Asian J Ophthalmol. 2017;15:135-142

The results of therapeutic keratoplasties performed in severely thinned or perforated corneas

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Abstract

Purpose: *To report the visual and anatomic outcomes of therapeutic keratoplasties performed in severely thinned or perforated corneas.*

Methods: *Medical records of 32 eyes of 32 patients operated between 2000 to 2014 were reviewed retrospectively. Indications, preoperative findings, surgical procedures, donor size, post-operative graft clarity, visual improvement, globe integrity and follow-up periods were analyzed. Main outcome measures were anatomical success, graft clarity and visual acuity.*

Results: *Mean age was 57,3 (20-85). Sixteen patients were male and 16 female. Mean follow-up was 28.9 (14-132) months. Surgical indication was infectious in 17 (53.1%) and non-infectious in 15 eyes (46.9%). Infectious causes were bacterial ulcer 8 (25.0%), herpes simplex 7 (21.9%) and fungus in two (6.3%) eyes. Non-infectious causes were traumatic in five (15.6%), Stevens-Johnson syndrome in two (6.3%), desmatocele in one (3.1%) other causes (bullous keratopathy, interstitial keratitis and lagophthalmos). The underlying cause of cornel melting was unknown in three eyes (9.3%). Combined PK was performed in 18 of 32 eyes (56.3%), PK alone in 14 (43.8%). Clear graft rate was 25/32 (78.1%) at 14th month. Anatomical integrity was restored in 19 (90.4%) of 21 perforated corneas. PK anatomical success was evaluated by the Kaplan-Meier survival analysis. Mean estimated graft survival was 46.3 ± 9.8 (27.2-65.5) months and median 30.0 ± 8.0 (14.3-45.7) months. Visual improvement was obtained in 23 eyes (71.9%). Visual acuity was ≥ 0.05 in five eyes (15.6%) preoperatively, it increased to 20 eyes (62.5%) post-operatively.*

Conclusion: *Therapeutic PK is an viable treatment option in the management of corneal thinning and perforation in the management of corneal melting and perforations due to varying aetiologies. It preserves the globe integrity and provide useful vision in majority of the cases.*

Keywords: *Corneal thinning, perforation, penetrating keratoplasty, therapeutic*

Introduction

Corneal melting and perforation may occur in infections, inflammatory conditions, ocular surface disorders, long term use of steroids and trauma.[1] It may lead to complicated cataract, secondary glaucoma, scleritis or endopthalmitis that may be reversed by prompt intervention, otherwise phthisis bulbi can occur. Recalcitrant bacterial or fungal keratitis unresponsive to medical treatment are usually

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progressive and may cause scleral invasion or corneal perforation. Corneal perforation is an emergency situation which may result in irreversible visual loss, thus early intervention to restore the anatomical integrity of the globe is mandatory. Prompt surgical intervention performed before actual corneal perforation arises is technically easier and reduces the risk of post-operative complications such as endopthalmitis, peripheral anterior synechia and secondary angle closure.[2]

In addition to nonsurgical treatments such as bandage contact lenses or tissue adhesives, surgical interventions including simple suturing, amniotic membrane transplantation (AMT), penetrating keratoplasty (PK) anterior lamellar keratoplasty (ALK) and lamellar or full thickness patch grafting may be utilized.[1] Developments in surgical techniques and tissue adhesives reduced the enucleation rate in corneal perforations.[3] Treatment preference is determined by the size and localization of the perforation as well as the underlying cause.[1,4] Therapeutic keratoplasty is a surgical procedure whose primary purpose is either to restore the structural integrity of the eye (tectonic keratoplasty) or to resolve an infectious or inflammatory keratitis. It is indicated in severely thinned, ectatic or perforated corneas, as well as corneal tissue loss, fistula and melting due to autoimmune diseases. It may also provide visual improvement in certain cases.[5,6] Aim of this retrospective study is to report the outcomes of 15 years of therapeutic PKs performed in a tertiary referral hospital in Turkey.

