ORIGINAL PAPER

Configuration of recipient corneal cut after mechanical trephination in keratoconus

Sepehr Feizi · Maryam Najafi · Mohammad Ali Javadi · Amir A. Azari

Abstract

Purpose To determine the roundness of recipient corneal cuts after mechanical trephination and to investigate possible factors that could affect the corneal bed configuration in deep anterior lamellar keratoplasty (DALK).

Methods This study enrolled 85 eyes with keratoconus that underwent DALK. Recipient corneas were partially trephined using a new, unused, disposable Hessburg-Barron suction trephine. Photographs that best represented the recipient corneal cut were selected, and ImageJ software was used to evaluate the roundness of recipient bed. The effect of potential variables on the roundness of cuts was investigated using the univariate analyses.

Results The mean patient age was 31.0 ± 9.0 years. The mean recipient trephine size was 8.04 ± 0.29 mm (range 7.5–8.50 mm). The recipient cut roundness was 0.922 ± 0.070, varying from 0.78 to 1.0. The roundness of the corneoscleral limbus (0.874 ± 0.074) which represented the shape of recipient cornea was the main predictor of the configuration of recipient cut ($r = 0.84$, $P < 0.001$). Other preoperative characteristics investigated were mean keratometry ($P = 0.63$), keratometric astigmatism ($P = 0.18$), central corneal thickness ($P = 0.64$), keratoconus severity ($P = 0.37$), and trephine size ($P = 0.50$) that demonstrated no significant associations with the roundness of cut.

Conclusions The recipient corneal cut after mechanical trephination may not be circular. The roundness of recipient bed was primarily affected by the roundness of corneoscleral limbus, indicating that the shape of recipient cut tends to follow the original shape of the cornea.

Keywords Hessburg-Barron suction trephine · Deep anterior lamellar keratoplasty · Recipient corneal cut · Roundness · Mechanical trephination

Introduction

Corneal transplantation is a sight-saving procedure in patients with corneal blindness.

Since microsurgical techniques and postoperative management have led to increased production of clear corneal transplants, post-keratoplasty astigmatism that prevents visual recovery is a major concern. Several factors can influence astigmatism after deep anterior lamellar keratoplasty (DALK) and penetrating keratoplasty (PK), including decentralized trephination, shape and size differences between the donor cornea and the opening in the recipient corneal bed, wound apposition and healing, recipient pathology,

S. Feizi (✉) · M. Najafi · M. A. Javadi · A. A. Azari
Ophthalmic Research Center, Labbafinejad Medical Center, Shahid Beheshti University of Medical Sciences, Boostan 9 St., Pasdaran Ave., Tehran 16666, Iran
e-mail: sepehrfeizi@yahoo.com

malposition of recipient and donor tissues, and suture tension [1]. Recipient trephination is the important step in DALK and PK and should ideally create a well-centered opening with round and regular edges. Inadequate recipient trephination, including noncircular trephination, results in the production of an irregularly shaped recipient bed that is a poor anatomical match with the round donor button [2]. Mismatching of the corneal donor button to the recipient opening can lead to high degrees of astigmatism postoperatively [2].

The factors that influence the roundness of recipient bed after mechanical trephination are not well defined. To the best of our knowledge, only a few laboratory studies investigated the features of recipient opening after mechanical trephination [3–6]. These studies showed that corneal distortion caused by the scleral fixation ring may result in a markedly oval cut, and different methods of trephination produce different shaped corneal openings [3–6]. The purpose of the present study was to quantitatively evaluate the roundness of the recipient cut after mechanical trephination in keratoconus-affected eyes that underwent DALK. A secondary objective was to investigate potential factors that might account for the configuration of the recipient cut after trephination.

