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Original Article

Long-Term Structural Changes Observed on Gonioscopy and Anterior-Segment OCT Following Gonioscopy-Assisted Transluminal Trabeculotomy

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Abstract

Objectives: To evaluate the long-term structural changes of the anterior chamber (AC) angle following gonioscopy-assisted transluminal trabeculotomy (GATT).

Methods: The AC angle of 10 eyes that underwent GATT at least 6 years previously was assessed for structural changes. A detailed gonioscopy was performed to determine the state of the cleft and the position of the trabecular flap. An anterior segment optical coherence tomography (AS-OCT) examination was performed on the corresponding areas on gonioscopy.

Results: The typical finding of the angle following GATT was an open cleft with a visible trabecular flap. However, the gonioscopy of our patients revealed three different cleft appearances: open, closed, and segmentally open cleft. In the long-term, the trabecular flap re-approximated the incision site in some areas resulting in the appearance of a closed cleft on gonioscopy. On AS-OCT the cleft was identified when the lumen of Schlemm's canal was connected to the AC, while the position of the flap differed. The cleft was observed as open in median 4.0 (IQR: 2.8–6.0) clock hours. The cleft was found open mostly in the superior quadrants of the angle (nine eyes). No correlation was found between the extent of open cleft and the percentage of IOP reduction.

Conclusion: AS-OCT, when used in conjunction with gonioscopy, was found helpful to evaluate the structural changes following GATT. As observed in the study, the cleft tended to close in some areas. It was found preserved mostly in the superior half of the angle in the long term.

Keywords: Anterior chamber angle, anterior segment optical coherence tomography, gonioscopy, gonioscopy-assisted transluminal trabeculotomy, structural changes

Introduction

Gonioscopy-assisted transluminal trabeculotomy (GATT), first described by Grover et al. in 2014, (1) has been increasingly preferred among a variety of minimally invasive glaucoma surgery methods by glaucoma surgeons. Long before GATT surgery, 360° suture trabeculotomy has been used and proven to be effective in the surgical treatment of primary and secondary open-angle glaucoma (2-4). Although, in their initial study Grover et al. used an illuminated microcatheter to cannulate the Schlemm's canal (SC), (1) they modified the

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technique later and used a 4-0 or 5-0 nylon suture, (5) and a 6-0 or 5-0 prolene suture in their further studies (6).

It is well known that the most important mechanism for IOP rise in glaucoma is the resistance to aqueous outflow built at the level of trabecular meshwork (TM), specifically at the juxtacanalicular meshwork (7). Both in suture trabeculotomy and in GATT the aim is to cleave the TM, thereby exposing the lumen of the SC directly into the anterior chamber (AC) and eliminating the resistance of the inner wall.

Previously, gonioscopic findings following GATT were described by Grover et al. (1) They named the cleaved trabecular tissue as a trabecular shelf, that is typically seen on gonioscopy as a leaflet of trabecular tissue protruding over the peripheral iris. Although currently numerous studies on the clinical results after GATT surgery are available, (8-10) scarce data exist elucidating the structural changes occurring in the AC angle. The condition of the cleft and trabecular flap (trabecular shelf) is particularly important in the long term, as tissue healing and remodeling are expected to occur over time. It has been recently demonstrated that the trabecular shelf, which represents the cleaved TM, and the SC could be clearly identified on an anterior segment optical coherence tomography (AS-OCT) after GATT surgery (11). In this study, we aimed to evaluate the long-term structural changes in the AC angle of patients who underwent GATT at least 6 years ago using gonioscopy and AS-OCT.

Methods

In this cross-sectional study, we performed a thorough ophthalmological examination including gonioscopy and AS-OCT on 10 patients who underwent GATT surgery at least 6 years ago and who were on routine follow-up in the glaucoma clinic of a tertiary eye hospital. An institutional review board approval was obtained to conduct the study (Date: November 30, 2022, No: 65/E-1). Each patient was informed about the risks and benefits of the procedure and a written informed consent was obtained. The study protocol adhered to the tenets of the Declaration of Helsinki.