Material and methods

This study was approved by the ethical committee of our hospital and followed the tenets of the Declaration of Helsinki. Thirty-two eyes of 32 patients who underwent therapeutic PK between 2000 and 2014 were reviewed retrospectively. Small perforations treated with non-surgical methods such as bandage contact lens and tissue adhesive or minor surgeries like primary suturation, AMT, conjunctival flap as well as tectonic patch grafts were excluded. Indications, preoperative findings, surgical procedures, donor size, postoperative corneal graft clarity, visual acuity, globe integrity and follow-up periods were analyzed. Main outcome measures were the anatomical success, graft clarity and visual acuity.

All sutures were removed at one year. Post-operative best spectacle corrected visual acuity (BSCVA) was measured one month after suture removal which corresponds to 14th postoperative month. The percantage of the eyes showing visual improvement and with a BSCVA ≥ 0.05 were analyzed. Percentage of anatomical success and graft clarity were also evaluated at this time point, since it contains full data for all cases. Transparent or semi-transparent corneal grafts with no sign of infection were defined as clear. If there is no melting or perforation in the graft, globe integrity has been saved and complete eradication of primary infection has been achieved, it was defined as anatomical success, yet the graft is not clear. The survival time for both PK anatomical success and optical clarity through follow-up were evaluated by Kaplan-Meier survival analysis. Cox regression model for survival analysis was performed to determine the factors that may have effect on graft survival.

After a detailed history, BCVA and slit lamp biomicroscopy was performed, intraocular pressure (IOP) was measured with Goldmann applanation tonometry at baseline and follow-up visits. Visual acuity was measured with a Snellen chart at six meters and given in decimal scores. Fundus examination was performed with a 90-D lens. If the fundus is not visible, ocular ultrasonography was utilized. In eyes with keratitis, culture material was taken via corneal scrapings or from the recipient corneal buttons during surgery. Samples were sent to microbiology laboratory for also direct microscopy, Gram and Giemsa staining. Previous surgeries were noted in patients with chronic anterior segment disease. Systemic and topical antimicrobial treatment was given in patients with keratitis. The treatment continued until the corneal infiltration and anterior segment inflammation subside. All surgeries were performed under general anesthesia within one to seven days of hospitalization. A Hessburg-Barron vacuum trephine was used for recipient trephination. Donor corneas were cut from the endothelial side with a disposable donor punch. In two cases with corneal melting extending to the sclera, a manual dissection was carried out by using a caliper and corneal scissors. The donor corneas were also trimmed to fit the recipient opening in these cases.

Concurrent procedures performed during PK were as follows: Open-sky extracapsular cataract extraction and intraocular lens (IOL) implantation, transsclerally fixated IOL implantation, removal of anterior chamber IOL, lateral tarsoraphy in eyes with decreased corneal sensitivity like in herpetic keratitis, synechiotomy in eyes with anterior or posterior synechiae, pupilloplasty in ectopic pupils and anterior vitrectomy in aphakic eyes. A single running 10-0 nylon suture was used for PK. Interrupted sutures were used in large PKs performed by manual preparation of both the donor and the recipient. A subconjunctival gentamycin and dexamethasone was injected in all patients at the end of surgery. Prophylactic oral acyclovir was used for one year following PK in patients with herpetic keratitis.

Results

Mean age was 57,3 (20-85). Sixteen patients were male and 16 female. Mean follow-up was 28.9 (14-132) months. Surgical indications were split into two groups; infectious and non-infectious. Seventeen (53.1%) of 32 eyes were infectious and 15 (46.9%) were non-infectious. Infectious causes were bacterial ulcer eight (25.0%), herpes simplex seven (21.9%) and fungus in two (6.3%) eyes. Non-infectious causes were traumatic in five (15.6%), Stevens-Johnson syndrome two (6.3%), desmatocele due to long-term topical steroid use one (3.1%), other causes three (bullous keratopathy, interstitial keratitis and lagophthalmos). The underlying cause was unknown in three of non-infectious corneal melt.

