The Influence of Ultrasound Ciliary Plasty on Corneal Parameters

Bartłomiej Bolek, MD, Adam Wylegala, MD, PhD, and Edward Wylegala, MD, PhD

Results: There was a significant difference in the anterior/posterior steep/flat keratometry and anterior/posterior astigmatism values immediately after UCP. However, 3 months postoperatively these parameters returned to their initial values and there were no significant differences noted. The mean ± SD values of anterior astigmatism preoperatively and at 1 week, and 1, 3, 6, and 12 months postoperatively were 1.12 ± 0.66 D, 2.17 ± 0.91 D (P < 0.001), 2.05 ± 0.93 D (P < 0.001), 1.55 ± 0.75 D (P = 0.004), 1.31 ± 0.70 D (P = 0.024), and 1.20 ± 0.73 D (P = 0.406), respectively. The astigmatism axis tended to approach 90 degrees meridian with a significant difference 1 week postoperatively. Central and minimal corneal thickness remained unchanged, whereas the intraocular pressure and the number of antiglaucoma medications decreased significantly.

Conclusions: UCP influenced the corneal topography parameters in the immediate postoperative period; however, with time, all parameters returned to their initial values.

Key Words: glaucoma, ultrasound ciliary plasty, cyclodestruction, astigmatism, corneal topography

Cyclodestructive methods are used to treat mild and severe forms of glaucoma. These methods reduce intraocular pressure (IOP) by decreasing the production of aqueous humor by partially damaging the nonpigmented epithelium of the ciliary body. Ultrasound ciliary plasty (UCP) for refractory glaucoma treatment, compared with the commonly used diode laser cyclodestruction, enables precise energy concentration through opaque structures, without uncontrolled absorption at the desired depth and area. Consequently, it reduces damage to the adjacent tissues. However, ultrasound energy can alter the morphology of the sclera that could possibly affect the corneal parameters and could be visually significant.

The primary outcome measures were the anterior and posterior curvatures of the cornea to determine how the values of corneal keratometry, astigmatism, and thickness change after UCP. Secondary outcome measures included IOP reduction, success rates, glaucoma medication use, and visual acuity.

MATERIALS AND METHODS

This prospective clinical study was approved by the institutional review board of the Medical University of Silesia (KNW/0022/KB1/78/18) and followed the tenets of the Declaration of Helsinki. Written informed consent was obtained from all enrolled patients.

In total, 78 patients with primary and secondary refractory glaucoma were enrolled to undergo UCP. The inclusion criteria for the study were as follows: adult patients (older than 18 y), uncontrolled glaucoma (IOP > 21 mm Hg, despite maximum-tolerated doses of antiglaucoma topical medications), and contraindication to incisional glaucoma surgery. The exclusion criteria were as follows: pregnant women, patients aged less than 18 years, IOP > 30 mm Hg, and neovascular glaucoma. Patients with a history of other treatments/surgeries for glaucoma were not excluded from the study. A total of 39 patients (39 eyes) fulfilled the above criteria and completed 12 months of the follow-up period. Patient characteristics are described in Table S1 (Supplemental Digital Content 1, http://links.lww.com/IJG/A399).

Complete ophthalmic examinations with measurements of corneal parameters were performed preoperatively and at 1 week, and 1, 3, 6, and 12 months postoperatively. Corneal parameters were analyzed with anterior segment swept-source optical coherence tomography (Caisa 2, Tomey Corp., Nagoya, Japan), and included anterior and posterior keratometry, anterior and posterior corneal astigmatism, steep and flat keratometry axis, and central and minimal corneal thickness (µm). In addition, data related to IOP (obtained with the standard Goldmann applation tonometer), the number of antiglaucoma medications, and best-corrected logMAR visual acuities were obtained for analysis. An IOP reduction of 20% or >5 mm Hg as compared with the baseline value was considered as successful treatment. Complete success was defined as a cessation of antiglaucoma medications.

