Eye (2003) 17, 1025–1031

www.nature.com/eye

CLINICAL STUDY

Development and progression of cataract in patients required repeated corneal transplantation

S Rumelt, T Blum-Hareuveni, V Bersudsky and U Rehany

Abstract

Purpose **To evaluate the incidence of cataract development in patients required repeated corneal transplantations, the types of cataract and the effect of cataract extraction on the corneal regrafts survival.**

Patients and Methods **The charts of all the patients that underwent repeated corneal transplantation between 1985 and 1998 were reviewed for the development of cataract after the first or subsequent keratoplasties. In all, 80 patients underwent 122 repeated corneal transplantations, of which six underwent surgery in both eyes. The average follow-up period of all the patients with repeated keratoplasty was 89.5 months from the first keratoplasty.**

Results **Of 86 eyes 19 (22%) that underwent repeated keratoplasties developed cataract. The cataract developed between 1 month and 17 years (average 61.3 months) after the first transplantation. The incidence of cataract development was independent of the number of repeated keratoplasties. In certain patients, such as patients with acute and severe regraft immune rejection, the cataract progressed more rapidly. Despite different cataract extraction procedures, the grafts in 17 eyes of the 19 (89.5%) failed following cataract surgery and 16 of them underwent additional corneal regrafting. The regrafts in eight of the 16 regrafted eyes (50%) remained clear with improvement in visual acuity. At the end of the follow-up, 10 eyes of the 19 had clear regraft (53%) comparable with the rate of clear grafts in the entire regrafted group (51%, $P = NS$).**

Conclusion **Corneal transplantation may be a trigger for slow development of cataract over years but repeated keratoplasties did not increase the risk for cataract development. Although failure of regrafts may occur after cataract extraction, subsequent corneal transplantation has a comparable survival and visual outcome with the entire regrafted group.**

Eye (2003) **17,** 1025–1031. doi:10.1038/sj.eye.6700725

Keywords: repeated corneal transplantation; regraft; cataract; corneal graft failure; survival

Introduction

Cataract formation has been found to develop in 24–60% of the patients after a single penetrating keratoplasty (PK).[1,2] The single most predictive factor for cataract development was the age of the patient. Advanced age was found associated with increased risk for the development of cataract after PK. Other attributing factors for cataract formation included the preoperative visual acuity, preoperative lens opacity, topical corticosteroid use, and the initial diagnosis. Certain preoperative diagnoses are associated with increased risk for cataract development. Sixty percent of the patients with Fuchs' endothelial dystrophy developed post-PK cataract and 44% of them required cataract extraction.[3] Topical corticosteroids attributed to the development of posterior subcapsular cataract in 32.5% of keratoconic patients undergoing PK in whom high doses and prolonged use were documented.[4] The development of cataract in patients required repeated corneal transplantation to the best of our knowledge has never been assessed before.

This study was designed to assess the incidence and timing of development and progression of cataract in patients required

Department of Ophthalmology, Western Galilee - Nahariya Medical Center, Nahariya, Israel

Correspondence:
S Rumelt
Department of Ophthalmology
Western Galilee - Nahariya Medical Center
P.O. Box 21 22100 Nahariya, Israel
Tel: +972-4-9107635;
Fax: +972-4-9107611

Presented in part at the 24th International Congress of Ophthalmology, Sydney, Australia, April, 2002

repeated corneal transplantations, the types of cataract and the influence of cataract extraction on corneal regraft survival and visual outcome.

Patients

The charts of all the patients who underwent repeated corneal transplantation between 1985 and 1998 at our tertiary referral centre were reviewed. The repeated corneal transplantation group included 86 primary grafts and 122 regrafts in 86 eyes of 80 patients out of 1040 penetrating keratoplasties (15.8%) that were performed during this period. In all, 86 eyes had primary transplantation, 55 eyes had one repeated keratoplasty, 27 eyes had two, three eyes had three, and one eye had four. The data for survival analysis were available in 110 of the 122 repeated grafts and were used for plotting a Kaplan–Meier curve.

