

The Role of Atopy in Corneal Graft Survival in Keratoconus

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Purpose: To compare the prevalence of endothelial rejection episodes and the probability of graft survival after initial and repeat penetrating keratoplasty (PK) in patients with keratoconus with and without atopy.

Methods: A retrospective review was conducted of all patients receiving PK for keratoconus at the University of Texas Southwestern Medical Center at Dallas from 1988 to 2009. Inclusion criteria involved those with both an International Classification of Diseases-9 code for keratoconus and a Current Procedural Terminology code for PK based on a computer database search. Patients younger than 18 years were excluded. These records were then reviewed for a history of atopic disorders. The main outcome measures included the prevalence of endothelial rejection episodes and the probability of graft survival. The probability of corneal graft survival in patients with and without a history of atopy was compared using the Kaplan–Meier method.

Results: There were 168 grafts in 122 patients. There were 66 (39.2%) and 102 (60.8%) grafts with and without a history of atopy, respectively. Bilateral first grafts were required in 32 patients, 14 and 18 patients with and without a history of atopy, respectively. The atopic and nonatopic groups had no significant differences with respect to age, preexisting ocular conditions, concomitant surgical procedures, and length of follow-up. Men received first grafts significantly more frequently than women in the nonatopic group ($P = 0.029$); however, there was no sex difference in repeat grafts. There were no significant differences in the prevalence of endothelial rejection episodes after the first ($P = 0.716$), second ($P > 0.999$), and third or further grafts ($P > 0.999$). Graft survival between the atopic and nonatopic groups did not differ significantly in the first ($P = 0.881$), second ($P = 0.752$), or third or further graft ($P = 0.157$). Among first grafts in the atopic group, no statistically significant difference in survival existed among patients analyzed with different manifestations of atopy ($P = 0.061$). One episode of allograft endothelial rejection created a statistically significant difference in ultimate graft survival probability in both the atopic ($P = 0.003$) and nonatopic ($P = 0.002$) groups.

Conclusions: Among patients with keratoconus receiving PK, there is no statistically significant difference in the prevalence of endothelial graft rejection episodes or probability of graft survival between patients with and without a clinical history of atopy.

Key Words: atopy, keratoconus, penetrating keratoplasty, corneal graft survival

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Corneal transplantation has been successfully performed for more than 100 years and is among the most common forms of solid tissue transplantation, with an estimated 42,606 corneal transplantations performed in the United States in 2009.^{1–3} The probability of corneal graft survival in first-time recipients approaches 90%, making penetrating keratoplasty (PK) one of the most successful forms of organ transplantation.^{2,4,5} Immunologic endothelial rejection is the leading cause of corneal graft failure.^{4,6,7}

Keratoconus is a progressive noninflammatory corneal ectasia with central thinning. The incidence is approximately 1 per 2000 in the general population.⁸ PK may be indicated to treat keratoconus for various reasons, including scarring in the visual axis, insufficient visual acuity with contact lens correction, or contact lens intolerance.^{8–10} Patients undergoing PK for keratoconus can expect a clear corneal graft in more than 90% of cases.^{6,11,12}

There is a known link between keratoconus and atopic disease.^{13–17} Patients with atopy have immune phenotypes skewed toward the type 2 T helper (Th2) cellular response.^{13,18} Clinical manifestations of atopy include asthma, allergic rhinitis, seasonal allergic conjunctivitis, atopic keratoconjunctivitis (AKC), and eczema.^{13,18}

Corneal allograft rejection classically has been considered as a type 1 T helper (Th1) cellular response.^{2,13,14,19} However, investigators recently have suggested that the Th2 cell response also could play a role in mediating transplant rejection after observing eosinophils in rejected cardiac and skin allografts in mice.^{20,21} To explore the role of atopy and the Th2 immune response in corneal graft rejection, investigators have created murine models that negate the Th1 immune response and are skewed toward the Th2 immune system.^{2,13,14,19} Grafts in these models experienced rejection, suggesting a role for the Th2 immune response in corneal graft rejection.^{2,13,14,19} One investigation using a murine model of atopic conjunctivitis suggested that this disorder induced a systemic Th2 response to corneal graft alloantigens with an associated increased incidence and tempo of graft rejection.¹⁹ Other studies in murine models of allergic airway hyperreactivity have shown that grafts transplanted

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during allergic exacerbations failed significantly more frequently than those placed during periods of allergic quiescence.²² This implies that transplantation occurring during periods of active allergy could have a decreased survival probability.

Given these data from animal models, investigators have explored the role of atopy in human corneal endothelial graft rejection and survival. Hargrave et al¹⁴ noted the presence of eosinophils in failed corneal graft pathology specimens, which implies that the Th2 immune response could play a role in endothelial graft rejection in humans. Wagoner et al²³ investigated the role of atopy in corneal graft rejection and failure by using survival analysis to compare 80 grafts in keratoconus with a history of vernal keratoconjunctivitis (VKC) and 384 cases without VKC. VKC is an atopic disorder with a Th2 immune bias.²³ No difference in postoperative complications, corneal graft survival, or graft rejection was found in this study.²³ Yildiz et al¹³ also explored the role of atopy in corneal graft rejection in keratoconus and observed an increased incidence of corneal graft rejection in patients with atopy, but this difference failed to reach statistical significance.

