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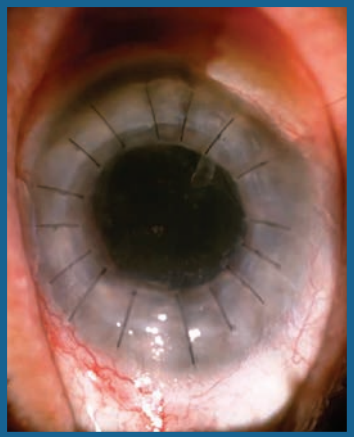

Autograft with clear cornea with tube *in situ*.

Volume 16 • Issue 4 • 2019 • 1560-2133

Asian Journal of OPHTHALMOLOGY

open access journal est. 1998

Asian Journal of
OPHTHALMOLOGY
open access journal est. 1998

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Publisher:
Kugler Publications,
P.O. Box 20538,
1001 NM Amsterdam,
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- To disseminate information that will improve the care of patients with all types of ophthalmological disorders, with a special focus on glaucoma.
- To increase the understanding of such disorders through reporting of educational activities.
- To publish the results of research programmes to expand knowledge about the causes, prevention, and treatment of ophthalmological disorders.
- To work closely with Asian and international researchers to achieve these aims.
- To provide a forum for young and relatively inexperienced researchers to present their research results as Original Articles via an international platform.
- To maintain and promote relationships with any organization with similar goals.

Although the focus of Asian Journal of Ophthalmology mainly was on glaucoma with close ties to the South-East Asian Glaucoma Interest Group (SEAGIG) in the past, the journal now focuses on the entire spectrum of Ophthalmology. This resulted in collaboration with the Asia Pacific Ophthalmic Trauma Society (APOTS).

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Asian J Ophthalmol. 2019;16:229-230

Diluting 5-fluorouracil with normal saline reduces patient discomfort

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5-Fluorouracil (5-FU) is an antimetabolite and is used to improve the success rate of trabeculectomies by inhibition of subconjunctival fibrosis. It can be administered postoperatively as a subconjunctival injection or given intraoperatively via cellulose sponge soaked in 5-FU and placed between the sclera and conjunctival flap. The advantage of injecting 5-FU subconjunctivally postoperatively is that the dose and frequency can be titrated according to patients' needs. Subconjunctival injection may be uncomfortable and this could be due to the alkaline nature of 5-FU (pH 9.20) and its osmolarity of 384 mmol/l. It would be beneficial if this discomfort can be minimised as the injection may need to be given several times.

A small study was performed to evaluate whether dilution of 5-FU with normal saline can improve discomfort. The cohort consisted of 31 patients who required subconjunctival 5-FU injection after trabeculectomy and needling of filtration bleb. They were given plain 0.2 ml 5-FU (50 mg/ml) on one occasion and diluted 5-FU (0.2 ml 5-FU and 0.2 ml normal saline) on another. Patients were administrated topical anaesthesia with Alcaine 0.5% (Proparacaine hydrochloride ophthalmic solution; Alcon, Fort Worth, TX, USA) and lignocaine 2% before the injection. The duration of the pain was recorded in seconds.

The average pain duration when plain 5-FU was administered subconjunctivally was 9.77 seconds, discomfort duration ranging from no pain to maximum pain lasted for 40 seconds. With diluted 5-FU, the average pain was 1.06 seconds, with discomfort duration ranging from no pain to maximum pain of 11 seconds among different patients. The average improvement of pain with the use of diluted 5-FU compared to plain 5-FU was 8.71 seconds.

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Three patients (9.7%) experienced no pain with both plain 5-FU and diluted 5-FU; 25 patients (80.6%) who had pain with plain 5-FU experienced no pain when 5-FU was diluted. Three patients (9.7%) experienced pain with both plain 5-FU and diluted 5-FU but had less pain with the use of diluted 5-FU.

