (Kidd & O'Connor 1985), however, as was also evident in a few eyes with this pressure level in the present study.

More eyes (65%) with stable VF had a final IOP level of 21 mmHg or lower (complete or qualified success) than did those (53%) who progressed, although this difference was not statistically significant. In this series we thus could not detect a significant relationship between VF progression and the final IOP level of 21 mmHg or lower. Moreover, the number of eyes with an IOP level less than 18 mmHg without any medication or additional glaucoma surgery at the final examination was similar in eyes with stable (38%) and with progressing VF (32%).

Significant risk indicators for progressive VF loss in the present series were severe VF defect preoperatively, use of preoperative oral antiglaucomatous medications, and smaller IOP reduction after surgery, all indicating glaucoma that was more therapy-resistant. The disease might have been so far advanced at the time of trabeculectomy that despite IOP lowering, VF progression continued after the operation. In some eyes, glaucoma surgery may have been used too late. Reasons for postponing glaucoma surgery in elderly patients are the risk for possible early complications requiring frequent follow-up visits and possibly additional surgery in the early postoperative period. On the other hand, in patients with poor general health, satisfactory IOP control without medication may be the main goal of glaucoma surgery because of the side-effects of medications or poor compliance in the use of topical glaucoma medication. In contrast with some previous findings, neither older age (Stewart et al. 2000, Lichter et al. 2001, Leske et al. 2003, Jonas et al. 2004) nor exfoliation (Leske et al. 2003) was a statistically significant risk factor for VF progression, although field progression was slightly more common in EG (52%) than in POAG (40%).

6.5 Visual impairment in operated eyes

Development of glaucoma-related visual impairment and blindness in various studies is difficult to compare, because the definition of blindness varies, stage of VF defects may not have been equally severe at the beginning of the follow-up, and some studies do not separate glaucoma-related blindness from blindness due to other causes. In this study, during the mean follow-up of 3.5 years after trabeculectomy the prevalence of glaucoma-related low vision (VA of <0.3 to 0.05) in the operated eye increased from 6% to 7% and that of blindness (VA of <0.05 or visual field constriction to <20º at its widest diameter) from 4% to 10%. Visual impairment at last follow-up was significantly more common in eyes with severe preoperative VF defect, as shown previously (Grant & Burke 1982, Parc et al. 2001, Chen 2003), but was not associated with patient age, as proposed by Hattenhauer et al. (1998).

The 10% prevalence of glaucoma-related blindness at about 10 years after diagnosis of glaucoma in one eye corresponds with findings of Kwon et al. (2001) and Chen (2003), although they did not consider various treatment modalities (medication, laser, filtration surgery) separately, and their definition of blindness was less severe (VA ≤20/200 and/or VF ≤20º at its widest diameter/in all quadrants). In the present series, at the end of the follow-up period only two patients (1.4%) were blind in both eyes.

Few studies have examined the probability of becoming blind after filtration surgery. According to Molteno et al. (1999), the probability of loss of useful vision (VA ≤20/400 or VF ≤5º radius) in one eye from any cause was 13%, 28%, and 40% at 5, 10, and 15 years, respectively, but only one-third was due to progression of glaucoma. Parc et al. (2001) reported higher figures, but the criteria were less severe (VA ≤20/200 and/or VF ≤20º in its widest diameter); the probability of blindness in one eye in patients with open-angle glaucoma was 22% at 5 years and 46% at 10 years. In the Advanced Glaucoma Intervention Study (The AGIS Investigators 2004), 10-year cumulative incidence of unilateral VA impairment (VA <0.2) or VF impairment or both in white patients in a trabeculectomy-ALT-trabeculectomy group was 30.4% from all causes.

6.6 Cataract surgery in trabeculectomized eyes

The progression of a cataract is considered to be a late complication of trabeculectomy (The AGIS Investigators 2001). Age, EG, diabetes, postoperative hypotony, marked inflammation, and flat AC after trabeculectomy have been associated with increased risk for cataract (Vesti 1993, The AGIS Investigators 2001). In the present study, patients undergoing cataract surgery during follow-up were significantly older at the time of trabeculectomy than were those without cataract surgery, but no other characteristics associated with increased risk for cataract emerged. The eyes that underwent cataract surgery had considerably worse VA prior to trabeculectomy, supporting the role of age as the most important risk indicator for cataract surgery in this series. During follow-up, 26% of POAG and 40% of EG eyes had cataract surgery (p=0.09), which corresponds to the 19% of POAG and 32% of EG eyes in Popovic & Sjöstrand (1999).