The current study uses a survival analysis to assess endothelial rejection episodes and the probability of graft survival in patients with keratoconus with and without a history of atopy. Survival analysis will be used to determine if there are differences among the various manifestations of atopy, including asthma, eczema, allergic rhinitis, seasonal allergic conjunctivitis, and AKC.

METHODS AND MATERIALS

This study was approved by the University of Texas Southwestern (UTSW) Medical Center Institutional Review Board. The clinical records of patients from 6 cornea and external disease faculty surgeons at UTSW Medical Center who underwent PK for keratoconus were located by a computerized review based on International Classification of Diseases-9 and Current Procedural Terminology codes. This yielded records of 122 patients who received 168 corneal allografts between 1988 and 2009. The records of each patient were reviewed to determine the presence of a clinical history of atopic disorders, including asthma, eczema, allergic rhinitis, seasonal allergic conjunctivitis, and AKC.

The diagnosis of keratoconus was based on previously described clinical features.⁸ Indications for surgery included visual axis scarring, contact lens intolerance, or insufficient best-corrected visual acuity with spectacles or contact lenses. The procedures were classified as primary grafts or re-grafts. Each graft was considered separately for data analysis purposes. Information was gathered on associated preoperative diagnoses, surgical procedures, and postoperative courses. Graft rejection episodes were studied separately and in detail. Graft clarity rather than visual acuity was used as the measurement of success.

Donor Corneas, Surgical Technique, and Postoperative Care

All surgeries were performed by faculty surgeons at the UTSW Medical Center. Donor tissue was obtained through the UTSW transplant services and stored in a standard fashion. Donor buttons were manually trephined with a disposable blade from the endothelial side, 0.25 to 0.5 mm larger than the recipient bed. Recipient tissue was removed by partial-thickness trephination and excision with corneal scissors, diamond knives, or microrazor blades. Simultaneous cataract extraction with or without intraocular lens placement or other indicated procedures was performed as indicated at the time of PK. The donor button was secured with 10-0 nylon sutures using a variable combination of interrupted and running suture techniques depending on the surgeon's preference. Subconjunctival injections of antibiotics and corticosteroids were administered at the conclusion of the procedure and included a combination of gentamicin, vancomycin, or cefazolin, and methylprednisolone. Postoperative management included topical antibiotics and corticosteroids used at the discretion of the operating surgeon. Typical regimens included topical antibiotics for 1 to 2 weeks, and corticosteroids were administered hourly for 1 to 2 weeks and gradually tapered at the discretion of the operating surgeon.

Patients were monitored for surgical complications and other comorbidities throughout the postoperative course. Sutures were removed at the surgeon's discretion, with most sutures typically being removed by 24 months postoperatively. Cataract was managed surgically when indicated. Glaucoma was managed initially with medical therapy and surgically

TABLE 1. Recipient Profile

	First Grafts		Second Grafts		≥3 Grafts	
	Atopy	No Atopy	Atopy	No Atopy	Atopy	No Atopy
Total grafts	59	92	5	6	2	4
Sex						
Male	26	58*	3	4	2	0
Female	33	34	2	2	0	4
Bilateral grafts	14	18	0	1	0	0
Average age (yr)	37.6 ± 12.5	39.1 ± 11.8	46.8 ± 9.7	43.83 ± 17.7	38.5 ± 19.1	45.75 ± 10.7
Range (yr)	14–71	18–74	36–61	27–74	25–52	30–54
Average follow-up (mo)	64.6 ± 52.6	61.6 ± 50.9	56 ± 66.6	29 ± 21.2	81.5 ± 58.7	13.3 ± 6.85

Student *t* test: *P* > 0.05 for all mean values.

**P* < 0.05 for Fisher exact test (sex analysis).

TABLE 2. Clinical Manifestations of Atopy

Manifestation	First Grafts	Second Grafts	Third or Further Grafts
Asthma (%)	15 (25.4)	1 (20)	0
Allergic rhinitis (%)	15 (25.4)	2 (40)	1 (50)
Seasonal allergic conjunctivitis (%)	20 (33.9)	0	0
AKC (%)	2 (3.4)	1 (20)	1 (50)
Multiple atopic manifestations (%)	7 (11.9)	1 (20)	0
Total	59	5	2

when indicated. Wound complications such as dehiscence were repaired as indicated. Phototherapeutic keratectomy was performed as necessary to manage postoperative astigmatism. Grafts complicated by infectious processes were cultured, and antimicrobial therapy was administered based on these results or the presumptive microbial organism. Cases of herpes simplex keratitis were treated with variable combinations of systemic and topical antiviral therapies administered at the surgeon's discretion.

Diagnosis and Treatment of Allograft Endothelial Rejection and Failure

Endothelial rejection was diagnosed using established criteria.⁶ Possible endothelial rejection was defined as an acute onset of ciliary flush, anterior chamber reaction, and/or keratic precipitates with or without corneal edema in a previously clear graft. Definite rejection was characterized by an endothelial rejection line. Rejection episodes were treated with intensive topical corticosteroids, typically with 1% prednisolone acetate. In some cases, periocular or systemic corticosteroids were administered. The duration and intensity of corticosteroid therapy were adjusted based on the clinical response.

