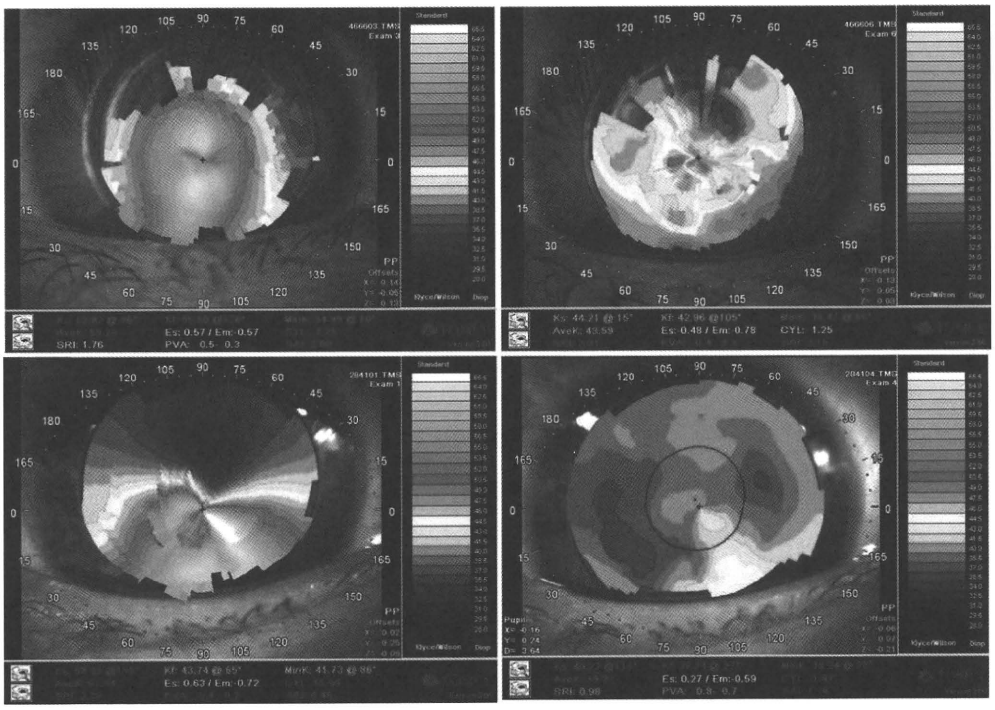

FIGURE 3. Representative cases with dramatic changes in corneal topography after topography-guided conductive keratoplasty. (Top) Case 5: A preoperative central protrusion (left) was flattened after topography-guided conductive keratoplasty at the next day of the surgery (right). (Bottom) Case 16: Another eye with a preoperative inferior protrusion (left) was centrally flattened at 1 week after topography-guided conductive keratoplasty (right).

round, the additional spots were placed to the appropriate area. The entire corneal thickness was assessed preoperatively, and the delivery probes were inserted perpendicularly as per the manufacturer's protocol. In areas where corneal thickness was less than 450 μm, the delivery probes were inserted obliquely, at angles of 45 to 60 degrees into the stroma, centrifugally from thinner point to thicker point, as needed, to avoid damaging the endothelium or penetrating the anterior chamber. These procedures were repeated until the configuration of the pupillary area became symmetrical (Figure 2).

Immediately after the procedure, all eyes received topical diclofenac sodium (Stafulmin, Kowa Company, Limited, Aichi, Japan), levofloxacine (Cravit, Santen, Osaka, Japan), and 0.3% hyaluronic acid (Hyalein, Santen) 5 times per day for 1 week after surgery.

• POSTOPERATIVE EXAMINATIONS: Postoperative examinations were performed 1 day, 1 week, 1 month, 3 months, 6 months, and 1 year after surgery. The UCVA, BSCVA, manifest refraction, corneal topography, intraocular pressure (IOP), and corneal endothelial count were measured, in addition to routine ophthalmologic and funduscopic examinations. Corneal topography was evaluated by TMS-4 (Tomey, Aichi, Japan). Corneal endothelial cells were counted with a specular microscope (Noncon Robo SP-9000, Konan, Hyogo, Japan).