GATT procedure was performed by a single surgeon (EB) between December 2015 and May 2016 as described previously by Grover et al. (6) At the time of examination, all patients had their best-corrected visual acuity on the Snellen chart, biomicroscopic anterior segment examination, intraocular pressure (IOP) measurement by Goldmann applanation tonometry, indirect fundoscopic examination by 90D lens, and gonioscopic examination using Latina SLT gonio lens (Ocular Instruments, Washington, USA). Additional information about the demographics of the patient, pre-operative data, operation notes, and early post-operative data were recorded from the patient's charts.

Gonioscopy was performed in dark room conditions and by applying a viscoelastic coupling agent to the lens. To define the location, the findings were noted based on four quadrants as nasal, superior, temporal, and inferior. To define the extent, each quadrant was divided into 3 clock hours, thus making a total of 12 clock hours for the circumferential examination. On gonioscopy, observing the cleft created by GATT was defined as open, and in the areas where the cleft was not identified, it was categorized as closed. The location was determined by the four quadrants and the extent as clock hours. In addition, the presence of peripheral anterior synechia (PAS) was also noted.

Anterior segment OCT was performed to image the AC angle structures using the anterior segment module of the Topcon DRI-Triton (Topcon, Tokyo, Japan, 2015) swept-source OCT device (wavelength of the laser of 1050 nm). Images were obtained with 3 mm line-scanning mode (100.000 A-scan images/s). The orientation of the scan line was modified to become perpendicular to the scanned limbus. Each eye was scanned at eight different locations (nasal, superonasal, superior, superotemporal, temporal, inferotemporal, inferior, and inferonasal). For visualization of the corneoscleral limbal area on AS-OCT, the patient was asked to fixate on the opposite side of the scanned limbus. That is, the eye was fixed nasally to visualize the temporal limbus, the eye was fixed inferiorly to visualize the superior limbus, and so on.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) software (version 23; SPSS Inc., Chicago, IL, USA) was used for the data analysis. Categorical variables were expressed as % (number) and continuous variables as median (interquartile rate). The Wilcoxon signed-rank test was used to compare the differences between pre-operative and post-operative values. The relationship between continuous data was evaluated by the Spearman correlation test. A $p<0.05$ was statistically significant.

Results

Ten eyes of 10 patients were included in the study. The demographic features of the patients and both pre-operative and final clinical data are displayed in Table 1. The median follow-up was 78.0 months (IQR: 75.0–78.2). Five eyes underwent 360° GATT whereas five eyes underwent hemi-GATT (120–270°). The surgery of five of the cases was combined with phaco (Table 1). In the post-operative period, only one eye of patient #6 underwent cataract surgery 5 years after the GATT procedure. The median pre-operative IOP decreased from 22.0 (IQR: 16.8–27.0) mmHg to 13.0 (IQR: 11.5–14.3) mmHg at the final visit ($p<0.001$) and median antiglaucoma medication decreased from 4.0 (IQR: 4.0–5.0) to 0.0 (IQR: 0.0–3.3) at final visit ($p<0.001$). During the follow-up, one

Table 1. The demographic features and clinical data of the patients

S. No.	Age (year), Sex, Eye	Glaucoma type, C/D	Pre-operative IOP (mmHg)	Pre-operative Medication	Surgery	Final IOP (mmHg)	Final Medication	Final open cleft (CH) on gonioscopy	Cleft location (quadrant)	PAS (location)	Blood reflux
1	73, F, L	PEX, 1.0	18	4	Phaco+ Superior 120 GATT	12	0	3	N, S	-	-
2	65, M, R	POAG, 0.8	20	3	360 GATT	13	2	9	N, S, T	S-PAS (IN)	+
3	63, M, L	POAG, 0.9	30	4	360 GATT	10	4	6	N, S	S-PAS (I)	+
4	66, M, R	Post-vitrectomy, 0.4	26	5	Superior 270 GATT	14	3	4	N, S	-	-
5	74, F, R	POAG, 0.9	25	5	Phaco+ Superior 180 GATT TRAB	14	4	4	SN, ST	-	+
6	30, M, L	Post-vitrectomy, 0.8	40	4	360 GATT	16	0	3	SN, ST	-	+
7	30, M, R	Juvenile, 0.9	17	4	360 GATT	8	0	5	SN, ST, N	B-PAS (T), S-PAS (S)	-
8	69, M, R	PEX, 0.9	20	4	Phaco+ Superior 180 GATT	10	0	2	SN	S-PAS (ST)	+
9	47, M, L	POAG, 1.0	24	5	Phaco+ 360 GATT	13	0	2	N	S-PAS (I)	-
10	72, M, R	PEX, 0.5	20	4	Phaco+ Superior 180 GATT	15	0	4	SN, S	-	-