On initial examination, corneal perforation was present in 21 of 32 eyes (65.6%). Other biomicroscopic findings were superficial/deep neovascularization 12 (37.5%), cataract nine (28.1%), iris prolapse five (15.6%), anterior/posterior synechiae five (15.6%), symblepharon two (6.3%), aphakia two (6.3%) and Fuch's dystrophy one (3.1%). Previous surgeries, attempted to alleviate the corneal problems, included AMT in 14 eyes (43.8%), lateral tarsoraphy six (18.8%), PK in five (15.6%), conjunctival

flap two (6.3%), tissue adhesive two (6.3%), primary suturation one (3.1%) and limbal autograft in one eye (3.1%).

Surgical techniques performed on patients with corneal thinning or perforation are as follows: Combined PK (with aforementioned procedures) in 18 eyes (56.3%) and PK alone in 14 (43.7%). The donor corneal diameter varied between 7.50-7.75 mm in six eyes (18.7%) and 8.0-11.0 mm in 26 eyes (81.3%). The anatomical integrity was preserved in 19 (90.4%) of 21 eyes with corneal perforation. Overall PK anatomic success rate was 96.8% and graft clarity rate was 78.1% at postoperative 14th month. The survival time for PK anatomical success was evaluated by the Kaplan-Meier survival analysis (Fig. 1). Mean estimated graft survival time was found as 46.3 ± 9.8 (27.2-65.5) months and median 30.0 ± 8.0 (14.3-45.7) months. The survival time for PK optical clarity was also evaluated by the Kaplan-Meier survival analysis. Mean estimated survival time for optical clarity was found as 31.3 ± 5.1 months and median 26.0 ± 3.0 months.

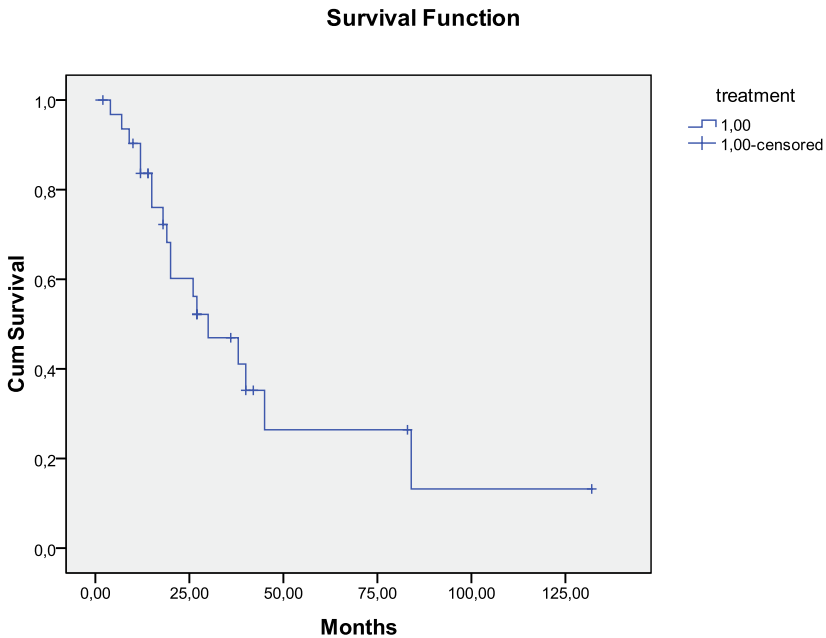

Fig. 1. Kaplan-Meier analysis for cumulative survival for PK anatomical success.

Cox regression model for survival analysis was performed to determine the factors which may affect the graft survival (clarity). It revealed no association between age, gender, presence of infection, previous surgical procedure or corneal perforation with graft survival ($p = 0.268$; $p = 0.270$; $p = 0.296$; $p = 0.065$; $p = 0.238$ respectively), whereas presence of postoperative complications showed a negative effect on graft survival ($p = 0.031$).