Materials and methods

This cross-sectional study was conducted on consecutive eyes with keratoconus that underwent DALK between June 2016 and September 2017. Complete preoperative ocular examinations were performed, including best spectacle-corrected visual acuity (BSCVA), manifest refraction (when possible), slit-lamp examination, tonometry, and dilated funduscopy. Preoperatively, no peripheral corneal vascularization, deep stromal scar, or defect in the Descemet membrane indicating previous hydrops was observed. Keratoconus was clinically diagnosed based on slit-lamp findings (Fleischer ring, Vogt's striae, and stromal thinning) and keratometry and was confirmed by elevation tomography (Pentacam HR, Oculus Optikgeräte GmbH, Wetzlar, Germany, software version 1.17r139). The Pentacam system was used to measure mean keratometry, keratometric astigmatism, central corneal thickness (CTT), and corneal thickness at the site of trephination. Keratoconus severity was

categorized according to the Amsler-Krumeich classification, which is based on myopia, induced astigmatism, central keratometry, corneal transparency, and corneal thickness [7].

All eyes were operated on under general anesthesia using the big-bubble technique as described previously [8]. A new, unused, disposable Hessburg-Barron suction trephine (Katena Products Inc, Denville, NJ) was used to cut the recipient cornea to approximately 80% of corneal thickness at the site of trephination. Prior to use, all blades were inspected for defects under the operating microscope (Zeiss, Jena, Germany). The size of recipient trephine was chosen to be 2.5 mm less than the vertical corneal diameter to prevent sutures from being placed very close to the limbus, thereby reducing suture-related complications. After partial trephination, the recipient cornea was blotted dry and a 1.0-mm scale was placed adjacent to the corneoscleral limbus. The operating microscope equipped with a digital camera was focused on the corneal epithelial surface to capture images of the recipient corneal cut at a magnification of $5\times$.

Evaluation of the recipient cut centration and configuration

From the records obtained intraoperatively, the photographs that most clearly represented the entire recipient corneal cut after trephination were prepared (Fig. 1). Only those photographs with sharp and distinct cuts were included in the analysis. Next, the centration and roundness of recipient cuts were measured using ImageJ software (http://imagej.nih.
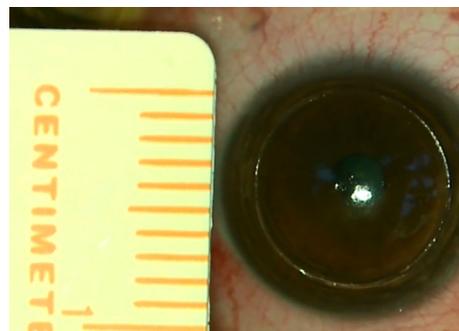

Fig. 1 A photograph of a recipient cornea after partial trephination. The photograph clearly represents the entire trephine cut. The scale on the image is used to provide the pixel-to-millimeter conversion

gov/ij/; provided in the public domain by the National Institutes of Health, Bethesda, MD, USA). The distance of the trephination cut from the limbus was measured at the vertical and horizontal meridians with the software. The eccentricity index, which evaluated the centration of the recipient trephination, was defined as the ratio of the minimum to the maximum distance of the trephination cut from the limbus at each meridian. Higher index values reflect more central recipient cut. To measure the configuration of the recipient cut, the outlines of the cut were delineated using the oval selection tool within ImageJ. Roundness was defined as $4 \times$ (area)/($\pi \times$ maximum diameter^2) with a value of 1.0 indicating a perfect circular cut. As the value approaches 0.0, it indicates an increasingly noncircular shape.

Statistical analysis

The data were analyzed using SPSS statistical software version 24 (IBM Corp., Armonk, NY, USA). The normal distribution of continuous variables was checked by a Kolmogorov–Smirnov test and a Q–Q plot. Normally distributed data were presented as the mean and range. The univariate analyses were used to evaluate the effect of potential variables (including recipient age and sex, mean keratometry, keratometric astigmatism, CCT, keratoconus severity, recipient trephine size, roundness of the corneoscleral limbus, and eccentricity index) on the roundness of cuts. The roundness of recipient cut was compared between two subgroups of keratoconus severity (stages 2 and 3 versus stage 4) using independent student test. A P value < 0.05 was considered statistically significant. All reported P values were two-sided.