C/D: Cup-to-disc ratio; CH: Clock hours; S-PAS: Small-based peripheral anterior synechia; B-PAS: Broad-based peripheral anterior synechia; N: Nasal angle; S: Superior angle; T: Temporal angle; I: Inferior angle.

of the eyes (patient #5) required further glaucoma surgery (trabeculectomy) to lower the IOP 4 years after GATT surgery. The median of IOP reduction from baseline is 46.0% (IQR: 23.4–54.7%). At the final follow-up, the success rate was 60.0% without medication and 90.0% with medication.

Gonioscopy and AS-OCT Findings

Gonioscopy of our patients revealed three different appearances of the cleft in the areas of trabeculotomy: (1) cleft being open; (2) cleft being closed; and (3) cleft being segmentally open. We further detailed the gonioscopic findings with the corresponding AS-OCT images as follows:

1. The typical gonioscopic finding following the GATT procedure was a wide-open cleft that was accompanied by a visible trabecular flap (Figs. 1a and b). The trabecular flap was clearly demonstrated on the corresponding AS-OCT image (Figs. 1c and d). On the other hand, the trabecular flap could not be identified in all areas where the cleft appeared open on gonioscopy (Figs. 2a-c). AS-OCT examination performed on the same areas revealed either a small, rounded trabecular flap that was undetectable on gonioscopy (only the SC appeared as an indented line on gonioscopy) (Figs. 2a and d) or a flap that was attached to the peripheral iris (Figs. 2b and e), or the flap was totally absent (Figs. 2c and f)
2. When the cleft appeared closed on gonioscopy, mostly no signs of trabeculotomy could be identified and the angle structures appeared as normal (Fig. 3). However, in some patients the closed cleft areas were accompanied by irregular hyperpigmentation (Figs. 4a-f), while small-based multiple PAS also coexisted in some areas (Figs. 3a and 4d). The corresponding image on AS-OCT showed either a near-total (Figs. 4b and c) or total re-approximation of the TM flap (Figs. 3c, 4e, and f). In some of the areas with closed cleft, the SC could not be identified on AS-OCT (Fig.3d) and in some SC was visible as being widely expanded (Figs. 4e and f)
3. Some areas of the angle showed segmental opening of the cleft on gonioscopy where short open cleft segments interchanged with closed cleft segments (Figs. 5a and b). AS-OCT images differed according to the segments scanned with an open or closed cleft (Figs. 5c-e).

The gonioscopic findings were analyzed as the cleft being open (both totally open and segmentally open) or closed. In the whole population, the cleft was observed as open in a median of 4.0 clock hours (IQR: 2.8–6.0). The median cleft opening in the eyes that had 360° GATT (five eyes) was 5.0 clock hours (IQR: 2.0–7.5) and in eyes that had hemi-GATT (five eyes) was 4.0 clock hours (IQR: 3.0–5.0). In most of the cases (nine eyes) the cleft was observed as open in the superior half of the angle (superior and supero-nasal), and in none of the eyes, the cleft could be identified in the inferior