Graft failure was defined as an irreversible loss of clarity in a graft that previously had been clear after surgery. These criteria were used for all causes of failure whether from endothelial rejection or from other causes such as infection. Irreversible rejection was diagnosed if the graft remained edematous after 4 weeks of intensive topical and/or systemic corticosteroid therapy. The date of failure was estimated from available clinical information. If not documented precisely, then it was assumed to have occurred midway between the last

TABLE 3. Associated Diagnoses

Preoperative Diagnoses	First Graft		Regrafts	
	Atopy (n = 59)	No Atopy (n = 92)	Atopy (n = 7)	No Atopy (n = 10)
Cataract (%)	3 (5.0)	5 (5.4)	0	1 (10)
Glaucoma (%)	0	0	2 (28.6)	3 (30)
Pseudophakia (%)	0	0	1 (14.3)	2 (20)

The difference between the atopy and nonatopic groups for each diagnosis was not significant ($P > 0.05$).

TABLE 4. Initial Procedures

	First Graft		Regrafts	
	Atopy (n = 59)	No Atopy (n = 92)	Atopy (n = 7)	No Atopy (n = 10)
PK with CE/PCIOL (%)	3 (5.08)	3 (3.26)	0	1 (10)
PK with CE/aphakia (%)	0	2 (2.17)	0	0
Peripheral iridectomy (%)	2 (3.44)	1 (10.8)	0	0
Tarsorrhaphy (%)	1 (1.69)	0	0	1 (10)
Glaucoma tube shunt (%)	0	0	1 (14.3)	0

The difference between the atopy and no atopy groups for each diagnosis was not significant ($P > 0.05$).

CE, cataract extraction; PCIOL, posterior chamber intraocular lens.

examination when the graft was clear and the first examination when the graft was noted to be cloudy.

Statistical and Survival Analysis

SigmaPlot 11.0 was used for statistical analysis. Comparisons were made between the atopic and nonatopic groups with respect to the endothelial rejection episodes in each graft and the Kaplan–Meier probability of graft survival was used after the initial graft, second graft, and third or further grafts. Statistical significance with the Kaplan–Meier method was determined with the Breslow method ($P < 0.05$). Pairwise multiple comparison procedures (Holm–Sidak method) were used to compare multiple curves to determine significance. Continuous variables were compared with the 2-tailed Student *t* test. Categorical data were compared with the Fisher exact test. Values were considered statistically significant if $P < 0.05$.

RESULTS

Demographic Data

Recipient demographic data are summarized in Table 1. The records of 122 patients were reviewed and yielded data from 168 total grafts. A clinical history of atopy was reported

TABLE 5. Postoperative Diagnoses

	First Graft		Regrafts	
	Atopy (n = 59)	No Atopy (n = 92)	Atopy (n = 7)	No Atopy (n = 10)
Cataract (%)	10 (16.9)	12 (13.0)	0	3 (30)
Glaucoma (%)	12 (20.3)	14 (15.2)	2 (28.6)	3 (30)
Anterior synechia (%)	0	3 (3.2)	1 (14.3)	0
Dehiscence (%)	1 (1.69)	3 (3.26)	0	0
HSV keratitis (%)	1 (1.69)	1 (1.09)	2 (28.6)	0
Infiltrate (bacterial) (%)	0	2 (2.17)	0	0
Fungal keratitis (%)	0	2 (2.17)	0	0
Retinal detachment (%)	0	1 (1.09)	0	0

The difference between the atopy and no atopy groups for each diagnosis was not significant ($P > 0.05$).

HSV, herpes simplex keratitis.

TABLE 6. Procedures in Postoperative Course

	First Graft		Regrafs	
	Atopy (n = 59)	No Atopy (n = 92)	Atopy (n = 7)	No Atopy (n = 10)
Cataract extraction with PCIOL (%)	6 (10.2)	4 (4.34)	0	2 (20)
Glaucoma tube shunt surgery (%)	2 (3.44)	1 (1.09)	0	0
Enucleation (%)	0	1 (1.09)	0	0
Wound dehiscence repair (%)	1 (1.69)	3 (3.26)	0	0
Astigmatism modifying procedure (%)	2 (3.44)	2 (2.17)	0	0
Retinal detachment repair (%)	0	1 (1.09)	0	0

The difference between the atopy and no atopy groups for each diagnosis was not significant ($P > 0.05$).