Results

A total of 85 consecutive eyes (57 right eyes) from 85 patients (51 male subjects) with keratoconus were operated on during the study period. The mean patient age was 31.0 ± 9.0 years (range 20–53 years). Mean preoperative BSCVA was 0.92 ± 0.50 logMAR (range 0.10–1.80 logMAR). Mean preoperative spherical equivalent refraction was -8.90 ± 4.57 D (range -18.13 to -2.0 D). Preoperatively, mean keratometry and keratometric astigmatism were 54.62 ± 5.55 D (range 46.18–67.41 D) and 6.91 ± 2.90 D (range

1.0–11.5 D), respectively. Mean CCT was 408.5 ± 62.5 μm (range 302–501 μm). Stromal opacities were present in ten eyes. According to the Amsler-Krumeich classification, 9 eyes (10.6%) had stage 2, 22 eyes (25.9%) had stage 3, and 54 eyes (63.5%) had stage 4 keratoconus.

The roundness of corneoscleral limbus was 0.874 ± 0.074 (range 0.69–1.0). The recipient cut roundness was 0.922 ± 0.070 (range 0.78–1.0). The eccentricity index was 0.797 ± 0.120 (range 0.47–1.0) at the vertical meridian and 0.80 ± 0.140 (range 0.43–1.0) at the horizontal meridian. Univariate analysis revealed that the roundness of the corneoscleral limbus had a statistically strong association with the roundness of the cut ($r = 0.84$, $P < 0.001$, Figs. 2 and 3). As illustrated, the roundness of the recipient cut increased with an increase in the roundness of the limbus. Other investigated characteristics including recipient age ($P = 0.83$) and sex ($P = 0.26$), presence of corneal scar ($P = 0.37$), mean keratometry ($P = 0.63$), keratometric astigmatism ($P = 0.18$), CCT ($P = 0.64$), keratoconus severity ($P = 0.37$), recipient trephine size ($P = 0.50$), and eccentricity index at the horizontal ($P = 0.97$) and vertical ($P = 0.29$) meridian demonstrated no significant associations with the roundness of cut (Fig. 2).

Subgroup analysis was performed to validate the results of the explanatory analysis. The study group was categorized into two subgroups on the basis of keratoconus severity; subgroup 1 consisted of patients with stage 2 and 3 keratoconus (31 eyes) and subgroup 2 consisted of patients with stage 4 keratoconus (54 eyes). We found that subgroups 1 and 2 were comparable in terms of the roundness of the recipient cut (0.938 ± 0.059 versus 0.917 ± 0.074, respectively, $P = 0.40$), confirming the results of the explanatory analysis.

Discussion

Disparity between donor and recipient tissue margins is one of the greatest contributors to post-keratoplasty astigmatism [9]. An exact circular trephine opening in the recipient cornea will facilitate uniform wound closure and will probably minimize postoperative astigmatism. In the current study, we evaluated the configuration of the recipient corneal cut and investigated if there were any characteristics that could