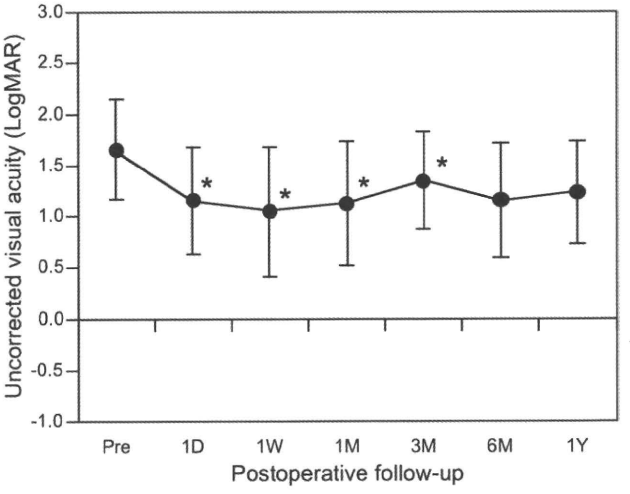

FIGURE 4. Change in average value of uncorrected visual acuity (UCVA) after topography-guided conductive keratoplasty. UCVA showed significant improvement immediately after the surgery; however, it returned to the preoperative value after 3 to 6 months. *P < .05, compared to the preoperative value. Pre = preoperative; D = day; W = week; M = month; Y = year.

Eighteen eyes were followed up for 3 months, 11 for 6 months, and 8 reached the 1-year postoperative examination. Four cases transferred to other clinics were

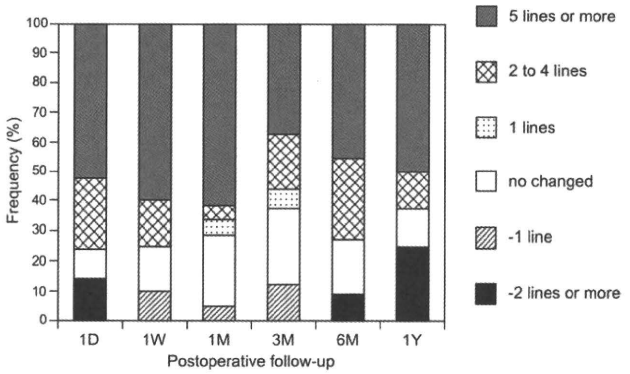

FIGURE 5. Change from preoperative value in uncorrected visual acuity (UCVA) after topography-guided conductive keratoplasty. UCVA improved in 60% to 70% of treated eyes throughout the follow-up period. The frequency of eyes in which UCVA improved more than 5 lines was around 60% at 1 month. Overall, 80% to 90% of eyes showed improved or stable visual acuity. D = day; W = week; M = month; Y = year.

interviewed by phone regarding any difficulties in visual performance, plans for additional surgical treatment, and their ability to wear contact lenses 1 year after the surgery.

• STATISTICAL ANALYSES: For statistical analysis, the Wilcoxon test was used. P values $< .05$ were deemed to indicate statistical significance.

RESULTS

THE INDIVIDUAL PATIENTS' DATA AND OUTCOMES OF THE topography-guided conductive keratoplasty are shown in the Table. Of the 21 eyes, corneal transplantation was avoided or delayed in 15 eyes (71.4%). We indicate the changes in corneal topography of typical cases in Figure 3.

• UNCORRECTED VISUAL ACUITY: The mean ± standard deviation of UCVA (logarithm of the minimal angle of resolution [logMAR]) was 1.65 ± 0.49 preoperatively, 1.15 ± 0.52 at 1 day ($P = .001$ compared to the preoperative value), 1.04 ± 0.64 at 1 week ($P < .001$), 1.12 ± 0.61 at 1 month ($P < .001$), 1.34 ± 0.48 at 3 months ($P = .008$), 1.15 ± 0.57 at 6 months ($P = .050$), and finally 1.23 ± 0.51 at 1 year after surgery ($P = .273$; Figure 4).