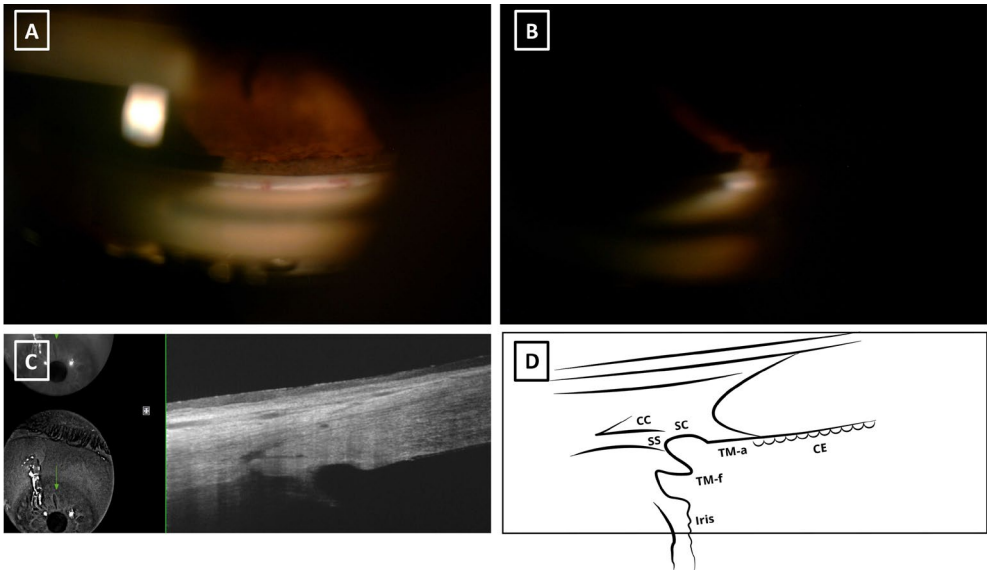

Figure 1. The typical angle finding following GATT. An open SC and a well-demarcated trabecular flap are visible on the gonioscopy viewing the superior quadrant of patient 2 **(a)**. The trabecular flap is better visualized by a slit light on the gonioscopy **(b)**. The corresponding AS-OCT image of the superior limbus **(c)**. The SC lumen is seen to be exposed to the AC and the trabecular flap is hinged to the scleral spur **(c)**. A drawing demonstrating the same structures as seen on the AS-OCT image in Figure 1c **(d)**. AC: Anterior chamber, AS-OCT: Anterior segment optical coherence tomography, CC: Collector channel, SC: Schlemm's canal, CE: corneal endothelium, SS: Scleral spur, TM-f: trabecular flap, TM-a: anterior non-pigmented trabecular meshwork.