The effect of cataract surgery on IOP or on the number of antiglaucoma medications in trabeculectomized eyes is controversial. Some studies show no negative effect (Park et al. 1997, Manoj et al. 2000, Mietz et al. 2001), while some reveal worsening of IOP control or greater number of antiglaucoma medications after phacoemulsification (Chen et al.1998, Crichton & Kirker 2001, Halikiopoulos et al. 2001, Casson et al. 2002, Derbolav et al. 2002, Rebolleda & Muñoz-Negrete 2002, Shingleton et al. 2003). In the present study, mean IOP at the last examination was higher, although not significantly so than before cataract surgery, but the mean number of topical antiglaucoma medicines had increased significantly. In 41% of the eyes, the use of topical antiglaucoma medicines had increased after cataract surgery, and four eyes had undergone cyclophotocoagulation. In this series, cyclophotocoagulations were done by either a krypton 647 nm or a diode 670 nm laser (Raivio 2002). However, in an eye with good IOP control (complete success), a cataract operation improved the chances that the eye remained a complete success.

In the present series, prior to cataract surgery, 48% of these eyes were categorized as complete successes, 22% as qualified successes, and 30% as failures. Of those categorized as complete successes prior to cataract surgery, 28% remained so during the follow-up. The number of failures increased from 30% before surgery to 61% after cataract surgery. Previously, continuing good or improved control of IOP without antiglaucoma medication after cataract surgery has been reported in 42% (Mietz et al. 2001), with even higher figures, up to 82%, reported (Crichton & Kirker 2001, Halikiopoulos et al. 2001, Casson et al. 2002, Derbolav et al. 2002, Rebolleda & Muñoz-Negrete 2002). In these studies, the high percentage of eyes with good postoperative IOP control without medication is in part explained by the higher percentages of eyes with good IOP control and functioning filtering blebs before cataract surgery (up to 100% in Rebolleda & Muñoz-Negrete 2002). The higher final failure rate in cataract eyes in this study was in part due to the fact that in 14 eyes cataract surgery was performed in eyes in which trabeculectomy had failed to control IOP, and of the 14 new failures, 6 had complicated cataract surgery.

7. Summary and conclusions

This retrospective study was planned to evaluate the long-term outcome of conventional trabeculectomy in POAG and EG. Based on the results of the various substudies, the following conclusions can be drawn.

In this consecutive series of single-surgeon trabeculectomies, females predominated (60%). The overall mean age was 70.1 years. The proportion of EG (60%) was higher than in most previous studies, possibly explaining some differences in the outcomes. Preoperative VF defect was considered severe in 40%.

Patients with EG were significantly older and had higher preoperative IOP, but the duration of their glaucoma was slightly shorter than that of the patients with POAG.

During the follow-up period, the initially highly significant IOP-reducing effect of trabeculectomy gradually decreased, as reported previously. At one year, 82% of the operated eyes had an IOP of ≤21 mmHg without or with a single topical medication; at 4 years the corresponding percentage was 52%. At the last examination, 53% of eyes were on antiglaucomatous medication, and 12% had had further glaucoma surgery during follow-up.

Early postoperative complications were common, and hyphema was significantly more common in the EG group, but in this series postoperative complications did not predict poor outcome. The only significant predictor of failure was an increased IOP at the end of the first postoperative month.

The location of the trephined block defined in histological preparations as anterior or posterior, did not correlate significantly with long-term success or complication rate.

In this unselected series of eyes, despite trabeculectomy, progression of FV defects was fairly common. Progression was associated with severity of initial VF defect. No significant correlation appeared between defect progression and the last IOP, but association between stability of VF and amount of IOP reduction after surgery, and the high standard deviation of the mean postoperative IOP both indicate that a lower target IOP level would be needed, particularly in eyes with an initially severe VF defect. However, even eyes with very low IOP (< 12 mmHg) did not escape progression of VF defect.

Development of visual impairment due to glaucoma occurred despite surgery. Glaucoma-related low vision in the operated eye increased from 6% to 7% and blindness from 4% to

10% during the follow-up period, but only 1.4% of the patients became bilaterally blind. Development of visual impairment was associated with the severity of initial VF defect.

In this series, patient age was the only significant risk indicator for cataract surgery. In eyes with cataract surgery, the BCVA was already reduced before trabeculectomy, possibly related to higher age. Patient age thus deserves more blame for cataract progression than does trabeculectomy. In an eye with complete success in IOP control, cataract surgery improved the chance of that eye's remaining a complete success through follow-up, but one-third (36%) of the eyes categorized as a complete success before cataract surgery were considered failures at the last examination. Altogether, the number of failures in the cataract surgery group increased from 30% before surgery to 61% at the last examination.

Based on these results, one can emphasize the importance of regular long-term follow-up examinations of patients following trabeculectomy. The early postoperative period is crucial to guarantee the development of the filtering bleb. It seems that in ordinary clinical settings, an adequate target IOP is not reached in every eye. Earlier surgery might improve the results in eyes with EG. In eyes with a fair surgical IOP outcome, more active remedication or new surgery should be considered. Regular VF examinations are important also in eyes with a good postoperative IOP result. In eyes with good IOP control, cataract surgery may not worsen the outcome, but as a whole, cataract surgery after trabeculectomy is likely to increase the need for antiglaucomatous medication.

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Pia Ehrnrooth

Pia Ehrnrooth

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