All the patients with preoperative clear crystalline lens that developed cataract at any time after the primary or subsequent keratoplasty were included in the study. Three patients with preoperative crystalline lens opacities were excluded from this study. Two of them with visual impairing cataract underwent triple procedure and one with minimal cataractous opacities underwent only PK. In none of the patients, an intraoperative trauma to the iris or the crystalline lens was reported. The average follow-up period of all the patients with repeated keratoplasty was 89.5 months and of those that developed cataract 89.8 months.

Methods

Several precaution measures to prevent trauma to the crystalline lens during PK included preoperative constriction of the pupil with topical pilocarpine 2%, use of Barron–Hessburg vacuum trephine with controlled penetration and covering the pupillary aperture with sodium hyaluronate to prevent lens desiccation and trauma before suturing the corneal transplant. The donor corneal button was sutured with 10-0 nylon suture usually in a continuous fashion after placement of 4 temporary cardinal sutures. The suture technique and the diameters of the donor corneal buttons and recipient bed were similar to the repeated transplantation patients that did not develop cataract. One expert in corneal transplantation (UR) performed all the repeated keratoplasties.

The patients were treated with topical corticosteroid drops every 2 h, which was tapered gradually, over 2 months and antibiotic drops every 2 h after surgery, which was discontinued after 2–3 weeks. Patients were followed-up regularly every day for the first postoperative week, weekly in the first month and then every 3 months. The patients were instructed to undergo an immediate ophthalmologic examination whenever they felt ocular pain or discomfort, decreased vision, redness of the eye, or following ocular trauma. The preoperative evaluation and the postoperative follow-up included visual acuity, applanation tonometry, slit-lamp examination with dilated pupils, direct, and indirect pupil-dilated ophthalmoscopy. The clarity of the crystalline lens or the type and density of the cataract were evaluated by pupil-dilated slit-lamp examination. Cataract was defined as any opacity in the crystalline lens. The definitions of complications such as immune graft rejection and their treatment are described elsewhere.[5,6] Statistical analysis for categorical covariates was performed with χ^2 test and two-tailed $P<0.05$ was considered statistically significant.

Results

Data on cataract development

Cataract developed in 19 of the 86 eyes (22%) (Table 1). The male to female ratio was 1 : 0.7. The age of the patients at first transplantation ranged between 4 and 70 years (average 41.6, median 44, SD$\pm$21.5). The cataract appeared between 1 month and 204 months (average 61.3, median 48, SD$\pm$66) after the first transplantation (Figure 1). The progression of the cataract from diagnosis to maturation in 10 eyes occurred between 1 day, due to penetrating ocular trauma, and 60 months (average 15.8 months, median 2, SD$\pm$24.4). The average time from the diagnosis of cataract to its extraction in the other nine eyes was 35.4 months (range: 2 weeks to 9 years). Figure 2 shows the progression time of the cataract from the first keratoplasty.

Cataract developed in 12 of the eyes after the primary transplantation (14% of all the first transplantation), in six after the second transplantation, (11% of all second transplantation) and in one after the third transplantation (4% of all third transplantation). The difference in the occurrence of cataract following successive penetrating keratoplasties was statistically insignificant. The indications for the first transplantation were similar to those reported previously by us for the entire regrafted patients.[5] In total, 10 patients had corneal scar (eight of them due to herpetic keratitis without uveitis), seven had keratoconus, one had Fuchs' corneal dystrophy, and one had perforated ulcer.

Types of cataract

The most common cataract type was nuclear sclerosis (10 of 19 eyes, 52%). Nuclear sclerosis and posterior subcapsular cataract were noted in two additional eyes (10%). Posterior subcapsular cataract developed in five

eyes (26%), of which three had cortical opacities as well. Cataract after trauma developed in two eyes (10%).

The clinical appearance of posterior subcapsular cataract in three eyes (15.8%) over an average period of 23 months (range 2–60 months) raises the possible aetiology of steroid-induced cataract. Two eyes (10.5%) had postoperative penetrating eye injury causing the development of mature cataract within 1–2 days. In three of the eyes (15.8%), nuclear sclerosis progressed to mature cataract over a period of 2 weeks in conjunction with severe immune graft rejection.