UCP was performed using the EyeOPI device (Eye Tech care, Rillieux-la-Pape, France) under intravenous or peribulbar...
anesthesia. In the present study, the second-generation probe was used, a ring-shaped probe containing 6 piezoelectric components (transducers) with a high frequency of 21 MHz (high-intensity focused ultrasound technology). The probe size was determined according to the axial length and white-to-white parameters measured preoperatively by IOL Master 700 (Carl Zeiss Meditec AG, Jena, Germany). The procedure involved precise adjustment of the positioning cone in the center of the eye under a surgical microscope and its stabilization by a mild vacuum system. The probe was then inserted into the cone and sequentially activated by footswitch transducers. The operation time of each of the 6 transducers was 8 seconds, with an interval of 20 seconds between the subsequent exposure, and the total time for the procedure was ~3 minutes. The preoperative antiglaucoma medications were either continued as before or modified according to the postoperative IOP. Postoperatively, patients were treated topically with ofloxacin (5 times a day for 2 weeks), dexamethasone (5 times a day for 2 weeks, followed by 3 times a day for 2 weeks), and atropine (3 times a day for 2 weeks).

Statistical analyses were performed using the Statistical Software version 13 (TIBCO Software Inc., Palo Alto, CA). Groups of data sets of a given parameter were compared using the Wilcoxon signed-rank test or *t*-test depending on the data distribution. A *P*-value of ≤0.05 was considered statistically significant.

RESULTS

The mean ± SD values of IOP preoperatively and at 1 week, and 1, 3, 6, and 12 months postoperatively were 22.7 ± 5.1 mm Hg, 16.2 ± 4.9 mm Hg (*P* < 0.001), 18.9 ± 5.6 mm Hg (*P* < 0.001), 17.3 ± 4.0 mm Hg (*P* < 0.001), 16.8 ± 2.8 mm Hg (*P* < 0.001), and 16.2 ± 2.9 mm Hg (*P* < 0.001), respectively (Table S2, Supplemental Digital Content 1, http://links.lww.com/IJG/A399; Fig. 1). The mean IOP at the last follow-up was reduced by 28.5% (Table S2, Supplemental Digital Content 1, http://links.lww.com/IJG/A399). The success rate and the complete success rate were 69.2% and 7.7%, respectively.

The mean ± SD values of the number of antiglaucoma medications preoperatively and at 1 week, and 1, 3, 6, and 12 months postoperatively were 3.9 ± 0.9, 1.1 ± 1.1 (*P* < 0.001), 1.3 ± 1.1 (*P* < 0.001), 2.1 ± 1.2 (*P* < 0.001), 2.4 ± 1.2 (*P* < 0.001), and 2.7 ± 1.2 (*P* < 0.001), respectively (Table S2, Supplemental Digital Content 1, http://links.lww.com/IJG/A399; Fig. 2).

The best-corrected logMAR visual acuities preoperatively and at 1 week, and 1, 3, 6, and 12 months postoperatively were 0.28 ± 0.36, 0.42 ± 0.37 (*P* < 0.001), 0.41 ± 0.39 (*P* < 0.001), 0.31 ± 0.34 (*P* = 0.191), 0.31 ± 0.35 (*P* = 0.113), and 0.33 ± 0.37 (*P* = 0.074), respectively.

The mean ± SD values of steep/flat anterior and posterior keratometry, and anterior/posterior astigmatism preoperatively, and at 1 week, and 1, 3, 6, and 12 months postoperatively are presented in Table S3 (Supplemental Digital Content 1, http://links.lww.com/IJG/A399; Figs. 3–5).

The mean ± SD values of central and minimal corneal thickness preoperatively and at 1 week, and 1, 3, 6, and 12 months postoperatively are presented in Table S4 (Supplemental Digital Content 1, http://links.lww.com/IJG/A399; Fig. 6).