Visual improvement was achieved in 23 of 32 eyes (71.9%). While BSCVA was 0.05 or better in only five eyes (15.6%) preoperatively, this rate increased to 20 eyes (62.5%) postoperatively. Postoperative complications are summarized in Table 1. None of the eyes were lost. Postoperative IOP elevation was controlled with topical antiglaucomatous medication in all cases. In three eyes with low postoperative vision, indirect ophthalmoscopy revealed total glaucomatous atrophy, retinal detachment and primary optic atrophy. Graft rejection was successfully treated with intravenous and topical steroids in two eyes, whereas a repeat PK was performed in another two eyes. AMT was performed in two of six eyes with postoperative persistent epithelial defect, one eye required repeat PK. Regrafting was carried out overall in five eyes including two graft rejections, one descematocele, one graft melting and one fungal keratitis recurrence.

Graft melting occurred in a 29-year-old female with Stevens-Johnson syndrome. Postoperative persistent epithelial defect and recurrent trichiasis were the main causes for failure in this patient. Vigorous treatment of trichiasis and permanent use of a soft bandage contact lens provided the second graft to be successfull. Fungal keratitis recurrence occurred in a 51-year-old male at two months of surgery. Patient presented with keratitis recurrence at wound margin and graft infiltration. Early suture loosening and fungal activation were the main causes for failure. A regraft resulted in complete cure in this patient. Full recovery was achieved in remaining eyes with keratitis by means of a single therapeutic PK (Fig. 2).

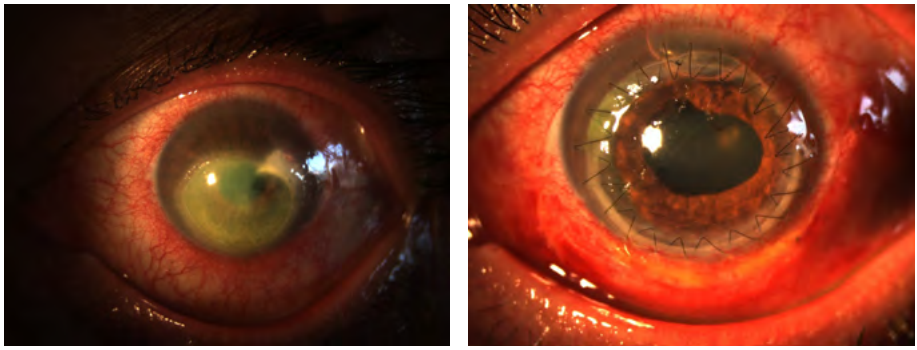

Fig. 2. 67-year-old male. Therapeutic PK for the treatment of a recalcitrant corneal ulcer resistant to medical therapy. Visual acuity was counting fingers at presentation (left). One week after surgery, visual acuity improved to 0.1 with complete cure (right).

Discussion

Despite the developments in medical treatment, surgical intervention is usually necessary in patients with severely thinned or perforated corneas.[7,8] In the current study, therapeutic PK was used to treat these conditions and anatomical integrity of the globe was preserved in 19 (90.4%) of 21 corneal perforations. Likewise, Sharma *et al.* reported an anatomical success in 89.7% of 506 therapeutic PKs for the treatment of refractory keratitis.[9] In another series, anatomical integrity was restored

in 91.3% of 23 corneal perforations.[2] Sukhija *et al.* reported that rate as 90.0%.[10] Although the primary goal of therapeutic PK is to restore the anatomical integrity of the globe, a visual improvement may also be achieved.[11] Visual acuity improved in 71.9% of our patients. Postoperative BCVA was over 0.05 in 62.5%. Jonas *et al.* reported visual gain in 90.0% (8). Hanada *et al.* reported a visual improvement in 85.0% and a graft survival in 67.0% of 20 cases.[12] Killingsworst *et al.* reported 70.0% graft survival rate and visual acuity over 0.3 in 43.0% in their series of PK for infectious keratitis.[5] In our study, PK anatomic success rate was 96.8% and graft clarity rate was 78.1% at postoperative 14th month.