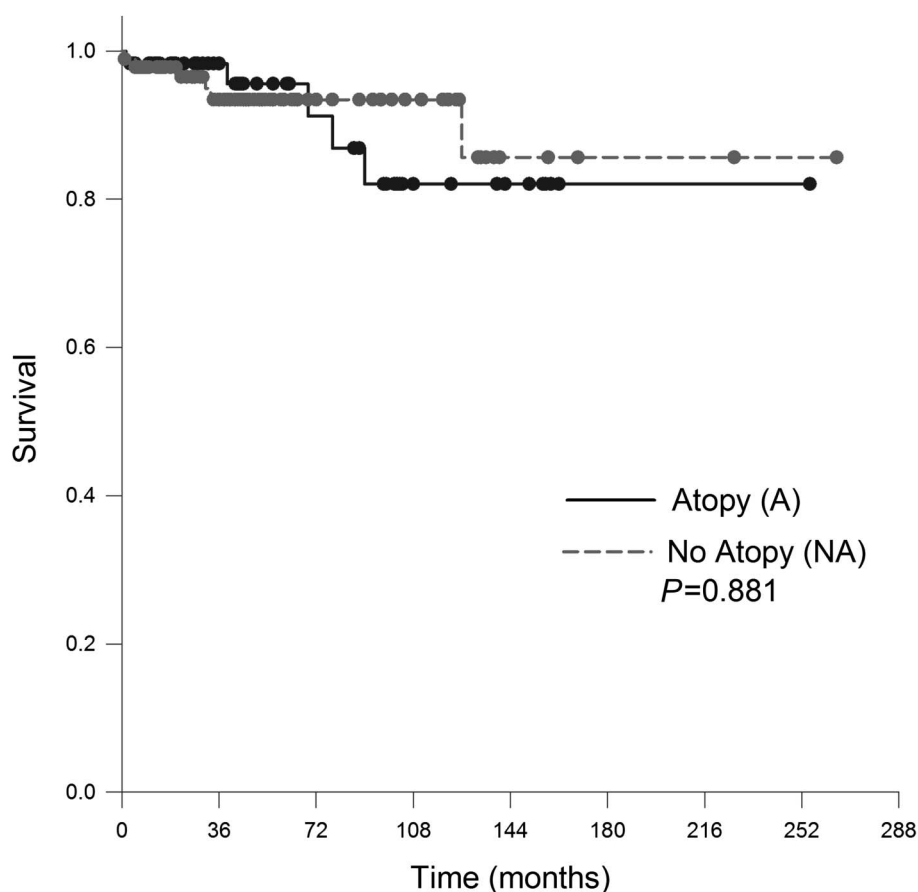
PCIOL, posterior chamber intraocular lens.

in 66 of all grafts (39.2%). Among those with a history of atopy, there were 59 first grafts, 5 second grafts, and 2 third or further grafts. There were 102 patients without a history of atopy, among whom there were 92 first grafts, 6 second

grafts, and 4 third or further grafts. Bilateral first grafts were performed in 32 patients, of whom 14 and 18 were atopic and nonatopic, respectively. Bilateral second grafts were required in 1 nonatopic patient. Among patients receiving first grafts, a statistically significant sex difference existed between the atopic and nonatopic groups, with more men receiving grafts in the nonatopic group ($P = 0.029$). Otherwise, there was no significant difference in sex, age, or duration of follow-up between the atopic and the nonatopic groups for first, second, or third or further grafts.

Among the 59 first grafts from patients with manifestations of atopy, 15 (25.4%) had a history of asthma, 15 (25.4%) had allergic rhinitis, 20 (33.9%) had seasonal allergic conjunctivitis, and 2 (3.4%) had AKC (Table 2). There were 7 patients (11.9%) with multiple atopic manifestations including asthma with allergic rhinitis (2 patients), asthma with seasonal allergic conjunctivitis (3 patients), asthma with eczema (1 patient), and allergic rhinitis and seasonal allergic conjunctivitis (1 patient). Manifestations of atopy in second grafts included 1 asthma, 2 allergic rhinitis, 1 AKC, and 1 with multiple features. Manifestations of atopy in those with third or further grafts included 1 allergic rhinitis and 1 AKC.