Surgical management of the cataract, graft clarity, and visual outcomes

The surgical management of cataract associated with failed graft was simultaneous cataract extraction and PK with or without IOL implantation. In cases of clear graft, cataract extraction alone was performed. Surgical intervention was indicated according to visual functions (visual acuity, glare etc) and patients' desire. Surgical intervention included triple procedure in eight eyes (42%), extra-capsular cataract extraction (ECCE) and posterior chamber intraocular lens (PC-IOL) in four eyes and phacoemulsification with PC-IOL in two eyes (Table 1). Cum-capsular cataract extraction (CCCE) and anterior vitrectomy was performed in three eyes. One had PK and intracapsular cataract extraction and another patient is waiting for corneal regrafting. Immune rejection was not encountered in any of those eyes before the extraction of the cataract.

After cataract surgery, two regrafts (11%) remained clear with visual acuity of 20/30–20/50. All the other regrafts failed due to various causes including immune graft rejection in nine eyes (47%), bullous keratopathy due to endothelial insufficiency in four eyes (20%), corneal graft ulcer in two (11%) and scarring in two (11%). The cumulative survival proportion (Kaplan–Meier curve) of the corneal grafts is presented in Figure 3. The regraft survival was comparable with the survival of the entire regrafted group. The causes for graft failure in the group that developed cataract were similar to those of the entire regrafted group.[5]

Sixteen of the 17 eyes with graft failure after cataract surgery had repeated corneal transplantation. In eight of them (50%) the corneal regraft remained clear, in seven of them the visual acuity improved from HM-20/200 to 20/100–20,/40 and in one, visual acuity remained poor due to cystoid macular oedema. In the other eight eyes (50%), the regrafts failed due to glaucoma (three eyes), immune rejection (2), suprachoroidal expulsive haemorrhage (1), regraft ulcer (1), and pseudophakic bullous keratopathy (1). All the eyes that underwent phacoemulsification or cum-capsular cataract extraction were complicated by bullous keratopathy.

The Kaplan–Meier curve of the grafts in the group that developed cataract showed a similar cumulative survival proportion compared with the entire repeated transplantation group during the first and the second year of follow-up and lower after the second year (Figure 3). The differences in the survival proportions were statistically insignificant. The cumulative graft survival proportions at 12, 24, and 36 months were 0.66, 0.61, and 0.44 for the group that developed cataract and 0.57, 0.38, and 0.29 for the entire regrafted group, respectively. However, at 90 months it was 0.143 and 0.18, respectively ($P = \text{NS}$, χ^2 test).

At the end of the follow-up, 10 of the 19 eyes (53%) that developed cataract had clear regraft and nine of them (47%) had remarkable visual acuity improvement. In the entire regrafted group, 44 of the 86 eyes (51% over an average period of 89.5 months) remained with clear regrafts and 39% with visual acuity improvement ($P = \text{NS}$, χ^2 test). The survival and visual outcome in regrafted eyes complicated by the development of cataract was slightly better than that of the regrafts complicated by immune graft rejection (37%, $P = 0.18$, χ^2 test) and statistically better than the regrafts complicated by glaucoma (17%, $P = 0.012$, χ^2 test).[5]

Discussion

Cataract development in patients with repeated corneal transplantation was rather frequent, complicating 22% of the eyes in an average follow-up of 89.5 months. However, this incidence of cataract development in the patients required repeated transplantation was lower than the reported incidence after a single corneal transplantation (24–60%).[1–3] The incidence was also lower than the reported incidence of cataract in the population of 49 to 96-years-old and in the general population of various geographic areas.[7,8] The lower incidence of cataract in the regrafted patients in the current study may be explained by the lower age range.