Recurrence is an important problem after PK for fungal keratitis. In Ti *et al.*'s series of 92 therapeutic PK for infectious keratitis, the treatment was uncessfull in 15 eyes that showed progression to endophthalmitis or evisceration. Of these 15 eyes, 11 were fungal keratitis.[13] Li *et al.* reported recurrence in 11.2% of 116 patients who had PK for fungal keratitis and four of these eyes were enucleated.[14] In our study, recurrence occurred in one of two fungal keratitis and full recovery was achieved by repeat PK. Acanthamoeba keratitis is associated with even higher recurrence rates.[15] In their series of therapeutic PK for keratitis, Chen *et al.* achieved a clear graft rate at one year in 68.8% of 32 bacterial keratitis, 51.3% of 39 fungal keratitis and 78.6% of 14 acanthamoeba keratitis.[16] The results were worse in fungal keratitis in terms of eradication of the infection, graft clarity and anatomical integrity. Graft rejection occurred in four eyes (12.5%) of our study. Three of these were herpes simplex keratitis patients already using prophylactic acyclovir.[17]

Preferred surgical technique is closely related with anatomical and functional results. In a series of 31 eyes, lamellar keratoplasty was used in seven eyes, PK in ten, patch graft in seven and AMT in seven eyes. Anatomical integrity was achieved in all and visual improvement in 25 of these eyes.[4] In another series of 41 eyes including 24 tectonic PK and nine lamellar keratoplasty, anatomical success was reported as 85.4%.[18] Soong *et al.* performed lamellar keratoplasty in 80 eyes with corneal thinning and suggested that lamellar surgery was superior to the full thickness grafting.[19] Lamellary keratoplasty may be preferred in non-perforated descemetoceles and infective lesions not involving deeper stromal layers.[13] However, interface haze may limit the visual improvement in some cases.[4] Surgical preference usually depends on clinical practise. Some surgeons prefer to attempt lamellar or patch grafts first to tide over the initial bout of inflammation, before a definitive graft to improve the chances of survival and reduce the complications.

The major complications of PK are peripheral anterior synechiae, secondary glaucoma and graft rejection. Larger donor size used in therapeutic PK may adversely affect the graft survival and IOP control.[14] In addition to 9.0 mm or larger donor, active inflammation, ocular surface disorder, corneal vascularization, lid deformities and corneal perforation are also reported as negative prognostic factors.[6] In our study, the graft diameter was between 8.0 to 11.0 mm in 81.3% of the eyes and it was ≥ 8.0 mm in four eyes with graft rejection. The most frequent complication observed in our patients was IOP elevation (18.9%) that was controlled with medication. Ang *et al.* reported epitheliopathy as the most often complication

followed by glaucoma, recurrence of bacterial or fungal keratitis and cataract.[6]

Limitations of the current study are its retrospective and single center nature with relatively few number of cases. Also our series include no lamellar keratoplasties which may be used in predescemetic lesions. Our study included PK cases with therapeutic indication in a relatively mixed patient group including perforated corneas in which a tectonic support has also been provided. However, purely tectonic patch grafts were excluded from the study to ensure patient homogenity.

In conclusion, therapeutic PK is a viable treatment option in the management of corneal thinning and perforation. If used in proper indication, it can restore the anatomical integrity of the eye and provide visual improvement in majority of the cases.

Table 1. Postoperative complications in 32 study eyes.

Postoperative condition	No of eyes	Percentage (%)	Mean time of occurrence (months ± SD)
IOP elevation	7	21.9	22.3 ± 5.2
Persistent epithelial defect	6	18.8	13.4 ± 8.6
Graft rejection episode	4	12.5	20.7 ± 7.0
Corneal vascularization	3	9.4	23.0 ± 4.2
Posterior synechiae	3	9.4	5.3 ± 5.2
Cataract	2	6.3	8.0 ± 4.2
Descematocele	2	6.3	63.0 ± 66.5
Graft melting	1	3.1	27.0
Fungal keratitis recurrence	1	3.1	2.0

IOP: Intraocular pressure.

Acknowledgement

Authors are thankful to Esra Erikmen from our eye bank staff for her efforts in data collection.

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