Survival Analysis for First Grafts: Atopy vs No Atopy

**FIGURE 1.** Survival analysis for first grafts: atopy vs. no atopy.

Remaining Cases

A	59	38	21	10	6	1	1	1	0
NA	92	59	26	17	5	2	2	1	0

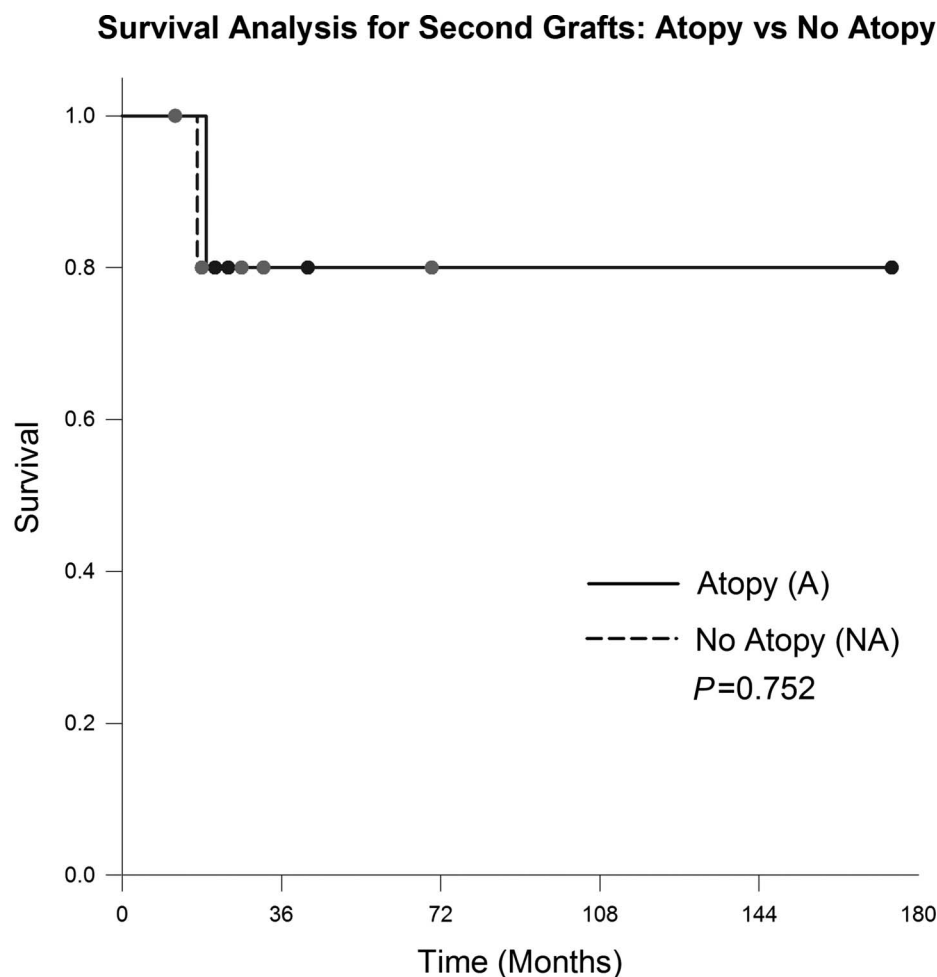


FIGURE 2. Survival analysis for second grafts: atopy vs. no atopy.

Remaining Cases							
A	5	2	1	1	1	0	
NA	6	1	0	0	0	0	

Associated Diagnoses and Procedures

The atopic and nonatopic groups receiving first grafts (Table 3) did not have a statistically significant difference in preoperative diagnoses of cataract, glaucoma, or pseudophakia. The atopic and nonatopic groups receiving re-grafts also did not differ significantly with regard to preoperative diagnoses.

Various surgical procedures were performed concomitantly at the time of initial PK as indicated based on the discretion of the attending surgeon (Table 4). Among first grafts, the atopic and nonatopic groups did not differ significantly with regard to the incidence of PK with concomitant cataract extraction with and without intraocular lens placement, peripheral iridectomy, tarsorrhaphy, or glaucoma tube shunt ($P > 0.05$). Among those receiving re-grafts, there was not a significant difference between the atopic and nonatopic groups with regard to concomitant procedures at the time of PK. The postoperative courses were reviewed in all patients (Table 5). The postoperative courses for first grafts in both the atopic and nonatopic groups did not differ significantly in terms of postoperative cataract,

glaucoma, anterior synechia, dehiscence, herpes simplex keratitis, corneal infiltrate, fungal keratitis, or retinal detachment ($P > 0.05$). Re-grafts in the atopic and nonatopic groups also failed to show a significant difference in the incidence of these postoperative diagnoses ($P > 0.05$). Surgical procedures were performed when indicated in the postoperative period (Table 6). The postoperative courses for first grafts did not differ significantly between the atopic and nonatopic groups with regard to the incidence of cataract surgery, glaucoma tube shunt procedure, enucleation, wound dehiscence repair, astigmatism modifying procedures, or retinal detachment repair. Enucleation was performed in 1 case within the nonatopic group because of fungal keratitis that resulted in the patient having no light perception and intractable pain.

Survival Analysis

The graft survival probability for first grafts in the atopic group was 98.3% at 12 months, 98.3% at 24 months, 95.6% at 60 months, and 82.1% at 90 months (Fig. 1). The probability of survival for first grafts in the nonatopic group was 97.8% at

Survival Analysis for Three or More Grafts: Atopy vs No Atopy

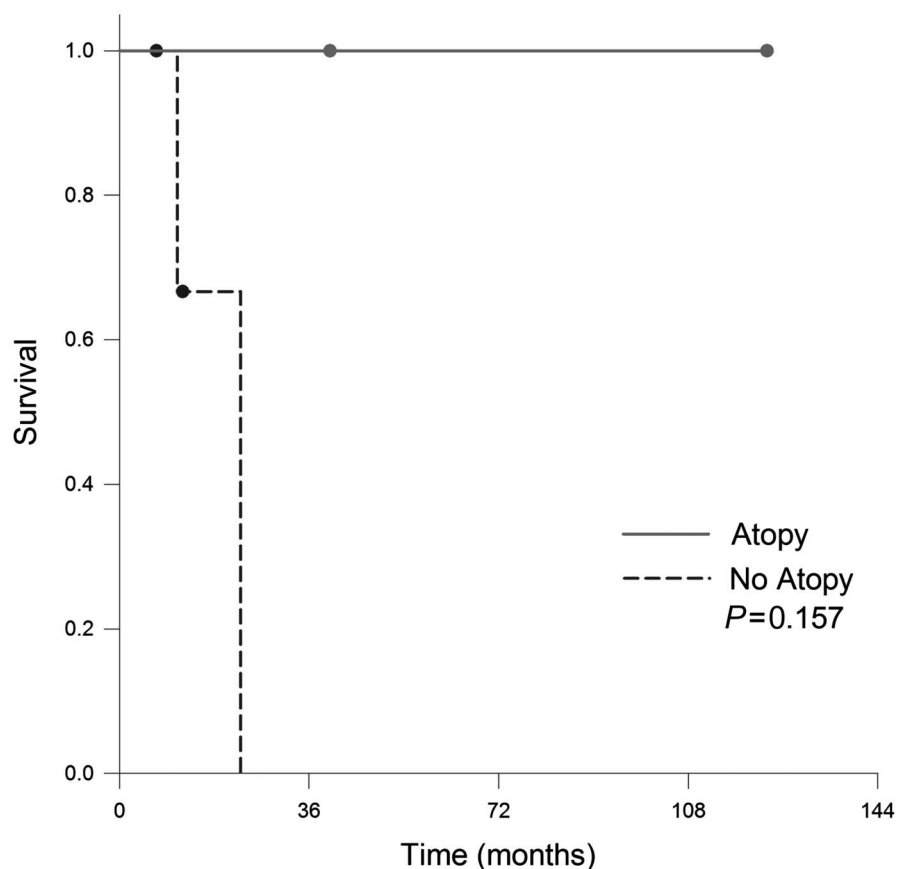


FIGURE 3. Survival analysis for third or further grafts: atopy vs. no atopy.