The mean ± SD values of steep astigmatism axis preoperatively and at 1 week, and 1, 3, 6, and 12 months postoperatively were 74.56 ± 38.56 degrees, 90.28 ± 33.48 degrees (*P* = 0.002), 90.67 ± 36.06 degrees (*P* = 0.006), 87.05 ± 42.05 degrees (*P* = 0.076), 80.87 ± 36.68 degrees (*P* = 0.187), and 81.15 ± 41.06 degrees (*P* = 0.465), respectively (Table S4, Supplemental Digital Content 1, http://links.lww.com/IJG/A399; Fig. 7).

A significant difference in corneal parameters was noted immediately after UCP. However, after 3 months, the parameters returned to their initial values and no significant
differences were noted compared with the baseline (Fig. 8; Table S3, Supplemental Digital Content 1, http://links.lww.com/IJG/A399). Central corneal thickness and minimal corneal thickness remained unchanged, whereas the astigmatism axis tended to approach 90-degree meridian immediately after surgery, with a significant difference only at 1 week postoperatively (Table S4, Supplemental Digital Content 1, http://links.lww.com/IJG/A399). The decrease in IOP and the number of antiglaucoma medications was statistically significant (Table S2, Supplemental Digital Content 1, http://links.lww.com/IJG/A399). The best-corrected logMAR visual acuity remained unchanged, at 1 month postoperatively.

DISCUSSION

Currently the only effective, proven method for glaucoma control is IOP reduction.1,2 This can be achieved by restricting aqueous humor production and/or improving its outflow, pharmacologically, and surgically. The aqueous humor production can be reduced by partially damaging the nonpigmented epithelium of the ciliary body using laser photocoagulation, cryotherapy, or ultrasound energy. The most common and effective method for this type of procedure is transscleral cyclophotocoagulation (TSCP). TSCP is mainly used in severe forms of refractory glaucoma, when previous pharmacological or surgical treatments (filtration or seton) have failed.3 The 2 main disadvantages of cyclo-destruction are limited selectivity of the target tissue, often causing damage to the adjacent structures (eg, laser energy is primarily absorbed by pigmented tissues, which can damage the iris or choroid), and the difficulty in predicting the dose-effect relationship. Further, the most common complications of TSCP are intraoperative and postoperative pain, conjunctival burn, scleral thinning, or uveitis.4–7 Rare, but more serious, complications are hypotension, choroidal detachment, choroiditis, retinal detachment, or extremely rare phthisis bulbi.8 Endoscopic cyclodestruction is safer and more selective than TSCP.9,10 However, it is an invasive procedure and is recommended in mild or moderate glaucoma for patients undergoing cataract surgery.11,12 This procedure also has side effects; the most common ones are IOP spikes, increased inflammation (compared with that in phacoemulsification without endoscopic cyclodestruction), or dislocation of the intraocular lens.13–14

The main advantage of high-intensity focused ultrasound technology, which is used in UCP through a specially designed probe, in comparison with the commonly used diode laser cyclodestruction, is the possibility of precise energy concentration through opaque structures, without uncontrolled absorption at the desired depth and the ciliary body area with less pain.15 As a result, it reduces the damage to the adjacent tissues because the amount of heat delivered to the tissue is independent of its properties, such as pigmentation (which in the case of the ciliary body may vary individually).16–18 Despite these advantages, the exact influence of the ultrasound energy on the conjunctival, scleral, and indirectly on the corneal tissues is still unknown.

The effect on the sclera in the proximity of the limbus may affect corneal topography and visual acuity. We aimed to assess the values of keratometry, astigmatism, and corneal thickness after UCP. The results showed a significant

FIGURE 3. Anterior keratometry after ultrasound ciliary plasty, 12-month follow-up.

FIGURE 4. Astigmatism after ultrasound ciliary plasty, 12-month follow-up.
FIGURE 5. Posterior keratometry after ultrasound ciliary plasty, 12-month follow-up.

FIGURE 6. Corneal thickness after ultrasound ciliary plasty, 12-month follow-up.

FIGURE 7. Steep astigmatism axis after ultrasound ciliary plasty, 12-month follow-up.