This small study shows that the pain of subconjunctival 5-FU injection is reduced when 5-FU is diluted with normal saline. The pH was measured by pH paper and pH meter (Edge pH meter; HI2020 Hanna Instruments, Woonsocket, Rhode Island). The pH of plain 5-FU is 9.20 and that of normal saline is 8.32. When combined together, the pH of diluted 5-FU is 9.09.

Osmolarity of plain 5-FU is 384 mmol/l and osmolarity of normal saline is 286 mmol/l. When 5-FU is diluted 50% with normal saline, the resultant osmolarity should be 335 mmol/l. This value is closer to plasma osmolality of 295 mOsm/kg.

Hence, this study demonstrates that if patients complain of pain and discomfort with subconjunctival 5-FU injections, diluting 5-FU with normal saline (1:1) can reduce the discomfort.

Conflict of interest

There is no conflict of interest and no funding was received for this work.

Asian J Ophthalmol. 2019;16:231-241

A modified technique for trabeculectomy

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Abstract
Aim or purpose: *To present a modified technique of trabeculectomy.*
Design**:** *Ahmad's modified trabeculectomy technique aims to utilize subtle modifications to the classical trabeculectomy technique in order to achieve a better filtering bleb leading to lesser complications.*
Methods: *Retrospective interventional case series.*
Results: *Thirty-four patients underwent this surgery. There was a significant difference in the preoperative and postoperative median intraocular pressure (IOP; $z = 3.928$; $p < 0.001$). The postoperative IOP (median = 12) was significantly lower than the preoperative IOP (median = 28; interquartile range = 9).*
Conclusion: *This modification can prove to be an effective method to reduce IOP with minimal complications.*

Keywords: *endophthalmitis, filtering surgery, glaucoma, intraocular pressure, sclerostomy, trabeculectomy*

Introduction

Glaucoma is a multifactorial disorder with the common denominator of retinal ganglion cell loss. There are a number of theories, including the mechanical, vascular and biochemical ones, which attempt to explain the causation of this multi-spectrum disorder called glaucoma.[1] The only risk factor that can be modulated currently is intraocular pressure (IOP). Thus, IOP is often used as a surrogate treatment goal to assess the efficacy of any glaucoma management strategy.

Surgical management of glaucoma still lacks a reliable, reproducible, resilient, and robust procedures to maintain a stable IOP throughout the lifetime of the patient without any complications. Since its introduction in the 1960s, trabeculectomy has remained the gold standard of glaucoma filtering surgeries (GFS). Following trabeculectomy, long-term control of IOP has been found to range from 55% to 98%.[2] However, this procedure remains unpredictable, with results varying from patient to patient and even from case to case performed by the same surgeon.[3] It is also known that the more the risk factors for the procedure,

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the higher the cumulative effect on the outcome.[4] Other weaknesses of this procedure include the safety profile, complications such as short- and long-term risks of infection (endophthalmitis, blebitis), ocular hypotony, and others.[5-13] As with all operative procedures performed on an open eye, this procedure carries the risk of infection. However, coupled with a thin, vulnerable conjunctival bleb, the situation is made grimmer.[14] Not surprisingly, patients with cystic blebs carry a lifetime risk of bleb-related infections.[15] Looking at the shortcomings of trabeculectomy, the door has opened for novel surgeries to be explored and improved upon.

The key factor that determines the success of trabeculectomy is the characteristic of the filtering bleb. Since bleb-related complications usually influence the outcome of GFS, we have developed some modifications to the classical trabeculectomy procedure. Our method, Ahmad's modified trabeculectomy technique (AMTT), is aimed primarily at overcoming the problems of bleb leakage and poor quality of blebs.