The incidence of cataract development after repeated keratoplasties was similar to the incidence after primary keratoplasty in the patients required repeated keratoplasty; therefore, we presume that regrafting did not substantially increase the risk for cataract development. The slow development and progression of cataract over years, in most of the corneal regrafted eyes, and the independence between the incidence of cataract development and the number of regrafts further support this presumption. In contrast, the incidence of other complications such as glaucoma after keratoplasty increased with subsequent regrafting.[9]

Table 1 Pre- and postoperative data of the repeated corneal transplanted group that developed postoperative cataract

Eye #	*Gender/ age*	*Initial diagnosis*	*Best-corrected VA before the first keratoplasty*	*No. of graft at cataract development*	*Corneal graft/ bed diameter (mm)*	*Total FU (m)*	*Type of cataract*	*Type of surgery*	*Other interventions*	*Complications*	*Final best-corrected VA*	*Success/ failure*	*Reason for failure*
1	F/44	Keratoconus S/p epi-keratophakia	20/200	1	8.5/8.0	43	Nuclear sclerosis	Phaco + PC−IOL	RI + CS	Graft decomp-ensation	2 ft CF	F	PBK
				2	8.5/8.0	11			Nd:YAG capsulotomy	Secondary cataract CME	6 ft CF	S	CME
2	M/65	Herpetic scar	1 ft CF	1	8.0/7.5	46	Nuclear sclerosis	ECCE + PC-IOL		Rejection herpetic keratitis, uveitis	2 ft CF	F	Rejection
				2	8.0/7.5	94					20/40	S	
3	M/40	Fuchs' dystrophy	13 ft CF	3	8.0/7.5	32	Nuclear sclerosis (mature)	Triple (PK, ECCE + PC−IOL)		Rejection.	HM	F	Rejection
				4	8.0/7.5	27			Cyclocryo, cyclophoto	Glaucoma	LPI	F	Glaucoma
4	M/70	Herpetic scar	13 ft CF	1	7.5/7.0	14	Nuclear sclerosis		Suture of wound dehiscence	Rejection, epithelial defect/ulcer, wound dehiscence after suture removal	10 ft FC	F	Ulcer
				2	7.5/7.0	28		Triple (PK, ECCE + PC−IOL)			20/60	S	
5	M/10	Keratoconus	HM	2	8.0/7.5	72	Nuclear sclerosis		RI + CS		HM	F	Rejection
				3	8.0/7.5	47		Triple (PK, ECCE + PC−IOL)			20/30	S	
6	M/42	Keratoconus	1 ft CF	1	8.5/8.2	204	PSC, steroid induced (mature)				HM	F	Rejection
				2	8.5/8.2	59		Triple (PK, ECCE + PC−IOL)		Rejection	3 ft CF	F	Rejection
				3	8.5/8.2	41			Nd:YAG capsulotomy	Secondary cataract	20/100	S	
7	M/72	Herpetic scar	20/200	1	7.5/7.0	18	Nuclear sclerosis (mature)			Epithelial defect, rejection	2 ft CF	F	Rejection
				2	7.5/7.0	12		Triple (PK, ECCE + PC-IOL)		Rejection	2 ft CF	F	Rejection
8	M/16	Keratoconus	4 ft CF	1	7.7/7.5	6	Traumatic cataract (lenticular perforation)	PK, CCCE + AV	Suture of traumatic wound	Traumatic wound dehiscence x2	20/30 (60 m FU)	S	
9	M/54	Herpetic scar	HM	1	8.5/8.0	132	Nuclear sclerosis			Rejection	HM	F	Rejection
				2	8.5/8.0	12		Triple (PK, ECCE + PC−IOL)			HM	F	ABK
				3	9.1/8.0	120				Glaucoma	LPI	F	Absolute glaucoma