When we compared the postoperative to preoperative UCVA values in individual subjects, postoperative UCVA improved more than 5 lines in 11 of 20 eyes (60%), 3 lines in 1 eye (5.0%), and 2 lines in 2 eyes (10.0%) at 1 week after surgery. However, postoperative UCVA was unchanged in 3 eyes (15.0%) and decreased 1 line in 2 eyes (10.0%) at 1 week after surgery. At the 1-month examination, the frequency of eyes with improved UCVA was not grossly changed, although it decreased slightly thereafter. Eyes with improved UCVA accounted for 60% to 70% of cases throughout the follow-up period (Figure 5).

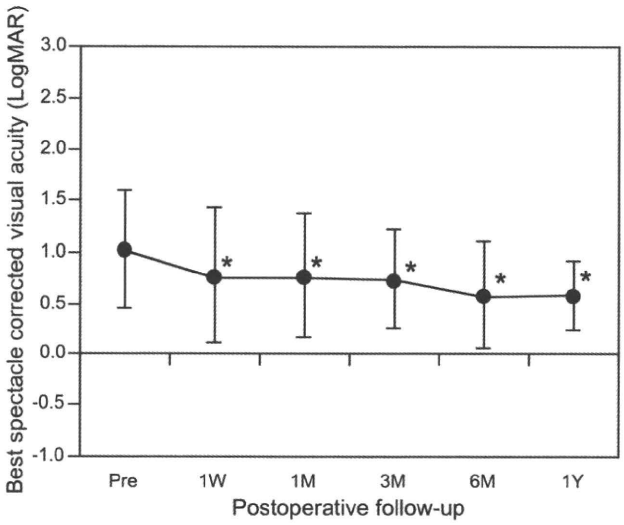

FIGURE 6. Change in average value in best spectacle-corrected visual acuity (BSCVA) after topography-guided conductive keratoplasty. BSCVA showed significant improvement immediately after the surgery, and up to 1 year later. *$P < .05$, compared to the preoperative value. Pre = preoperative; W = week; M = month; Y = year.

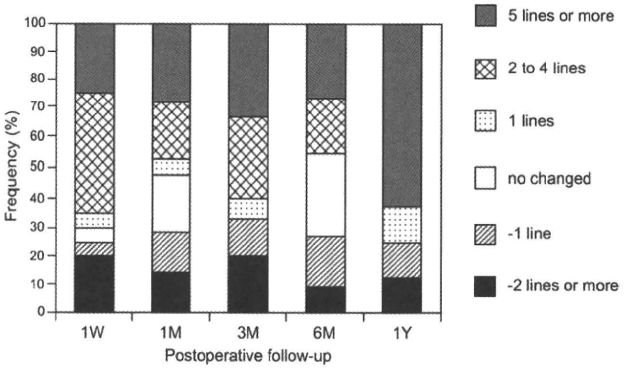

FIGURE 7. Change from preoperative value in best spectacle-corrected visual acuity (BSCVA) after topography-guided conductive keratoplasty. Seventy percent of all eyes showed improved or stable BSCVA values throughout the follow-up period. In particular, 30% of treated eyes gained more than 5 lines. W = week; M = month; Y = year.

• CHANGE IN BEST SPECTACLE-CORRECTED VISUAL ACUITY: The mean ± standard deviation BSCVA, which was 1.02 ± 0.56 before surgery, improved to 0.76 ± 0.65 at 1 week ($P = .026$), 0.76 ± 0.60 at 1 month ($P = .003$), 0.73 ± 0.48 at 3 months ($P = .034$), 0.57 ± 0.53 at 6 months ($P = .043$), and 0.58 ± 0.34 at 1 year after surgery ($P = .018$; Figure 6).