Remaining Cases				
Atopy	2	1	1	0
No Atopy	4	0	0	0

12 months, 96.5% at 24 months, 93.4% at 60 months, and 85.7% at 126 months. There was not a statistically significant difference in survival probability in first grafts between the atopic and nonatopic groups ($P = 0.881$). Regarding second grafts (Fig. 2), the probability of survival in the atopic group was 100% at 12 months, 80% at 24 months, 80% at 60 months, and 80% at 174 months. The nonatopic group survival probability was 100% at 12 months, 80% at 24 months, 80% at 60 months, and 80% at 70 months. There was not a statistically significant difference in survival probability between the atopic and nonatopic groups ($P = 0.752$). Patients receiving third or further corneal grafts (Fig. 3) in the atopic group demonstrated a 100% survival probability at 12 months, 24 months, 60 months, and 123 months. Those in the nonatopic group demonstrated a 1-year survival rate of 66.7%. No grafts survived beyond 23 months in this group. There was no statistically significant difference in survival probability between the atopic and nonatopic groups ($P = 0.157$).

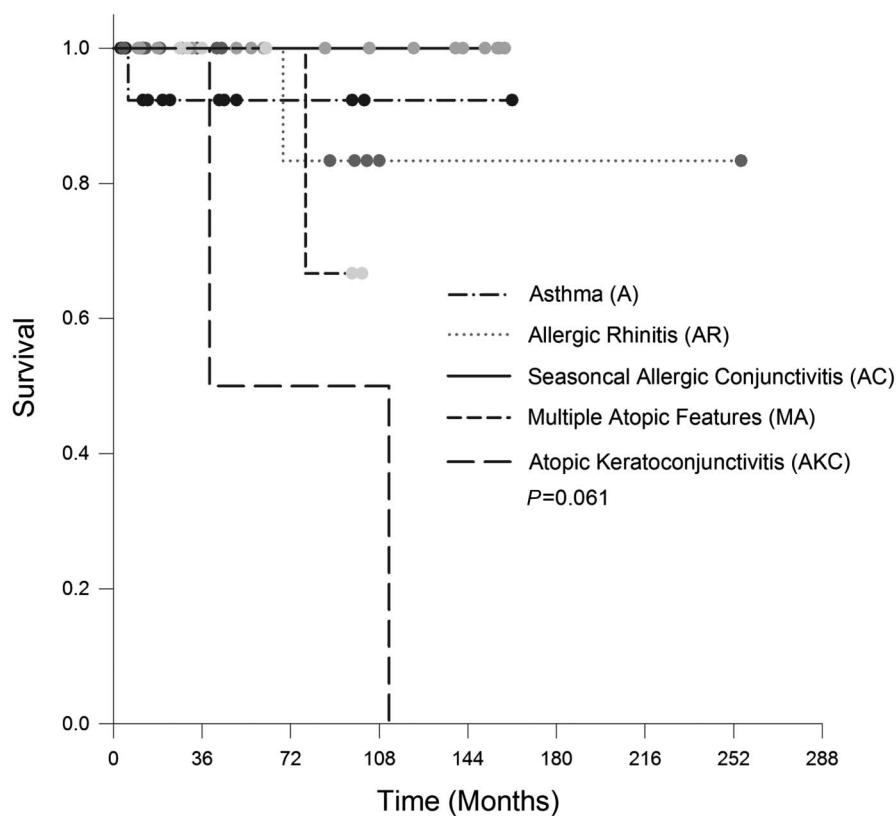
Survival analysis was also performed on first grafts in the atopic group to determine if the various manifestations of atopy had different survival probabilities (Fig. 4). Graft

survival probability for each manifestation of atopy did not differ significantly ($P = 0.061$). However, only 2 patients were included in the AKC analysis, and both grafts failed.

Allograft Rejection

Grafts in the atopic and nonatopic groups experienced endothelial rejection in 20 cases (30.4%) and 32 cases (31.3%), respectively. This provided a cumulative of 52 (30.9%) cases of endothelial graft rejection in this study. Among first grafts in the atopic group (Table 7), 16 (27.1%) experienced 1 episode of rejection and 1 (1.69%) experienced 2 or more episodes. Among first grafts in the nonatopic group, 1 rejection episode occurred in 28 cases (30.4%) and 2 or more rejection episodes occurred in 1 case (1.09%). The prevalence of endothelial rejection episodes in first grafts did not differ significantly between the atopic and nonatopic groups ($P = 0.7161$). Regrafts in the atopic group experienced 1 rejection episode in 4 cases (57.1%) and no cases of 2 or more episodes occurred. Among regrafts in the nonatopic group, 4 (40%) experienced 1 episode of rejection and none experienced 2 or more rejections. There was no statistically significant difference in the prevalence of endothelial rejection

Survival Analysis Atopic Manifestations: First Grafts



Remaining Cases

A	15	7	3	1	1	0	0	0	0
AR	15	10	5	2	1	1	1	1	0
AC	20	14	9	7	4	0	0	0	0
MA	7	5	3	0	0	0	0	0	0
AK	2	2	1	1	0	0	0	0	0

FIGURE 4. Survival analysis of atopic manifestations: first grafts.

episodes in the regrafts between the atopic and nonatopic groups ($P > 0.999$). The incidence of 2 or more rejection episodes also did not differ significantly for first grafts ($P > 0.999$) or regrafts ($P > 0.999$) between the atopic and nonatopic groups.