Table 1 Continued

Eye #	*Gender/ age*	*Initial diagnosis*	*Best-corrected VA before the first keratoplasty*	*No. of graft at cataract development*	*Corneal graft/ bed diameter (mm)*	*Total FU (m)*	*Type of cataract*	*Type of surgery*	*Other interventions*	*Complications*	*Final best-corrected VA*	*Success/ failure*	*Reason for failure*
10	F/52	Herpetic scar	2 ft CF	2	8.2/8.0	15	Nuclear sclerosis + PSC (mature)			Cataract + rejection	HM	F	Rejection
				3	8.5/8.0	34		PK + ICCE			HM	F	During 3rd transplant. Explosive hem.
11	F/57	Herpetic scar	20/200	1	7.5/7.0	12	PSC + cortical (mature), steroid induced	CCCE + AV + PC−IOL		PBK	3 ft CF	F	PBK
				2	8.0/7.5	39				Glaucoma	20/200	F	Glaucoma
12	M/24	Keratoconus	17 ft CF	2	9.0/8.75	56	PSC	Phaco + PC−IOL	Epikerato-phakia, Suture of wound	PBK, traumatic wound dehiscence x2	3 ft CF	F	PBK
				3	9.0/8.5	8			Suture of wound	Traumatic wound dehiscence	20/40	S	
13	F/70	Keratoconus	2 ft CF	1	8.5/8.0	50	Cortical + PSC (mature), steroid induced	CCCE + AV			2 ft CF	F	ABK
				2	8.5/8.0	33					20/80	S	
14	F/24	Keratoconus	20/200	1	8.25/8.0	56	Traumatic mature cataract	ECCE + PC−IOL	RD repair	Retinal detachment	3 ft CF	F	Scar
				2	8.25/8.0	8					20/50	S	
15	M/53	Perforated ulcer s/p chemical burn	10f ft CF	1	7.5/7.0	5	Nuclear sclerosis	ECCE + PC−IOL		Graft ulcer	10 ft CF	F	Ulcer
16	M/12	Alkali burn	LP	2	8.25/8.0	36	Nuclear sclerosis (mature)		Cataract after rejection		LP	F	Rejection
				3	8.25/8.0	58		Triple (PK, ECCE + AV + PC−IOL)	RD repair	Retinal detachment, rejection	NLP	F	Rejection
17	F/44	Herpetic scar	HM	2	8.0/7.5	7	Nuclear sclerosis (mature)	Waits for surgery		Cataract + rejection	HM	F	Rejection
18	F/4	Traumatic corneal scar	CF	1	8.5/8.0	252	Cortical + PSC			Amblyopia, Exotropia	6 ft CF	F	Graft scar
				2	8.5/8.0	51		Triple (PK, ECCE + PC−IOL)	Strabismus surgery	PBK	6 ft CF	F	PBK
19	M/37	Herpetic scar	3 ft CF	2	8.0/7.5	10	Nuclear sclerosis + PSC	ECCE + PC−IOL	Tarsorrhphy	Rejection	20/50	S	

BK, bullous keratopathy; ABK, aphakic bullous keratopathy; PBK, pseudophakic bullous keratopathy; KC, keratoconus; VA, visual acuity; ft, feet; CF, counting fingers; HM, hand movement; LPC, certain light perception; LPI, uncertain light perception; FU, follow-up; m, months; RD, retinal detachment; AV, anterior vitrectomy; CsA, cyclosporine-A; Trabec., trabeculectomy; F, failure; S-success.

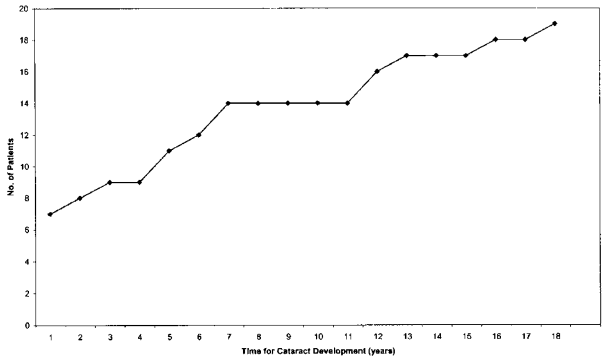

Figure 1 Interval between the first corneal transplantation and the appearance of cataract in years.

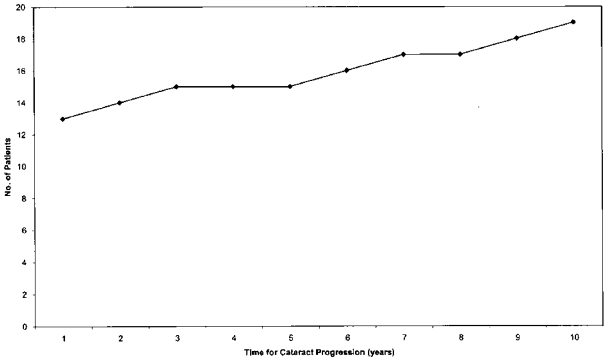

Figure 2 Interval from the first corneal transplantation to cataract maturation or extraction in years.