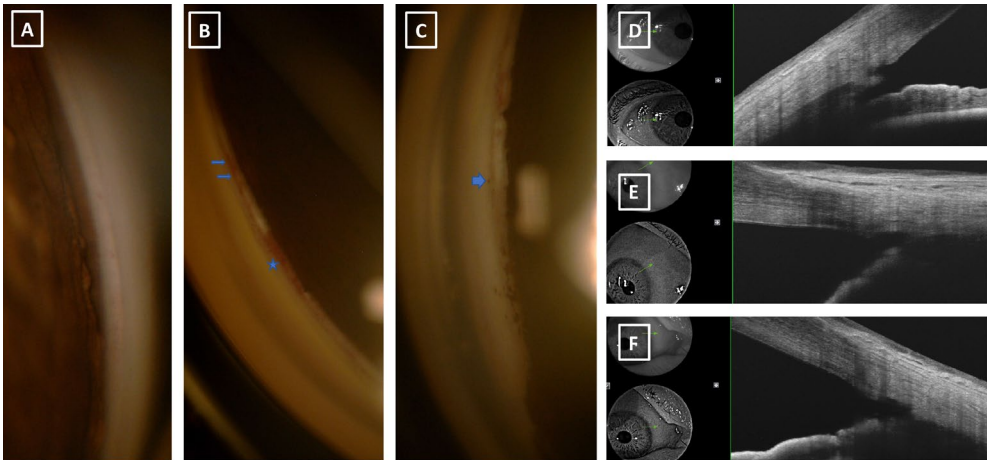

Figure 2. Examples of gonioscopic view of the angle where the cleft appears open, however, the trabecular flap cannot be identified **(a-c)**. The angle view of the temporal quadrant of patient 2. The SC appears as an indented line and the trabecular flap is not visible **(a)**. The angle view of supero-nasal quadrant of patient 8. The cleft appears wide-open, no flap is visible and blood reflux into the canal is visible as large spots (asterisk) and small dots (arrows) **(b)**. The nasal quadrant of the same patient (patient 8, superior 180° GATT on the right eye) demonstrates the beginning of the goniotomy incision (arrow) **(c)**. A small and rounded trabecular flap is seen on the corresponding AS-OCT image of the angle in Figure 2a **(d)**. The trabecular flap is seen attached to the peripheral iris on the corresponding AS-OCT image of the angle in Figure 2b **(e)**. The trabecular flap is absent on the corresponding AS-OCT image of the angle in Figure 2c **(f)**. In all images, the SC is connected to the AC. AC: anterior chamber, AS-OCT: anterior segment optical coherence tomography, SC: Schlemm's canal.

quadrant (Table 1). No correlation was present between the extent of the open cleft and final IOP (p=0.73) or the percentage of IOP reduction (p=0.47).

Other Findings Observed on Gonioscopy

PAS were noted as small-based structures on the angle of five of the eyes. The multiple small PAS (Figs. 3a, 4d, 6) were observed mostly in the quadrants of the closed cleft (Table 1). Furthermore, blood reflux into the SC was identified during gonioscopy as small dots and larger spots through the open cleft in five of the eyes (Table 1, Figs. 1a and 2b).

Discussion

A circumferential slit opening (cleft) in the TM and the inner wall of SC is created by trabeculotomy surgery (1,12). This cleft permits direct communication between the AC and the SC which gives the accessibility for aqueous directly into the collector channels. Following GATT, a flap of TM tissue is formed that is hinged at the scleral spur level (1). This flap was termed as "trabecular shelf" which is easily observed on gonioscopic examination as a leaflet that protrudes from the spur (Fig. 1) When the inner wall of the SC is cleaved, the resistance to aqueous flow is eliminated to an important extent which results in increased conventional outflow after trabeculotomy (13). In perfusion studies of ex vivo human eyes, it has been demonstrated that 75% of the resistance was eliminated in normal eyes after the removal of the TM (7).

Previously, animal studies showed that the trabeculotomy area in monkey eyes was repaired within a few months after the surgery and no communication between the SC and the AC was found at 1 year (14,15). Although there are histological studies examining failed trabeculotomy segments, (16,17) there has not been yet any report on human subjects demonstrating the structural changes involving the whole circumference of the angle following GATT surgery. In this study, we aimed to evaluate the AC angle by gonioscopy and AS-OCT imaging and to demonstrate the alterations that have occurred in the long term.

The expected finding on gonioscopy following GATT is an open cleft and a visible trabecular shelf (Fig. 1). However, on gonioscopy and AS-OCT examination of our patients, we observed different findings apart from the typical appearance of the post-surgery angle. The cleft, when observed as open, was not always accompanied by a visible trabecular shelf on