Fig. 2 Effects of limbus roundness, eccentric trephination, and keratoconus severity on the shape of recipient cut after mechanical trephination. The edge of the recipient cut follows the contour of the limbus irrespective of the centration of trephination and keratoconus severity. **a** A perfectly round cornea yields a recipient cut with the same configuration. **b** The edge of the recipient cut is oval in an oval cornea. **c** An eccentric trephination in a round cornea results in a round cut. **d** The recipient cut is round in a cornea with advanced keratoconus and stromal scars
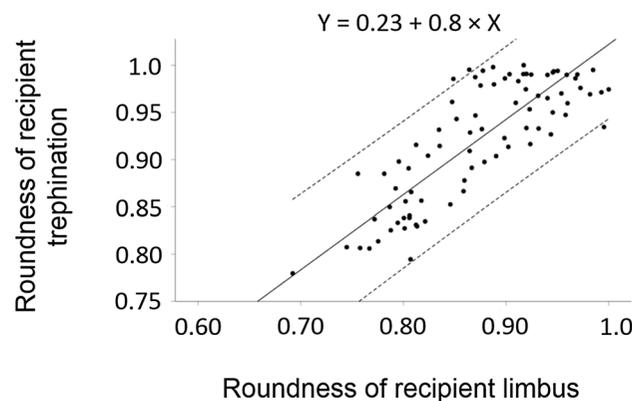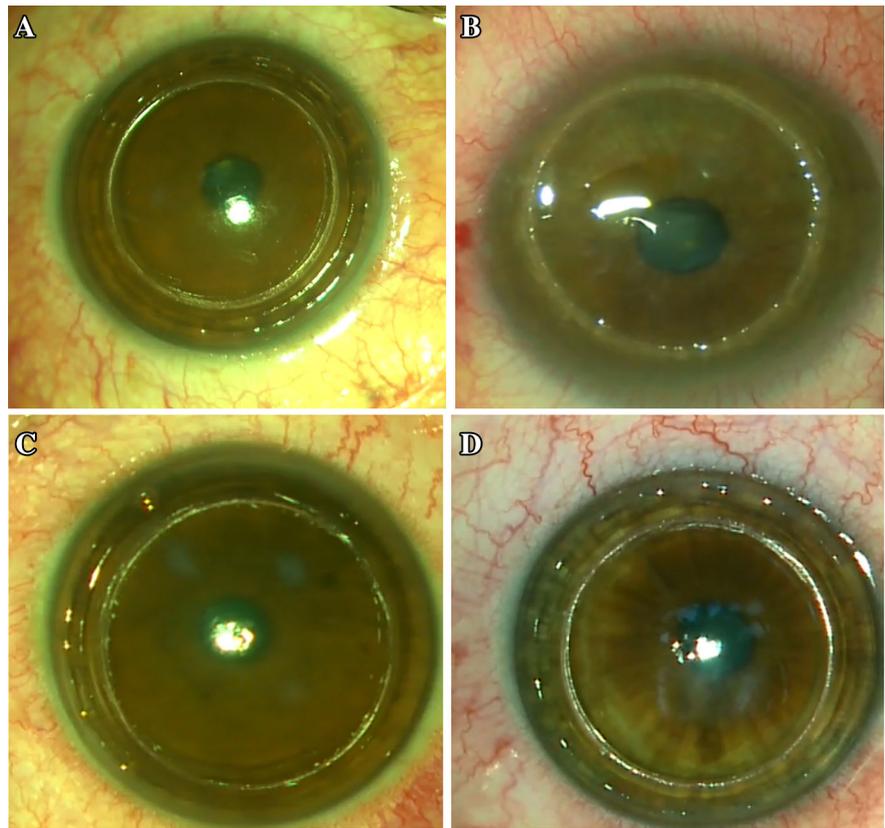

$$Y = 0.23 + 0.8 \times X$$

Fig. 3 A scattergram illustrating the effect of the roundness of recipient corneoscleral limbus on the roundness of recipient cut. As illustrated, the roundness of recipient cut increases with an increase in the roundness of limbus ($r = 0.84$, $P < 0.001$). The regression formula is provided. Dotted lines indicate 95% confidence intervals for the regression line

affect the roundness of cuts using the ImageJ software. This software has routinely been used in several studies to analyze the size of epithelial lesions in dry eye [10], DNA double strand break repair [11], fluorescence cell images and western blots [12, 13], immunohistochemical probes [14], cell size [15], and to quantify wound healing [16] or identify soft tissue in tomography images [17].

In the present study, we included eyes that underwent DALK because the anterior chamber remains formed after partial-thickness trephination. However, the edges of the opening collapse irregularly after full-

thickness trephination performed in PK, making it difficult to measure directly the roundness of the corneal opening. It is possible that the measurements of roundness after removing corneal stroma would be closer to the actual roundness of recipient cuts. However, the accuracy of the measurements made after baring the Descemet membrane can be negatively influenced by two factors. First, the peripheral cornea becomes emphysematous and thick after air injection making it difficult to accurately identify the edge of the recipient cut. Second, anterior chamber is decompressed before puncture of the bubble. The resultant hypotony can alter the dimensions of the recipient bed. Therefore, we believe that the eye is in more physiological state after partial trephination where our photographs were taken. Our results demonstrate that the recipient corneal cut after mechanical trephination may not be circular. It has been previously reported that a 0.1-mm cutting error in either the recipient bed or the donor cornea will induce as much as 1 D of post-keratoplasty astigmatism [2]. Therefore, we can expect to encounter a significant amount of postoperative astigmatism based on the degree of recipient bed acircularity observed in this study.