We also compared the postoperative to preoperative BSCVA values in the individual subjects. One week after

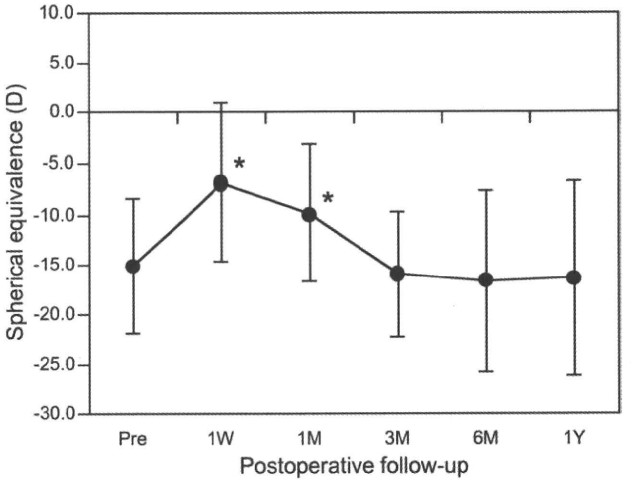

FIGURE 8. Change in average value in manifest refraction after topography-guided conductive keratoplasty. Manifest refraction decreased significantly shortly after surgery; however, it returned to the preoperative value at 3 months. *P < .05, compared to the preoperative value. Pre = preoperative; W = week; M = month; Y = year.

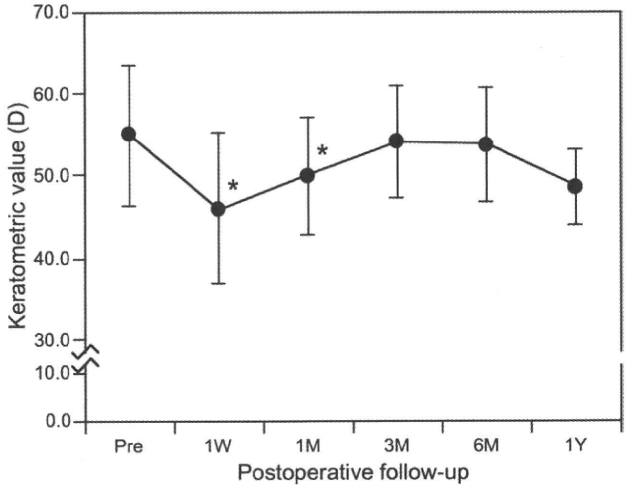

FIGURE 9. Change in average keratometric value after topography-guided conductive keratoplasty. The average keratometric value decreased significantly shortly after surgery; however, it returned to the preoperative value at 3 months. *P < .05, compared to the preoperative value. Pre = preoperative; W = week; M = month; Y = year.

surgery, postoperative BSCVA improved more than 5 lines in 5 of 20 eyes (25.0%), 4 lines in 2 eyes (10.0%), 3 lines in 1 eye (5.0%), 2 lines in 5 eyes (25.0%), and 1 line in 1 eye (5.0%). However, it was unchanged in 1 eye (5.0%) and decreased 1 line in 1 eye (5.0%) and 2 lines or more in 4 eyes (20.0%) 1 week after surgery. Eyes with improved BSCVA accounted for around 50% to 70% of cases throughout the follow-up period (Figure 7).

- MANIFEST REFRACTION: The mean ± standard deviation preoperative manifest refraction (spherical equivalents) was −15.13 ± 6.66 D (range, −6.50 to −28.50 D) before surgery. This value was −6.92 ± 7.70 D (+3.00 to −20.00 D) at 1 week after surgery, and −9.97 ± 6.71 D (+3.00 to −20.00 D) at 1 month, −16.03 ± 6.30 D (−5.00 to −25.00 D) at 3 months, −16.68 ± 9.04 D (−10.00 to −30.00 D) at 6 months, and finally −16.44 ± 9.77 D (−4.00 to −30.00 D) at 1 year after surgery. Postoperative manifest refraction was significantly better than the preoperative value at the 1-week and 1-month examination points (P = .005 and .002, respectively; Figure 8).

- KERATOMETRIC VALUES: The mean ± standard deviation of preoperative average keratometric value (54.95 ± 8.47 D; range, 39.05 to 69.09 D) was 45.98 ± 9.13 D (32.16 to 62.88 D) at 1 week after surgery, and 50.05 ± 7.13 D (38.75 to 60.84 D) at 1 month, 54.14 ± 6.78 D (43.63 to 66.07 D) at 3 months, 53.70 ± 6.88 D (43.00 to 64.05 D) at 6 months, and finally 48.63 ± 4.52 D (42.90 to 55.52 D) at 1 year after surgery. The postoperative keratometric value decreased significantly compared to the preoperative value at the 1-week and 1-month examination points (P = .003 and .039, respectively; Figure 9).