Figures 5 and 6 demonstrate the influence of endothelial rejection on survival. A single episode of endothelial rejection significantly affected the survival probability of grafts in the atopic group ($P = 0.003$); this finding was also seen in the nonatopic group, with a single episode of rejection significantly influencing survival ($P = 0.002$). Both the atopic and

nonatopic group involved only 1 case each of 2 episodes of allograft rejection, and neither of these grafts failed.

Causes of Graft Failure

All 6 cases of graft failure in the atopic group resulted from endothelial graft rejection. The nonatopic group involved 9 graft failures, 7 (77.8%) from rejection and 2 (22.2%) from fungal keratitis. One of these cases of fungal keratitis occurred in an eye with no light perception and intractable pain leading to enucleation. Grafts experiencing endothelial rejection episodes were significantly more likely to fail in the atopic ($P = 0.0017$) and nonatopic groups ($P = 0.0278$). Fungal keratitis was a significant risk factor for graft failure in the nonatopic group ($P = 0.0278$). Corticosteroid therapy was too variable to enable the determination of its impact on the incidence or timing of rejection episodes or to comment on differences between the various groups.

DISCUSSION

Our study compared the preoperative and postoperative courses of the atopic and nonatopic groups. No statistically

TABLE 7. Allograft Rejection Episodes

	First Grafts		Regrafts	
	Atopy	No Atopy	Atopy	No Atopy
Total grafts	59	92	7	10
Grafts with 1 rejection episode	16 (27.1)	28 (30.4)	4 (57.1)	4 (40)
≥2 rejection episode	1 (1.69)	1 (1.09)	0	0

The difference between first grafts and regrafts for both groups was not significant. The difference between the atopy and no atopy groups, for first grafts and regrafts, was not significant ($P > 0.05$, Fisher exact test).

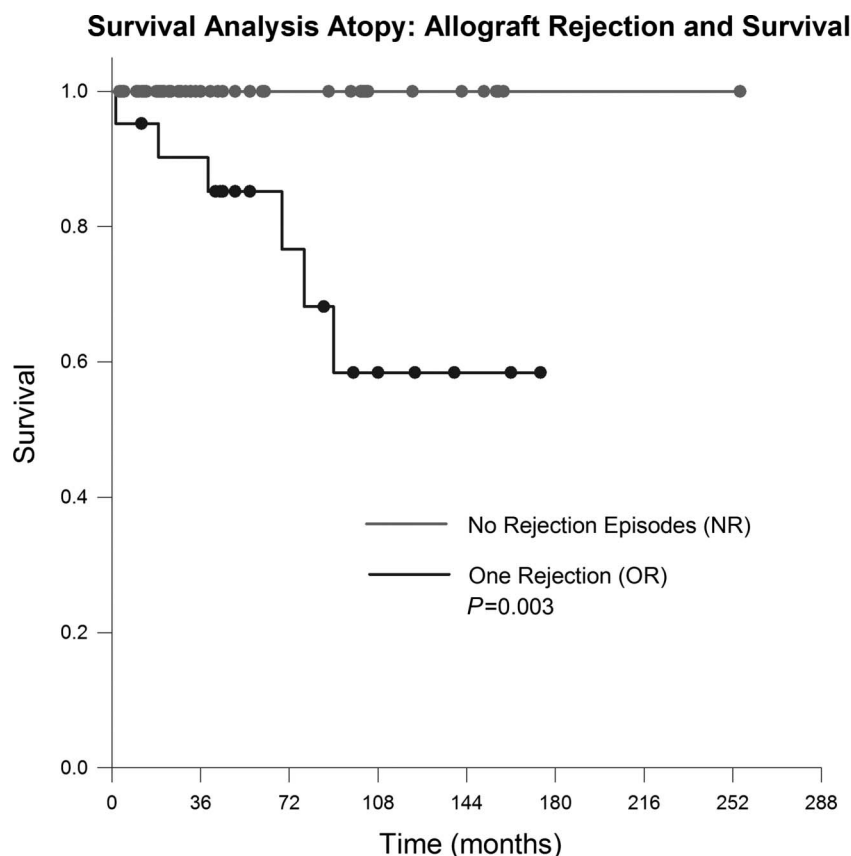


FIGURE 5. Survival analysis of atopy: allograft rejection and survival.

Remaining Cases

NR	45	24	14	7	5	1	1	1	0
OR	21	18	9	5	2	0	0	0	0

significant difference in terms of preoperative diagnoses, initial procedures, postoperative complications, or procedures was noted between the atopic and nonatopic group. Wagoner et al²³ explored the postoperative course of patients receiving PK for keratoconus with and without VKC and found no difference in the incidence of postoperative glaucoma, cataract, secondary cataract, and infectious keratitis between the 2 groups. These results are consistent with our study.