The present study investigated factors that could affect recipient cut configuration after trephination. The results of the explanatory analysis revealed that the roundness of the recipient cornea measured at the limbus was the most important explanatory variable that had influence on the roundness of the recipient cut; the roundness of recipient cut increased with an increase in the roundness of recipient corneal limbus. This finding indicates that the shape of recipient cut tends to follow the original shape of the cornea which is horizontal oval in human beings. The observed association is attributable to the amount of the corneal tissue inside the trephine as the cut is made. We hypothesize that when trephination is performed, more tissue balloons up into the trephine along the longer horizontal meridian, while less tissue balloons up into the trephine along the shorter vertical meridian. Thus, after a perfectly circular-appearing cut is made in an oval cornea, the surgeon will end up with an oval cut with the longer diameter along the longer meridian (Fig. 2b). We also performed a similar analysis for the donor tissue and correlated the roundness of the donor cornea before trephination with the roundness of the resultant donor button [18]. Interestingly, we observed

a strongly significant association between these two measurements [18]. Given that, we can further hypothesize that matching the anatomical orientation of the donor tissue with the opening in the recipient corneal bed (i.e., horizontal meridian of donor with horizontal meridian of recipient) during corneal transplantation may result in a better fit of the donor corneal button in its recipient bed and subsequently improve refractive outcomes.

It has been proposed that good centration of the trephine on the cornea during trephination is a key factor in achieving round recipient corneal opening [4]. The results of the current study, however, demonstrate no significant association between the eccentricity and roundness of the recipient corneal cut (Fig. 2c). In line with our results, van Rij et al. [19] compared the ovality of the trephine hole in the eccentrically trephined eyes versus the centrally trephined eyes in a laboratory study and observed no significant difference between these two groups [19]. From this observation, it can be concluded that severe astigmatism associated with a markedly eccentric keratoplasty is caused by optical aberrations rather than the acircularity of the recipient opening.

The present study enrolled keratoconus-affected eyes which can produce an irregular cut in recipient trephination due to corneal thinning, increased corneal curvature, and decreased biomechanics. An interesting result of the present study is a nonsignificant association of mean keratometry, keratometric astigmatism, and CCT (keratoconus severity) with recipient cut roundness (Fig. 2d). Similarly, van Rij and Waring [4] found that corneal astigmatism that was induced with 1 or 2 silk sutures at the limbus had no effect on the roundness of the recipient corneal opening. The lack of association between keratoconus severity and the configuration of recipient cut can explain why keratoconus severity has no significant influence on postoperative visual and refractive outcomes as reported by previous studies [20, 21].

This study has two limitations. One limitation was the relative difficulty to determine the interface between the limbus and cornea in some eyes. We used the definition stated by van Buskirk [22] to determine the limbus (peripheral loss of corneal transparency). However, exact determination of the limbus may not be straightforward in all cases. Furthermore, this study is limited by using only one trephine to prepare the recipient bed. The method used

in the present study is one of the most commonly used clinical techniques and most corneal surgeons currently prefer to perform recipient corneal trephination using the same technique because suction trephination systems are considered technically reliable and easy to use [6]. However, there are a wide variety of trephine types which produce different shaped corneal openings. In addition, numerous modifications have been made in instrumentation to produce more accurate corneal cuts and less tissue disparity. For example, innovative surgical strategies including femtosecond laser-assisted corneal trephination have been developed to cut recipient corneas. This innovation may result in more regular cut, independent of the original shape of the recipient cornea [23].