- CORNEAL ENDOTHELIAL COUNT: The corneal endothelial count was only measured in 12 eyes before surgery and in 6 eyes 1 month after surgery, because of an irregular corneal reflex or corneal stromal haze. The corneal endothelial cell count was 2434.4 ± 687.8 cells/mm^2 before surgery, and 2721.7 ± 121.4 cells/mm^2 at 1 month after surgery; these were not significantly different.

- INTRAOCULAR PRESSURE: IOP was not sufficiently measured in all subjects because of corneal irregularities caused by epithelial impairment or stromal scars. The IOP was 11.5 mm Hg in 6 eyes before surgery, 8.5 mm Hg in 8 eyes at 1 week after surgery, 9.3 mm Hg in 14 eyes at 1 month, 8.2 mm Hg in 6 eyes at 3 months, 9.0 mm Hg in 4 eyes at 6 months, and 10.2 mm Hg in 2 eyes at 1 year after surgery.

- COMPLICATIONS AND EVENTUAL OUTCOMES: *Complications*. No severe and/or irreversible complication, such as corneal perforation or microbial infection, was observed.

Contact lens wearing. Eleven of 21 subjects performed daily activities while wearing hard contact lenses; some of these wear special contact lenses for keratoconus and others wear normal ones, even though all of these subjects had been unable to tolerate contact lenses before the procedure. The best-corrected visual acuity using hard contact lenses in these eyes varied from 20/50 to 20/12.5.

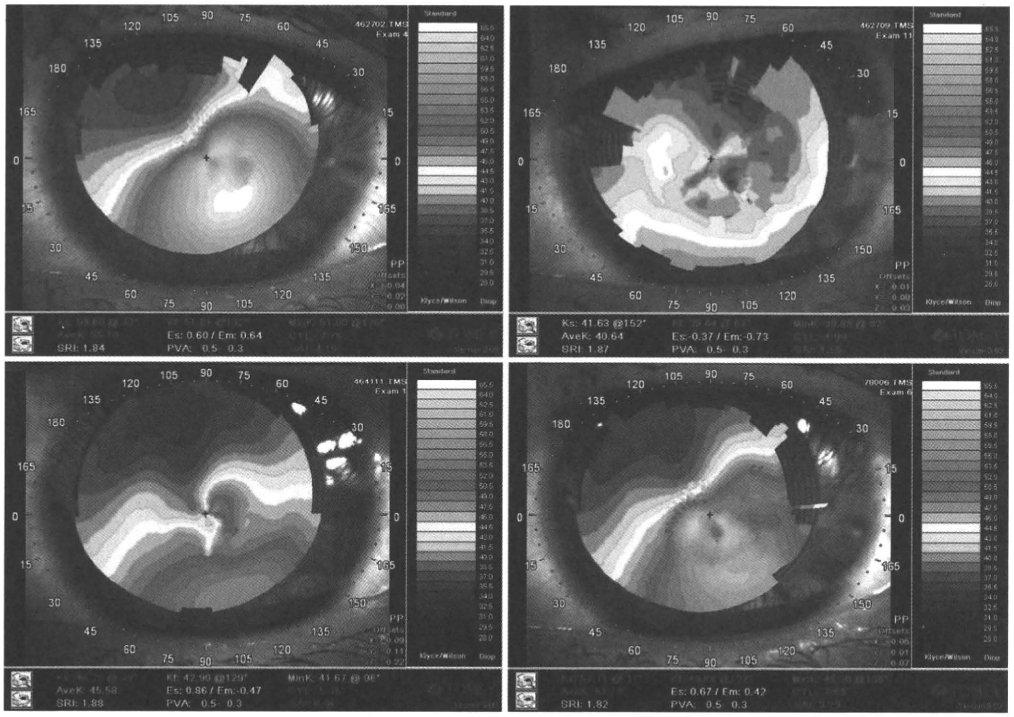

FIGURE 10. Regression of keratoconus after topography-guided conductive keratoplasty (Case 4). (Top) Typical inferior protrusion of a keratoconic cornea (left) was dramatically improved at 1 day after surgery (right). (Bottom) However, the protrusion had recurred by 1 month (left) and finally resumed the preoperative configuration at 3 months after surgery (right).

