Thermokeratoplasty for Keratoconus: A More Than 30-Year Follow-Up Study

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Purpose: The aim of this study was to investigate the long-term outcomes of thermokeratoplasty (TKP) surgery in patients with keratoconus (KC).

Methods: We retrospectively reviewed our clinical database of 2949 patients with KC seen at the Department of Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan, between April 1979 and December 1991. Patients with KC who underwent TKP with a greater-than-30-year postoperative follow-up were included. The occurrence of adverse events including infectious keratitis, corneal perforation, corneal melting, bullous keratopathy, consistency of contact lenses (CL) wear at the final visit, and a history of corneal transplantation post-TKP was assessed.

Results: Forty-two patients (29 male and 13 female patients) with a mean age at initial visit of 23.4 years (range: 13.9–39.5 yrs) were included, and TKP was performed unilaterally in all cases. The mean follow-up period was 35.2 years (range: 30.1–41.6 yrs). As for adverse events/complications, no cases of infectious keratitis, corneal perforation, corneal melting, and/or BK were observed. However, 11 eyes received corneal transplants at an average of 24.9 years postoperatively because of the inability to wear CL continuously. At the last visit, 31 eyes were able to continue wearing CL without corneal transplantation, and the remaining 11 eyes were able to continue wearing contact lenses in all cases after corneal transplantation.

Conclusions: TKP for KC resulted in relatively favorable surgical outcomes over the long-term postoperative period.

Key Words: TKP, KC
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Keratoconus (KC) is a corneal disease characterized by progressive corneal thinning and protrusion, thus resulting in loss of vision due to irregular astigmatism.1,2 Traditionally, rigid gas-permeable contact lenses (RGP-CLs) have been used to correct corneal irregular astigmatism.3 However, patients with advanced KC often experience ocular discomfort when wearing RGP-CLs, which can ultimately lead to lens wear discontinuation and the need for corneal transplantation. First reported by Gasset et al4 in 1973, thermokeratoplasty (TKP) has been used as an alternative treatment to penetrating keratoplasty (PKP) for patients with advanced KC because it uses thermokeratophore to produce controlled thermal shrinkage of corneal collagen and alter the corneal curvature in such patients. Numerous TKP methods have been reported,5–9 which consequently lead to variation of the surgical outcomes. In a Japanese study by Itoi et al,10 the authors reported the postoperative results of TKP and the related complications due to the varied surgical techniques. However, it is important to note that these previous studies on TKP only reported the short-term surgical outcomes, that is, up to 2 years postoperatively,4,5,7,10 and to the best of our knowledge, there have been no previously published studies on the long-term outcomes of TKP. Thus, the purpose of this retrospective study was to analyze the long-term outcomes of TKP in the eyes of patients afflicted with KC.

MATERIALS AND METHODS

Subjects
The protocols of this retrospective study were approved by the Clinical Research Review Board, an independent organization to approve ethical issues, of Kyoto Prefectural University of Medicine, Kyoto, Japan (Approval No. 1235-3), and the research was conducted in accordance with the tenets set forth in the Declaration of Helsinki. Because this study involved the retrospective analysis of patient medical records and because there were no anonymity issues involved, the need for patient consent was waived by the above-referenced Clinical Research Review Board.

In this study, we retrospectively reviewed our clinical database dedicated to patients with KC, which was created in
April 1979 and consists of 2949 patients with KC treated at Kyoto Prefectural University of Medicine through December 1991. As a primary focus, this study centered on the following patients with KC with a history of undergoing TKP: 1) patients who were diagnosed with KC preoperatively and 2) patients with a greater than 30-year postoperative follow-up. The definitive diagnosis of KC was made based on the presence of slit lamp microscopy findings of both corneal stromal thinning and corneal protrusion. Patients with a history of ocular surgery or other ocular pathologies at the initial visit were excluded from the study.