FIGURE 8. Corneal map one of the patient preoperatively (A), at 1 week (B), 1 (C), 3 (D), 6 (E), and 12 months (F) after ultrasound ciliary plasty, 12-month follow-up.
change in the values of anterior/posterior and steep/flat keratometry, and anterior/posterior astigmatism for 3 months postoperatively. The largest difference between preoperative and postoperative values in keratometry and astigmatism was observed 1 week postoperatively. However, 6 months postoperatively and later, all parameters returned to the initial values, with no lasting changes detected in any of the measurements. The astigmatism axis showed a tendency to approach 90-degree meridian immediately after the surgery. With time, the values returned to baseline. Central corneal thickness and minimal corneal thickness remained unchanged during the follow-up period, with no significant differences. We considered all these changes to be related to the area of ultrasound energy application during the procedure. The ultrasound probe has 6 transducers placed radially at regular intervals on the superior and inferior circumference, avoiding the nasal and temporal meridian. Therefore, slightly more energy is applied and concentrated in the superior and inferior quadrants. Probable focal scleral shrinkage19 of tissues superiorly and inferiorly causes a steeper curvature of the cornea in that meridian.

Several studies have reported on the influence of ultrasound energy on the sclera.20–24 Mastropasqua and colleagues assessed the alternative outflow of aqueous humor through the uveoscleral pathway after UCP. A scleral cyst was reported in the area where the ultrasound energy was applied. The authors hypothesized that heat induces scleral fiber delamination. Other studies have reported the appearance of scleral marks after UCP in the area of ultrasound energy application.21–24 However, these studies evaluated only the efficiency of the procedure and did not further examine the reason for the occurrence of scleral marks. Histologically, scleral marks are described as rearrangement of the collagen tissue, which results in a denser structure.19 Considering the different types of cyclodestructive methods, like TSCP, limited studies have investigated the influence of thermal energy on the sclera. One study reported no injury,25 whereas 2 studies reported transient scleral trauma.26,27 Recently, Consejo and Rozema28 proved that the shape of the sclera influenced the occurrence of astigmatism. A review on the influence of cyclodestructive procedures on corneal topography revealed only 2 studies each, on UCP and TSCP. Both studies on UCP reported surgically induced astigmatism (SIA) only when it exceeded > 1 D. The results revealed that SIA occurred in 1/3023 and 2/73 patients (2.7%),22 but it was transient. The first TSCP study reported the occurrence of persistent SIA of 0.83 ± 0.69 D, 2-3 years postoperatively.29 Conversely, the second study reported that corneal topography was not influenced by the procedure.30 All 4 studies presented SIA as the only examined parameter, without a more detailed assessment of corneal parameters. A difference between our results and the 2 reports on SIA after UCP may appear apparent, with a predominance of astigmatism occurrence. However, our study used different assumptions to examine corneal parameters by presenting them more accurately and not excluding an SIA < 1 D; therefore, a direct comparison is impractical. Furthermore, a study conducted by Deb-Joardar and Reddy22 did not specify the time of occurrence of SIA after UCP, and only mentioned that the SIA was transient. Aptel et al.23 reported that SIA > 1 D occurred in a patient 1 month postoperatively. Nevertheless, SIA > 1 D occurred in 41.0% of our patients, 1 month postoperatively. In a meta-analysis on UCP,25 the author suspected that induced astigmatism and pupil irregularities were uncertain but may be related to cases where the ultrasound probe was too close to the limbus. However, another study reported that pupil irregularities after UCP are unrelated to the method of treatment, and are related to the individual and to the somewhat unpredictable response to the procedure.22 We performed UCP with utmost attention to cone centration; hence, in our opinion this cause is unlikely. In addition, we analyzed images of the eye with visible scleral marks and found that they were usually equidistant from the limbus. We suggest that it was more likely that the induced astigmatism was an effect of energy distribution that led to scleral shrinkage and further caused the change in the astigmatism axis, and the occurrence of scleral marks. However further analysis is required to confirm this.