Retreatment. Five eyes revealed marked regression after the initial surgery and underwent retreatment with topography-guided conductive keratoplasty between 3 months and 1 year postoperatively. These eyes revealed no significant improvement in visual acuity and corneal topography after the retreatment. Among them, 3 cases resumed normal daily lives with hard contact lenses, and the other 2 cases underwent corneal transplantation because of unsatisfactory results after repeat topography-guided conductive keratoplasty.

Subsequent surgical measures. In total, 6 of 21 eyes had already undergone or were planning to undergo additional keratoplasty because of poor visual performance 6 to 18 months after the initial topography-guided conductive keratoplasty. One eye underwent collagen cross-linking (using the riboflavin/UVA method) 2 months after topography-guided conductive keratoplasty. As a result, the patient's preoperative UCVA (20/200) improved to 20/25 at the most recent examination, and BSCVA improved from 20/60 to 20/20 and was stable at 10 months after the procedure. In this case, contact lenses became unnecessary.

DISCUSSION

OUR SURGICAL APPROACH FOR ADVANCED KERATOCONUS, topography-guided conductive keratoplasty, markedly improved UCVA, BSCVA, manifest refraction, and keratometric values immediately after surgery. No severe perioperative or postoperative complication was observed, and 11 of 21 subjects (53%) were able to perform daily activities using hard contact lenses alone; another individual who underwent subsequent cross-linking 2 months after topography-guided conductive keratoplasty is wearing neither contact lenses nor spectacles. Considering that all of the enrolled subjects were candidates for corneal transplants prior to topography-guided conductive keratoplasty, this procedure may allow patients to delay or even avoid the need for transplantation.

Advanced keratoconus is characterized by severe asymmetry or astigmatism of the cornea that interferes with spectacle-corrected visual acuity. Alió and associates[17] reported excellent results with the placement of thermal spots at 6.0 to 7.0 mm of the optical zone on the flat area of the cornea, leading to a "belt-tightening" effect. Lyra and associates put 8 or 16 thermal spots on the circumstance with 4 and 5 mm diameter according to the severity of the disease.[18] In the modified topography-guided conductive keratoplasty procedure described here, the thermal spots were placed concentrically on the smaller circumstance with 3 to 5 mm diameter in the optical zone and additionally on the protruded area. This topography-guided correction enables the alignment of corneal configuration more effectively, probably because stronger belt-tightening effect and flattening power of the close-placed thermal spots make the central

cornea more symmetric. The present results demonstrate that this procedure was quite effective in the correction of corneal irregularities in various cases.

However, we concede that topography-guided conductive keratoplasty was not effective in all eyes. Eyes with severely advanced keratoconus, showing extreme thinning accompanied by a focal protrusion at the central or paracentral area, could not be effectively reshaped by topography-guided conductive keratoplasty. Moreover, corneas with a stromal scar or a previous history of acute hydrops were also unaffected by this treatment. We speculate that the shrinking power may not evenly be carried to the expanded collagen fibers in the too-thin cornea. In addition, when the corneal stroma has scars, which contain aberrant collagen and other extracellular matrix materials, the constructive power may not work as well.[19–21]

A second problem to be resolved is the issue of postoperative regression (Figure 10). Although topography-guided conductive keratoplasty reshaped the affected cornea quite effectively and improved visual performance immediately after surgery, corneal configuration rapidly reverted to preoperative conditions within 3 to 6 months. These results are inconsistent with many previous studies reporting that CK provides stable improvement for hyperopia[15,22–29] and also after CK for keratoconus.[17,18] Especially, Lyra and associates reported that cases with keratoconus treated by CK and followed for 18 months showed few regressions.[18] On the other hand, Erhlich and Manche reported that even the CK for hyperopia led to significant regression of refractive and keratometric effects in the follow-up period.[30] The rapid regression after topography-guided conductive keratoplasty may be the result of the more precipitous correction of the protrusion treated on the more fragile keratoconic cornea causing less resistance against IOP, compared to healthy hyperopic or presbyopic eyes.