**Surgical Technique**

In all subjects, TKP surgery was performed using the previously described standard method with the thermopencil, which is a probe consisting of a small stainless steel tip with a thermocouple placed within the steel head and connected to a control box that can continuously read the temperature. In brief, the temperature of the TKP probe was set to between 85°C and 90°C, with the probe then applied to the apex of the cone toward the cone base. The elapsed time of each application was less than 1 second. Normal 4°C saline was continuously applied on the treated site, just under the tip of the probe. After the desired flattening was obtained, the operation was halted. It should be noted that in this study, the indication for TKP included patients with KC who ultimately were candidates for PKP due to inability to wear RGP-CLs or in whom adequate vision with RGP-CLs was not obtained.

**Clinical Evaluations**

In this study, the following demographic and clinical data of all patients was obtained through a close review of the medical records: 1) the occurrence of adverse events including infectious keratitis, corneal perforation, corneal melting, and bullous keratopathy (BK), 2) any history of corneal transplantation post-TKP, 3) the consistency of contact lenses (CL) wear at the final visit, 4) the best-corrected visual acuity (BCVA) with RGP-CLs at the first and last visits, and 5) the average keratometry at the final visit. BCVA was converted from decimal to logarithm of the minimum angle of resolution values, with the values obtained at the initial and final visits then compared. The consistency of CL wear was classified into 1 of the following 3 categories depending on the times per week lenses likely to be worn: 1) dropout (no CL use), 2) occasional use (under 4 d of CL use), and 3) continuous use (more than 4 d of CL use). As for the average keratometry values at the last visit, those obtained from Placido disc-based corneal topography images were assessed. On the other hand, keratometry values before surgery, including the values obtained at the initial and final visits, could not be evaluated because keratometry measurements using a corneal topography or autokeratometry were not performed at 1970s in our hospital.

**Statistical Analyses**

Statistical analyses were performed using R version 3.1.0 (The R Foundation) statistical software, with the data being presented as mean ± SD where applicable.

**RESULTS**

Of the 2949 cases in our database, 42 patients (29 male and 13 female patients) in whom TKP for KC was performed unilaterally met the study criteria. A flowchart illustrating the design of this retrospective study is shown in Figure 1. The mean patient age at the initial visit was 23.4 years (range: 13.9–39.5 yrs), and the mean follow-up period was 35.2 years (range: 30.1–41.6 yrs). The demographic data of the patients in this study are summarized in Table 1. Corneal topographic findings of 9 representative patients at 1, 10, 20, and 30 years postoperatively are shown in Figure 2.

As for adverse events/complications, no cases of infectious keratitis, corneal perforation, corneal melting, and/or BK were observed. However, 11 of the 42 eyes did not continue to wear CL because of poor CL vision or discomfort associated with CL wear and underwent corneal transplantation, on average, 24.9 years (range: 15.8–33.4 yrs) after surgery.

**TABLE 1. Patients Demographics**

| No. Patients    | 43 |
|-----------------|----|
| Mean baseline age yrs (range) | 23.4 (13.9–39.5) |
| Male patients, n (%) | 29 (69.0) |
| Mean follow-up periods | 35.2 (30.1–41.6) |
| Clinical features at the last visit | |
| Mean Ave K (range) | 51.8 (41.9–64.8) |
| Mean age at final visit yrs (range) | 58.5 (44.0–74.9) |

Ave K, average keratometry.

**FIGURE 1.** Flow diagram of the study. Of the 2949 cases in our database, 75 KC eyes underwent TKP. Of these 75 eyes, 33 eyes were excluded because of observation periods were less than 30 years. Thus, the remaining 42 eyes were included in this retrospective study.
Table 2 summarizes the BCVA with RGP-CLs, consistency of contact lens wear at the initial and last visits, and the number of patients who had undergone corneal transplantation at the last visit. At the last visit, 31 eyes were able to continue wearing contact lenses without corneal transplantation, and the remaining 11 eyes were able to continue wearing contact lenses after corneal transplantation.

**FIGURE 2.** Placido disc–based corneal topography images at 1-, 10-, 20-, and 30-year post-TKP in 9 representative KC cases (a: case 1 to case 5, b: case 6 to case 9).