Cataract development may be triggered by postoperative altered lens metabolism and inflammation or by microtrauma during keratoplasty. The development of cataract in 21% of the patients, who were under the age of 25 years, suggests that PK might have had a certain role in its development. The appearance of nuclear sclerosis as early as 1 month following the primary keratoplasty in 15.8% of the eyes may further support the assumption that PK might have been a trigger for cataract development in these eyes.

Cataract that developed and progressed due to perforating ocular trauma, prolonged topical corticosteroids instillation[4,10,11] and in conjunction with acute and severe immune graft rejection had a specific appearance and rapid progression. After penetrating ocular trauma, cortical cataract maturated by 1–2 days. Corticosteroids presumably induced a posterior subcapsular cataract that developed over a period of 2–60 months although the total amount of corticosteroid given was similar to that given to the rest of the eyes in the total regrafted group. The reported average amount of topical dexamethasone 0.1% that may cause cataract was 765 units equivalent (approximately eight bottles of 5 ml)

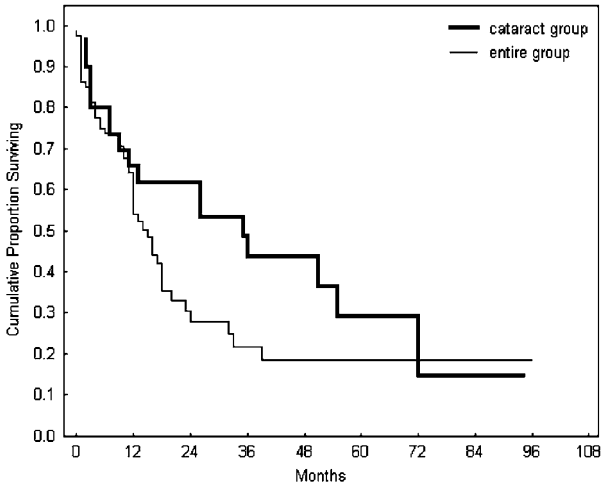

Figure 3 Kaplan–Meier cumulative survival proportion of the corneal grafts from the extraction of the cataract until failure (bold line) compared with the survival proportion of the rest of the repeated corneal transplantation group (thin line). The survival time is in months.

over 10.5 months.[10] Although our three patients received approximately one-third of that amount, it is still in the range of the reported amount that may induce cataract.[10] Another distinctive type of cataract was associated with acute and severe immune graft rejection, in which nuclear sclerosis progressed to mature cataract within 2 weeks due to severe anterior chamber inflammatory response.

Some of these cataracts may be preventable. Traumatic cataract may be prevented by protective eyewear given primarily to protect the corneal graft. Corticosteroid-induced cataract may be prevented or at least attenuated by substituting corticosteroids with nonsteroidal anti-inflammatory drugs and cyclosporine-A when reasonable anti- inflammatory effect can be achieved.

Despite different surgical approaches for cataract extraction, the regrafts in most cases failed and additional corneal regrafting was required. The surgical visual outcome in our study differs from previous studies reporting on cataract development after single PK. These studies reported on a good visual outcome and graft survival following a triple procedure as well as sequential surgeries.[12–16] However, the current study deals with patients required repeated corneal transplantations, which were at a higher risk for postoperative complications and failure than primary transplantation. The causes for graft failure and graft survival proportion were similar in the group that developed cataract and the entire regrafted group, suggesting that cataract surgery had no direct deleterious effect on graft survival.

The cumulative graft survival proportion as plotted in Kaplan–Meier curve showed similar proportion of

survival in the group that develop cataract and the regrafted group that did not developed cataract. Although the survival rate was relatively low, the data analyses could not be compared with previous studies that addressed single keratoplasty.[17–21] Graft clarity and visual outcome in our study were similar to that of the entire repeated corneal transplanted group and higher than the rate of regraft clarity in eyes complicated by immune graft rejection or glaucoma.[5,9]

In conclusion, cataract development after repeated corneal transplantation is a frequent short- and long-term complication. However, cataract surgery, when indicated, does not decrease the overall survival rate of the repeated corneal grafts.

Acknowledgements

The authors thank Orly Yakir, MA, for the statistical analysis.

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