We performed retreatment with a second topography-guided conductive keratoplasty in 5 patients; however, the outcomes were not outstanding: The repeat topography-guided conductive keratoplasty did not improve the visual acuity, manifest refraction, and corneal topography in all 5 cases. However, further investigation with larger numbers of cases is required to conclude whether the repeat topography-guided conductive keratoplasty is effective or not.

To prevent postoperative regression, several measures might be adopted. The first is to perform corneal collagen cross-linking[31] simultaneously or shortly after topography-guided conductive keratoplasty, thus fixing the reshaped cornea into an ideal shape. In fact, we have already observed 1 case of corneal cross-linking 2 months after topography-guided conductive keratoplasty. The treated eye has maintained stable visual acuity, refraction, and corneal configuration for up to 10 months after cross-linking. When performing corneal cross-linking with riboflavin/UVA irradiation, the cornea should be more than 400 μm in thickness at the thinnest part to avoid corneal endothelial decompensation attributable to the cytotoxicity of ultraviolet radiation.[32] This criterion coincides with topography-guided conductive keratoplasty being more effective in not-too-thin corneas without focal protruding areas.

Six patients are planning or have already undergone corneal transplantation after topography-guided conductive keratoplasty. One patient, who had a preoperative UCVA of 20/1000 and corrected visual acuity of 20/125 (with a hard contact lens), showed a positive outcome immediately after the initial topography-guided conductive keratoplasty, with a UCVA of 20/50, a BSCVA of 20/32, and a visual acuity of 20/20 with a hard contact lens up to 3 months after the surgery. This case, however, showed dramatic regression thereafter and required a corneal transplant at 18 months after topography-guided conductive keratoplasty. The other 5 cases showed no marked improvement in vision after topography-guided conductive keratoplasty, probably because the corneas were too thin and/or had stromal scars, thus making a favorable outcome unlikely. All of these cases were treated in the first half of the trial; based on our subsequent experience, we would no longer consider such cases for the topography-guided conductive keratoplasty procedure.

In the present investigation, 50% to 70% of eyes increased BSCVA by more than 1 line; notably 25% to 50% achieved BSCVA gains of 5 lines or more postoperatively. On the other hand, 10% to 20% of treated eyes lost 2 lines or more of BSCVA. We could not define the accurate causes for decreased BSCVA and the tendency for some eyes to have decreased BSCVA. In some cases, BSCVA could vary several lines at each examination, affected by the condition of corneal epithelium or prior contact lens wearing.

In summary, we believe that topography-guided conductive keratoplasty may be effective to reshape keratoconic eyes, as it provides marked improvements in corneal symmetry, contact lens tolerance, and visual performance. However, our experience has given the impression that only patients with diffusely protruded corneas without focal protrusion or stromal scar are likely to benefit from this procedure. More experiences with larger numbers of cases are required to address the precise indications for topography-guided conductive keratoplasty.

THE AUTHORS INDICATE NO FINANCIAL SUPPORT OR FINANCIAL CONFLICT OF INTEREST. INVOLVED IN DESIGN AND CONDUCT of study (N.K., C.S.); collection of data (N.K., I.T., K.T.); management (N.K.), analysis, and interpretation of data (N.K., C.S.); and preparation (N.K., C.S.), review (I.T., T.K.), or approval of the manuscript (K.T.). The study protocol was approved by the institutional review board of the Minamiaoyama Eye Clinic and Keio University School of Medicine, and was conducted in accordance with the tenets of the Declaration of Helsinki. This clinical trial is registered at the Clinical Trial Registry of the University Hospital Medical Information Network (UMIN-CTR; UMIN000000886).

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