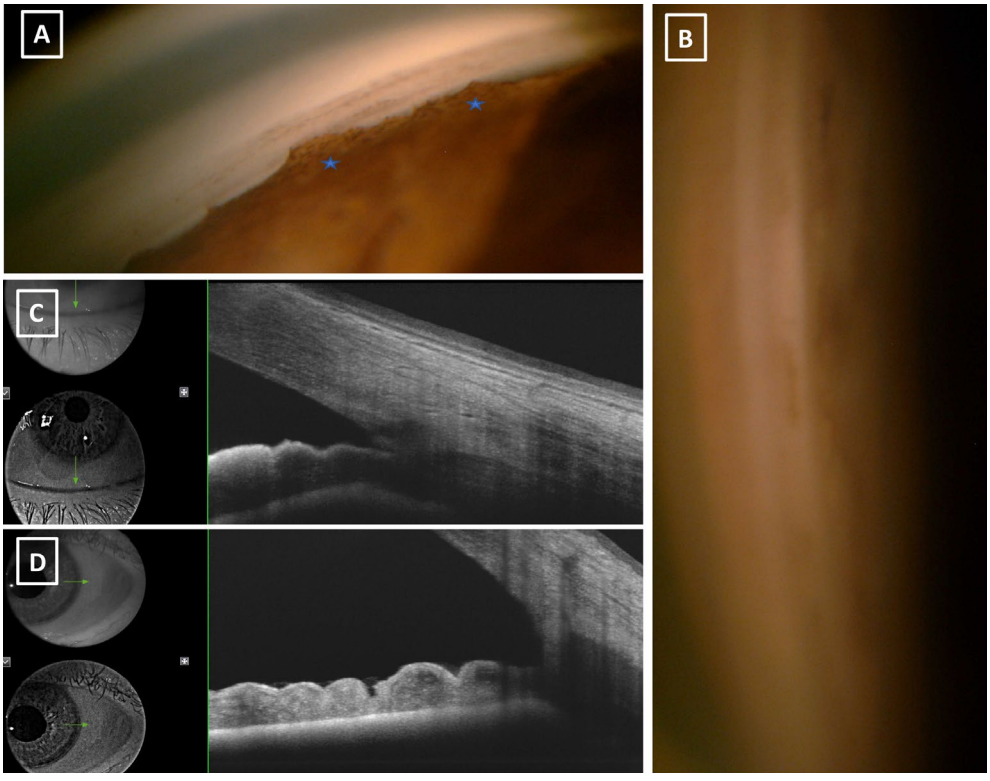

Figure 3. Gonioscopic appearance of the closed cleft **(a and b)**. The angle appears normal without any sign of trabeculotomy. Small peripheral anterior synechiae (asterisk) are visible on the inferior angle of Patient 2 **(a)**. The corresponding AS-OCT image of the angle is in Figure 3a **(c)**. The flap is seen as apposed and the SC is visible. The cleft is observed as closed in the gonioscopy of the temporal angle of patient 3 **(b)**. On the corresponding AS-OCT image, the SC and the flap cannot be identified **(d)**. AC: anterior chamber, AS-OCT: anterior segment optical coherence tomography, SC: Schlemm's canal.

the gonioscopy (Fig. 2). In parallel with our findings, histologic studies demonstrated that the disconnected TM might show swelling or degeneration at the cut end, (17) which might be the reason for the small or the absent trabecular flap on gonioscopy. Rarely, a small segment of the trabecular flap might have been removed or peeled off during the surgery.

If on gonioscopy the cleft was seen as closed, the corresponding AS-OCT showed either a total or a near total re-approximated flap (Fig. 4). Histologically, reconnection or fusion of the TM to the incision site was demonstrated to occur following trabeculotomy, (17) and the healing process involved scarring by fibrosis or endothelial spread from the SC endothelium or rarely from corneal endothelium (16,17). In the present study, in some of the eyes the closed cleft was accompanied by an irregular and wide-spread hyperpigmentation (Fig. 4). In addition, PAS was mostly found also in the closed-cleft areas (Table 1). It is impossible to conclude from the study whether PAS or hyperpigmentation has a direct association to the reattachment of the flap and therefore to the closure of the cleft. However, invasion of melanocytes into the TM has been previously reported as one of the causes of failure in trabeculotomy (17).

The segmentally open cleft was evident as short segments of open cleft interchanged by short segments of closed cleft. The state of the cleft and the configuration of the flap on OCT differed depending on the segment scanned (Fig. 5). It was a frequent finding observed mostly in nasal and temporal quadrants in our series. On a standard gonioscopic examination, the segmentally open cleft is difficult to differentiate and therefore might be easily interpreted as being closed. However, as it is obvious on the AS-OCT images a communication between the AC and the SC lumen is present.

In our series, there was no case with a circumferential closure of the cleft and at least 2 clock hours opening was evident. Interestingly, the two patients (patient #8 and 9) with 2 clock hours opening were free of antiglaucoma medication at the final visit and the patient with failed GATT (patient #5) had 4 clock hours open cleft. Although in the current study, the sample size was small to conclude, no correlation could be demonstrated between the extent of the open cleft observed on gonioscopy and IOP reduction. Hamanaka et al. (16) could demonstrate that in the eyes with large openings in the TM, a failure of trabeculotomy might be observed due to closure of the lumen by endothelial cells, fibrotic tissue deposition around the canal, or shrinkage of the lumen of the SC. Nevertheless, they found that IOP reduction was significantly higher in the eyes with open-type