The decrease in IOP and the number of antiglaucoma medications was statistically significant at each follow-up time point. The mean IOP at the last follow-up was reduced by 28.5%, which is similar to other studies.21–23,33 A significant difference was noted in visual acuity, 1 week, and 1 month postoperatively; however, the long-acting mydriatics used postoperatively might have accounted for this.

The present study had some limitations. The sample size was relatively small and heterogenous. However, we did not observe any discrepancy in the IOP reduction or corneal parameters, considering previous glaucoma treatments or types of glaucoma. Some patients had previous cyclodestructive procedures, which could have influenced the IOP. However, there was no difference in the IOP reduction in these patients as compared with those without previous cyclodestructive glaucoma surgery. A long-term study with a larger sample is needed to confirm our results.

Despite assuming that the energy applied to the neighboring tissue in UCP is less, the present study suggested that this type of cyclodestructive method influenced the sclera and indirectly, the cornea; however, the effect was transient. The clinician must be aware that increasing astigmatism during the first 3 months postoperatively may affect visual acuity and the patient should be informed of this possibility. UCP is safe and well-tolerated to reduce IOP in patients with refractory glaucoma, and can help in halting the process of vision loss.

In conclusion, UCP affects corneal topography immediately postoperatively; however, with time, all parameters return to their initial values.

REFERENCES

1. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002;120:701–713.
2. Heijl A, Leske MC, Bengtsson B, et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol. 2002;120:1268–1279.
3. Jankowska-Szmul J, Dobrowski D, Wylegala E. CO2 laser-assisted sclerectomy surgery compared with trabeculectomy in primary open-angle glaucoma and exfoliative glaucoma. A 1-year follow-up. Acta Ophthalmol. 2018;96:e582–e591.
4. Vernon SA, Koppens JM, Menon GJ, et al. Diode laser cyclolysis in adult glaucoma: long-term results of a standard protocol and review of current literature. Clin Exp Ophthalmol. 2006;34:411–420.
5. Walland MJ. Diode laser cyclophotocoagulation: longer term follow up of a standardized treatment protocol. Clin Exp Ophthalmol. 2000;28:263–267.
6. Frazzotti P, Mittica V, Martone G, et al. Long-term follow-up of diode laser transscleral cyclophotocoagulation in the treatment of refractory glaucoma. Acta Ophthalmol. 2010;88:150–155.
7. Pucci V, Tappainer F, Borin S, et al. Long-term follow-up after transscleral diode laser photoacoagulation in refractory glaucoma. Ophthalmologica. 2003;217:279–283.
9. Pantcheva MB, Kahook MY, Schuman JS, et al. Comparison of acute structural and histopathological changes in human autopsy eyes after endoscopic cyclophotocoagulation and trans-scleral cyclophotocoagulation. *Br J Ophthalmol*. 2007;91:248–252.

10. Lin SC, Chen MJ, Lin MS, et al. Vascular effects on ciliary tissue from endoscopic versus trans-scleral cyclophotocoagulation. *Br J Ophthalmol*. 2006;90:496–500.

11. Berke S, Cohen A, Sturm R, et al. Endoscopic cyclophotocoagulation (Ecp) and phacoemulsification in the treatment of medically controlled primary open-angle glaucoma. *J Glaucoma*. 2000;9:129.

12. Siegel MJ, Boling WS, Faridi OS, et al. Combined endoscopic cyclophotocoagulation and phacoemulsification versus phacoemulsification alone in the treatment of mild to moderate glaucoma. *Clin Exp Ophthalmol*. 2013;45:531–539.

13. Noecker RJ. ECP Collaborative Study Group. Complications of endoscopic cyclophotocoagulation. ASCRS Symposium on Cataract, IOL and Refractive Surgery, San Diego, CA; 2007.

14. Noecker RJ. Transscleral diode laser cyclophotocoagulation on autopsy eyes with abnormally thinned sclera. *Ophthalmic Surg Lasers*. 2007;38:266–272.