### DISCUSSION

This retrospective study involved the review of all patients who underwent TKP for KC and who underwent follow-up examinations for more than 30 year postsurgery. Although several previous studies have reported on the short-term postoperative course of TKP, to the best of our knowledge, this study is the first report of the long-term outcomes.
TABLE 2. Visual Acuity, Consistency of Contact Lens Wear, and Number of Cases That Underwent Corneal Transplantation at the Last Visit

| No. yr After Surgery | BCVA With RGP-CLs | Consistency of CL Wear | Corneal Transplantation After TKP |
|----------------------|------------------|------------------------|----------------------------------|
|                      | ≥20/200          | ≥20/30                 | ≥20/20                           | Dropout | Occasional Use | Continuous Use |
| Baseline (n = 42)    | 17 (40.5%)       | 24 (57.1%)             | 1 (2.4%)                         | 25 (59.5%) | 3 (7.1%)       | 14 (33.3%)     |
| Last visit (n = 31) | 5 (16.1%)        | 11 (35.5%)             | 15 (48.4%)                       | 0 (0%)   | 1 (3.2%)       | 30 (96.8%)     |

It has previously been reported that some of the postoperative problems accounting for TKP failure that subsequently required PKP included delayed epithelial healing and stromal melting. However, our findings revealed that, no cases of corneal melting or corneal perforation were observed in our database. This variance with that of the previous reports may possibly reflect a characteristic feature of our TKP technique, that is, namely the slightly lower TKP-probe temperature setting of 80°C to 90°C. Artensen stated that he chose a temperature setting of 90 to 95 degrees for the probe because the postoperative corneal striae recovered more quickly at 90 to 95 degrees than at 110 degrees. In addition, Aquavella et al also stated that they changed the setting from 105 degrees or higher to 95 degrees or lower in consideration of damage to the corneal epithelium. Although other factors related to the amount of heat given to the cornea, such as corneal thickness and probe contact time, need to be verified, in addition to histological findings, it is possible that the temperature of the probe affected the results.

By flattening the cornea and reducing the size of protrusion, TKP is expected to not only reduce corneal astigmatism but also facilitate CL wear. In our results, 31 of 42 eyes were able to continue wearing contact lenses without corneal transplantation. In addition, even in the 11 eyes that had undergone corneal transplantation, it was estimated that continuous CL wear was possible until corneal transplantation was performed. Although this was a long-term retrospective study and there was a lack of evaluation of CL wear time, visual acuity, and keratometry values along the way, the results are relatively favorable in that they were able to return patients who were unable to wear contact lenses to CL wearers and delay corneal transplantation.

There have been several findings on the effects of TKP on corneal endothelium. For example, a study using porcine eyes showed transient swelling of endoplasmic reticula in corneal endothelial cells immediately post-TKP, and another study using human eyes also showed endothelial edema with marked nuclear pyknosis and cytoplasmic blebs post-TKP. Conversely, the findings in this study revealed no cases of prominent corneal edema or BK. However, because no qualitative or quantitative evaluation of the corneal endothelium was conducted, our findings provide no conclusive information regarding the effect of TKP on corneal endothelial cells.

It should be noted that one of the strengths of this study was the long-term follow-up period. As stated earlier, to the best of our knowledge, this is the first time such a long-term follow-up has been reported on TKP. TKP is an invasive procedure that causes thermal shrinkage of corneal collagen. Therefore, it is very important to elucidate not only the short-term but also the long-term safety postsurgery. Despite the encouraging results, it is important to note that this study did have some limitations. Because this was a retrospective study, we were unable to collect the data on all patients who underwent TKP at our hospital, so the data on some patients who progressed poorly might have been missed. Therefore, it is important to note that the safety of TKP for KC is difficult to determine based on our findings.

In conclusion, the findings in this retrospective long-term-postoperative study on TKP in patients with KC revealed that, of these 42 eyes, no cases of corneal melting, corneal perforation, and/or BK were noted, 31 eyes were able to continue wearing contact lenses without corneal transplantation, and the remaining 11 eyes were able to continue wearing contact lenses after corneal transplantation.

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