In summary, this study provides insights into the configuration of the recipient corneal bed after being cut by the currently available trephine. Our results show that marked variance in the shape of recipient bed could be noted after mechanical trephination. This study also identified the roundness of corneoscleral limbus as the main predictor of cut; an oval recipient cornea will lead to ovality of the resultant bed. We continue to follow up with these patients to examine the actual correlation between the shape of the recipient bed and the ultimate astigmatism. Further studies are warranted to evaluate the shape of the recipient corneal bed prepared using different methods including femtosecond laser-assisted cut.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Fares U, Sarhan AR, Dua HS (2012) Management of post-keratoplasty astigmatism. J Cataract Refract Surg 38:2029–2039

2. Troutman RC (1979) Astigmatism considerations in corneal graft. Ophthalmic Surg 10:21–26

3. Villacriz E, Smith RE (1986) Corneal recipient bed distortion due to scleral fixation rings. Cornea 5:75–79

4. Van Rij G, Waring GO (1988) Configuration of corneal trephine opening using 5 different trephines in human donor eyes. Arch Ophthalmol 106:1228–1233

5. Wilbanks GA, Cohen S, Chipman M et al (1996) Clinical outcomes following penetrating keratoplasty using the Barron-Hessburg and Hanna corneal trephination systems. Cornea 15:589–598

6. Moshirfar M, Calvo CM, Kinard KI et al (2011) Comparison of Hanna and Hessburg-Barron trephine and punch systems using histological, anterior segment optical coherence tomography, and elliptical curve fitting models. Clin Ophthalmol 5:1121–1125

7. Amsler M (1946) Keratocone classique et keratocone fruste, arguments unitaires. Ophthalmologica 111:96–101

8. Feizi S, Javadi MA, Jamali H et al (2010) Deep anterior lamellar keratoplasty in patients with keratoconus: big-bubble technique. Cornea 29:177–182

9. Spadea L, Bianco G, Mastrofini MC et al (1996) Penetrating keratoplasty with donor and recipient corneas of the same diameter. Ophthalmic Surg Lasers 27:425–430

10. Courrier E, Lépine T, Hor G et al (2016) Size of the lesions of superficial punctate keratitis in dry eye syndrome observed with a slit lamp. Cornea 35:1004–1007

11. Djuzenova CS, Elsner I, Katzer A et al (2013) Radiosensitivity in breast cancer assessed by the histone γ-H2AX and 53BP1 foci. Radiat Oncol 8:98

12. Wiesmann V, Franz D, Held C et al (2015) Review of free software tools for image analysis of fluorescence cell micrographs. J Microsc 257:39–53

13. Wu KH, Madigan MC, Billson FA et al (2003) Differential expression of GFAP in early v late AMD: a quantitative analysis. Br J Ophthalmol 87:1159–1166

14. Woeffler-Maucler C, Beghin A, Ressnikoff D et al (2014) Automated immunohistochemical method to quantify neuronal density in brain sections: application to neuronal loss after status epilepticus. J Neurosci Methods 225:32–41

15. Tchoukalova YD, Harteneck DA, Karwoski RA et al (2003) A quick, reliable, and automated method for fat cell sizing. J Lipid Res 44:1795–1801

16. Rifkin LH, Stojadinovic S, Stewart CH et al (2012) An athymic rat model of cutaneous radiation injury designed to study human tissue-based wound therapy. Radiat Oncol 7:68

17. Irving BA, Weltman JY, Brock DW et al (2007) NIH ImageJ and Slice-O-Matic computed tomography imaging software to quantify soft tissue. Obesity 15:370–376

18. Feizi S, Masoudi A, Rahimi B et al (2019) Geometric properties of donor corneas after mechanical trephination in deep anterior lamellar keratoplasty. Cornea 38:35–41

19. van Rij G, Cornell FM, Waring GO 3rd et al (1985) Postoperative astigmatism after central vs eccentric penetrating keratoplasties. Am J Ophthalmol 99:317–320

20. Buzard KA, Fundingsland BR (1997) Corneal transplant for keratoconus: results in early and late disease. J Cataract

Refract Surg 23:398–406

21. Liu Y, Seitz B, Langenbucher A et al (2003) Impact of preoperative corneal curvature on the outcome of penetrating keratoplasty in keratoconus. Cornea 22:409–412

22. van Buskirk EM (1989) The anatomy of the limbus. Eye 3:101–108

23. Angunawela RI, Riau A, Chaurasia SS et al (2012) Manual suction versus femtosecond laser trephination for penetrating keratoplasty: intraocular pressure, endothelial cell damage, incision geometry, and wound healing responses. Invest Ophthalmol Vis Sci 53:2571–2579