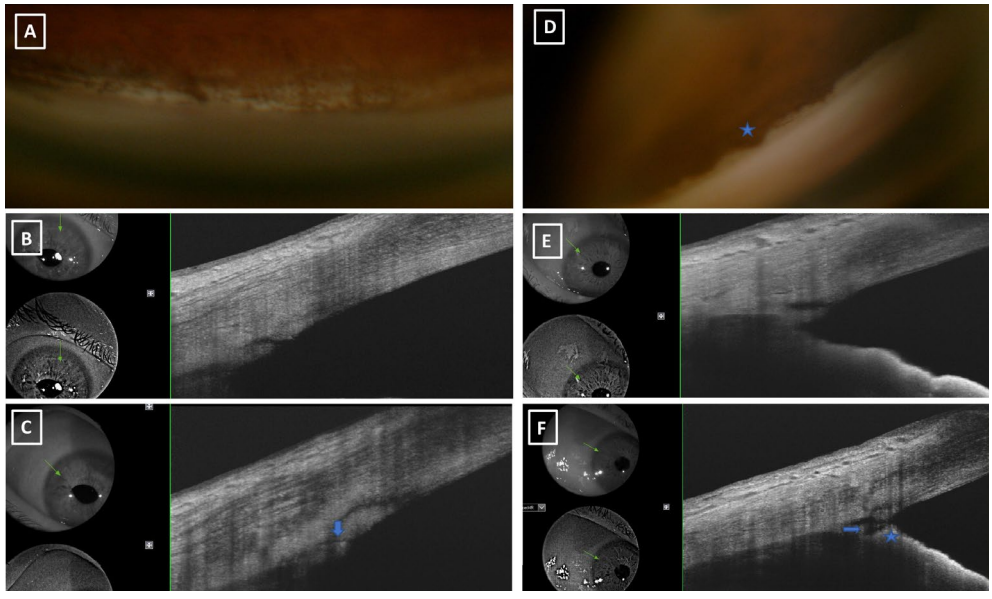

Figure 4. Gonioscopic view of the closed cleft that is accompanied by irregular hyperpigmentation of the superior angle of patient 4 **(a)** and the corresponding AS-OCT images of the superior limbus where the SC and the cleft are seen as a narrow slit-opening into the AC **(b)**. The slit is seen almost closed (arrow) on an image from a different section (supero-nasal limbus) **(c)**. Gonioscopic view of the supero-nasal angle of patient 8. Multiple peripheral anterior synechiae (asterisk) coexisted in the areas of closed cleft **(d)**. The trabecular flap is identified to re-approximate the cleavage line created by GATT on the corresponding AS-OCT. The SC is visible as expanded **(e)**. Another AS-OCT image from a section that involves a peripheral synechia (asterisk). The trabecular flap (arrow) that is sandwiched between the corneoscleral wall and the synechia is clearly identified **(f)**. AC: anterior chamber, AS-OCT: anterior segment optical coherence tomography, SC: Schlemm's canalç