Survival analysis was performed to compare graft survival probability in the atopic and nonatopic groups. There was not a statistically significant difference in survival probability for the first, second, or third or further grafts when the atopic and nonatopic groups were compared. This is consistent with the survival analysis performed by Wagoner et al²³ in which no difference was found between patients with and without a history of atopy. Survival analysis for first grafts within the atopic group comparing the various manifestations of atopy failed to demonstrate a statistically significant difference in survival probability. The sample size of the AKC cohort receiving first grafts included only 2 patients. The literature has reported a poor prognosis for cornea transplants in AKC.²⁴ The limited sample size in the AKC cohort could explain why there was not a statistically significant difference between this group and those with other atopic manifestations.

Despite the lack of survival difference between the atopic and nonatopic groups and the various manifestations of atopy, one should still consider the data from Niederkorn et al²² when considering PK in patients with atopy. In this animal model of airway hyperreactivity, performing PK during periods of active allergy resulted in a significant increased incidence of graft rejection and failure. However, no difference in survival was noted if transplantation was delayed 30 days from the time of allergic stimulation during a period of immunologic quiescence.²² It may be prudent to extrapolate this concept to humans and delay transplantation in patients with atopy until periods of active allergy have resolved and immunologic quiescence is maximized.

The prevalence of endothelial graft rejection episodes in this study was 30.9%, with graft rejection episodes occurring in 30.4% and 31.3% of the atopic and nonatopic groups, respectively. This difference was not statistically significant ($P > 0.999$). The literature reports a variable prevalence of at least 1 graft rejection episode ranging from 4.3% to 31%.^{9,13,25,26} Additionally, Yildiz et al¹³ reported that patients with atopy had an increased incidence of graft rejection; however, this difference failed to reach statistical significance. In this study, endothelial rejection was also the most common cause of graft failure in both the atopic and nonatopic groups. Fungal keratitis was a significant risk factor for graft failure in the nonatopic group. One case of

Survival Analysis in No Atopy: Allograft Rejection and Survival

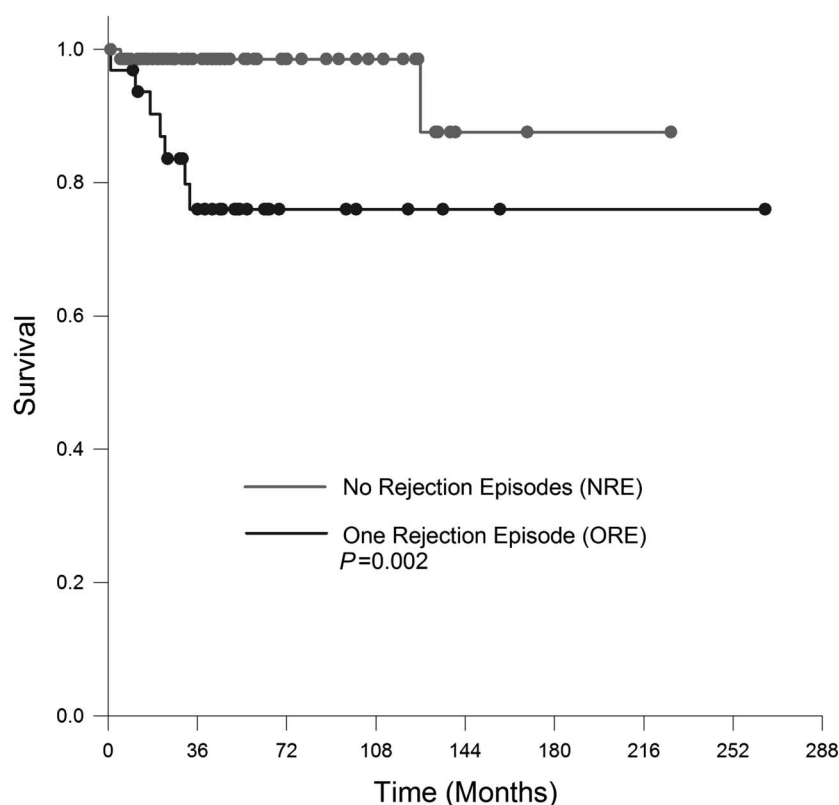


FIGURE 6. Survival analysis in no atopy: allograft rejection and survival.

Remaining Cases	70	40	20	13	3	1	1	0	0
NRE	70	40	20	13	3	1	1	0	0
ORE	32	20	6	4	2	1	1	1	0

fungal keratitis required enucleation, because the eye had no light perception and intractable pain developed.

Survival analysis was performed comparing grafts with and without a history of endothelial graft rejection. In both the atopic and the nonatopic groups, those with 1 episode of endothelial rejection developed a statistically significant decrease in graft survival. This finding differs from the data from Epstein et al⁶ in which a single rejection episode was not associated with a significant decrease in graft survival. Limitations of this study include its retrospective design. Sample size also limited the statistical analysis in some subgroups. For example, the AKC cohort among first grafts did not demonstrate a statistically significant difference in survival compared with the other atopic manifestations despite the previously reported poor prognosis of grafts in this disorder.²⁴ This is likely explained by the fact that there were only 2 primary grafts transplanted into patients with AKC in this study.

In conclusion, in patients with keratoconus receiving PK, these data suggest that a clinical history of atopy does not provide a statistically significant difference in endothelial graft rejection prevalence or graft survival probability in comparison to those without a history of atopy. Furthermore, among those with a history of atopy, no statistically significant difference in survival was noted between the various manifestations of atopy.

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