15. Aptel F, Charrel T, Birer A, et al. Development of a miniaturized high-intensity focused ultrasound device in patients with glaucoma: a clinical pilot study. *Investig Ophthalmol Vis Sci*. 2011;52:8747–8753.

16. Aptel F, Charrel T, Paluzzi X, et al. Histologic effects of a new device for high-intensity focused ultrasound cyclocoagulation. *Investig Ophthalmol Vis Sci*. 2010;51:5992–5998.

17. Charrel T, Aptel F, Birer A, et al. Development of a miniaturized HIFU device for glaucoma treatment with conformal coagulation of the ciliary bodies. *Ultrasound Med Biol*. 2011;37:742–754.

18. Aptel F, Lafon C. Therapeutic applications of ultrasound in ophthalmology. *Int J Hyperthermia*. 2012;28:405–418.

19. Lim KS. Ultrasound cycloplasty in glaucoma – mechanisms of action and their possible impact on intraocular pressure. *Eur Ophthalmic Rev*. 2017;11:35–39.

20. Mastrospasqua R, Agniffili L, Fasanella V, et al. Uveo-scleral outflow pathways after ultrasonic cyclocoagulation in refractory glaucoma: an anterior segment optical coherence tomography and in vivo confocal study. *Br J Ophthalmol*. 2016;100:1668–1675.

21. Denis P, Aptel F, Rouland JF, et al. Cyclocoagulation of the ciliary bodies by high-intensity focused ultrasound: a 12-month multicenter study. *Investig Ophthalmol Vis Sci*. 2015;56:1089–1096.

22. Deb-Joardar N, Reddy K. Application of high intensity focused ultrasound for treatment of open-angle glaucoma in Indian patients. *Indian J Ophthalmol*. 2018;66:517–523.

23. Aptel F, Denis P, Rouland JF, et al. Multicenter clinical trial of high-intensity focused ultrasound treatment in glaucoma patients without previous filtering surgery. *Acta Ophthalmol*. 2016;94:e268–e277.

24. Aptel F, Dupuy C, Rouland JF. Treatment of refractory open-angle glaucoma using ultrasonic circular cyclocoagulation: a prospective case series. *Curr Med Res Opin*. 2014;30:1599–1605.

25. Palmer DJ, Cohen J, Torczynski E, et al. Transscleral diode laser cyclophotocoagulation on autopsy eyes with abnormally thinned sclera. *Ophthalmic Surg Lasers*. 1997;28:495–500.

26. Coleman AL, Jampel HD, Javitt JC, et al. Transscleral cyclophotocoagulation of human autopsy and monkey eyes. *Ophthalmic Surg*. 1991;22:638–643.

27. Ferry AP. Histopathologic observations on human eyes following cyclocryotherapy for glaucoma. *Trans Am Acad Ophthalmol Otolaryngol*. 1977;83:315–336.

28. Consejo A, Rozema JJ. Scleral shape and its correlations with corneal astigmatism. *Cornea*. 2018;37:1047–1052.

29. Hasan S, Theilig T, Unterlauft JD. Comparing the efficacy of trabeculectomy and diode laser cyclophotocoagulation in primary open-angle glaucoma. *Int Ophthalmol*. 2019;39:2485–2496.

30. Arikian G, Yaman A, Ozbek Z, et al. Effect of diode laser cyclophotocoagulation on the anterior segment: an Orbscan study. *Cornea*. 2008;27:152–155.

31. Denis P. Clinical research of ultrasound ciliary plasty and implications for clinical practice. *Eur Ophthalmic Rev*. 2016;10:108–112.

32. Sousa DC, Ferreira NP, Marques-Neves C, et al. High-intensity focused ultrasound cycloplasty: analysis of pupil dynamics. *J Curr Glaucoma Pract*. 2018;12:102–106.

33. Giannaccare G, Vagge A, Sebastiani S, et al. Ultrasound cycloplasty in patients with glaucoma: 1-year results from a multicentre prospective study. *Ophthalmic Res*. 2019;61:137–142.