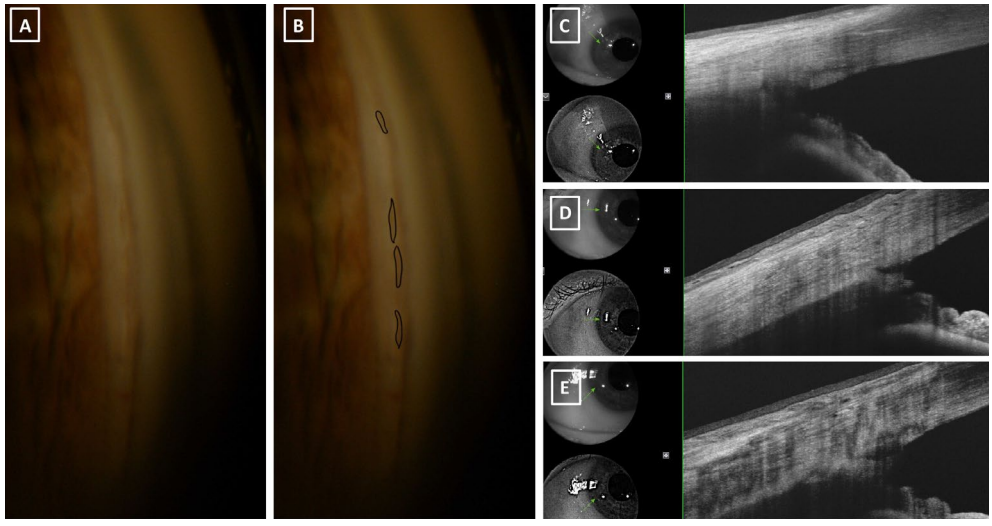

Figure 5. The gonioscopic appearance of the nasal quadrant in patient 3. A segmentally open cleft is seen in the photograph **(a and b)**. The black lines in Figure 1b are drawn to show the locations of the open segments of the cleft in Figure 1a. The AS-OCT images differed according to the segments scanned with an open **(d)** or closed cleft **(c and e)**.

TM opening than in the eyes with closed-type, thus concluding the importance of the accessibility of aqueous into the SC. Moreover, a well-functioning distal outflow system is required for success in trabeculotomy (18). It was demonstrated that in some cases of glaucoma eyes, the collector system and the intra-scleral plexus were narrower and even obliterated (19). The exact reason for the lack of correlation is yet to be clarified in further studies.

In our series, in the eyes that underwent 360 GATT, the cleft persisted specifically in the superior half of the angle, and in none of the eyes, the typical appearance of the trabecular shelf or the open cleft could be visualized in the inferior quadrant. The extent of the open cleft was found similar between hemi-and circumferential GATT, most probably because all the eyes that underwent hemi-GATT had their trabeculotomies performed in the superior angle, and the cleft in superior angle was preserved in contrast to the inferior angle where the flap mostly re-apposed and the cleft closed.

On OCT examination the TM flap was observed to be hinged at the scleral spur, which supports the previous observations that the cleavage line of TM is localized behind Schwalbe's line (1). In the superior quadrant when the cleft appears to be open, the trabecular flap is oriented from superior to inferior in a patient who stays in up-right position. However, in the inferior quadrant for the cleft to remain open the direction of the trabecular flap must be oriented from inferior to superior. It is not known how the trabecular flap behaves in response to gravity, however, in the inferior quadrant the TM flap was observed to be re-approximated to its original attachment site in all patients and the cleft appeared closed on gonioscopy. Another reason might be hyphema and hyphema-related inflammation that also involves the inferior quadrant in the early post-operative period.

The major limitation of the study was the small case number that limited us to conclude about the correlations between the extent of the open cleft and the IOP reduction. In addition, the heterogeneity of cases in the series (etiology and surgery) might have an impact on the clinical results. However, the primary aim of the study was to evaluate the structural changes of the AC angle in the long term, and examining the factors contributing to these changes was out of the scope of the study. For a better understanding of the structural alterations in the AC angle and showing their time course, prospective studies should be conducted involving also the early post-operative period.

Conclusion

AS-OCT was found helpful when used in conjunction with gonioscopy to determine the state of the cleft and the position of the trabecular shelf following GATT. The present study showed us that the trabecular cleft created by the GATT procedure tended to close in some areas of the angle in the long term. It was observed that the cleft was mostly preserved in the superior half of the angle, while the inferior quadrant was the one in which the flap re-approximated.

Disclosures

Ethics Committee Approval: An institutional review board approval was obtained to conduct the study (Date: November 30, 2022, No: 65/E-1).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Use of AI for Writing Assistance: Not declared.
Authorship Contributions: Concept – N.A., I.C., C.A., E.B., Z.I., E.E., T.Y.; Design – N.A., I.C., C.A., E.B., Z.I., E.E., T.Y.; Supervision – N.A., I.C., C.A., E.B., Z.I., E.E., T.Y.; Resource – N.A., I.C., C.A., E.B., T.Y.; Materials – N.A., E.B.; Data Collection and/or Processing – N.A., Z.I.; Analysis and/or Interpretation – N.A.; Literature Search – N.A.; Writing – N.A.; Critical Reviews – N.A., C.A., E.E., T.Y.

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