AMTT does not attempt to radically change the classical trabeculectomy procedure. Our modifications can be performed by any surgeon adept in trabeculectomy. AMTT targets to achieve the "much desired diffuse, non-cystic bleb" by promoting posterior flow by making an innovative "spout" configuration in the sclerostomy, tight suturing of the scleral flap anteriorly, and better healing by leaving a cuff of conjunctiva near the limbus.[16]

Materials and methods

Inclusion criteria for this prospective study were patients above 14 years of age who were diagnosed to have glaucoma based on their visual field defects, optic disc changes, uncontrolled IOPs despite maximal tolerable medical therapy, retinal nerve fibre thickness changes, central corneal thickness values, and gonioscopic appearance. Patients who did not achieve the target IOP consistently or had progressive visual field changes on at least two consecutive examinations despite maximal medical treatment underwent trabeculectomy using the AMTT procedure.

Surgical technique

Aseptic precautions were taken prior to starting surgery. A corneal traction suture was often used to rotate the eye downwards in order to obtain a good surgical exposure of the field of surgery. Subsequently, a conjunctival flap was fashioned. Unlike the usual fornix-based flaps which are flush to the cornea, we start the peritomy about 0.5 mm posterior to the limbus, leaving a margin of conjunctiva there. Adequate haemostasis is achieved by using a bipolar cautery.

We routinely use mitomycin-C (Kyowa Hakko Kirin Co., Japan). The agent is diluted to a concentration of 0.02% solution. Subsequently, soaked gel sponges are applied to the episcleral tissues. The sponges are kept for 2 to 3 minutes, with the conjunctival flap blanketed over them by holding the edges away from the sponges. After 2 to 3 minutes, the sponges are removed and the area irrigated with nearly 20 ml of balanced salt solution (BSS).

A bevelled limbal stab incision is made in the 9 o'clock region after the mitomycin-C is washed out. Using a 15° knife, a square or trapezoidal scleral flap measuring around 4 × 4 mm is fashioned, hinged at the limbus. The dissection is completed using a crescent knife. Subsequently, a stab incision is made into the anterior chamber just behind the hinge of the scleral flap. Using a 15° blade, the anterior chamber is entered from the centre. A Kelly Descemet punch (1 mm diameter) is then used to cut the deep scleral/trabecular layer in order to perform the sclerostomy. Either two adjacent or overlapping snips are made by the punch. Subsequently, we go back to the centre of the sclerostomy and, tilting the punch downwards, make a half-thickness snip in the posterior lip of the sclerostomy. This produces a spout-like configuration in the centre, allowing aqueous to flow posteriorly rather than towards the sides (Figs. 1 and 2).

A peripheral iridectomy is then made. The scleral flap is sutured with five 10/0 nylon sutures. We keep the anterior two sutures on either side relatively tight while the rest of the three are kept loose. BSS is injected from the limbal stab incision to titrate the flow. The sutures are adjusted to have a smooth flow through the fistula without collapse of the anterior chamber on applying pressure.

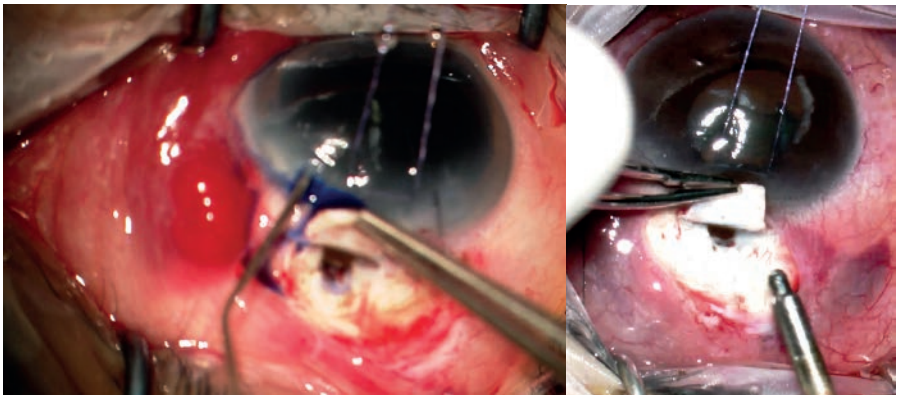

Fig. 1. Left, right: An intraoperative view of the spout configuration.

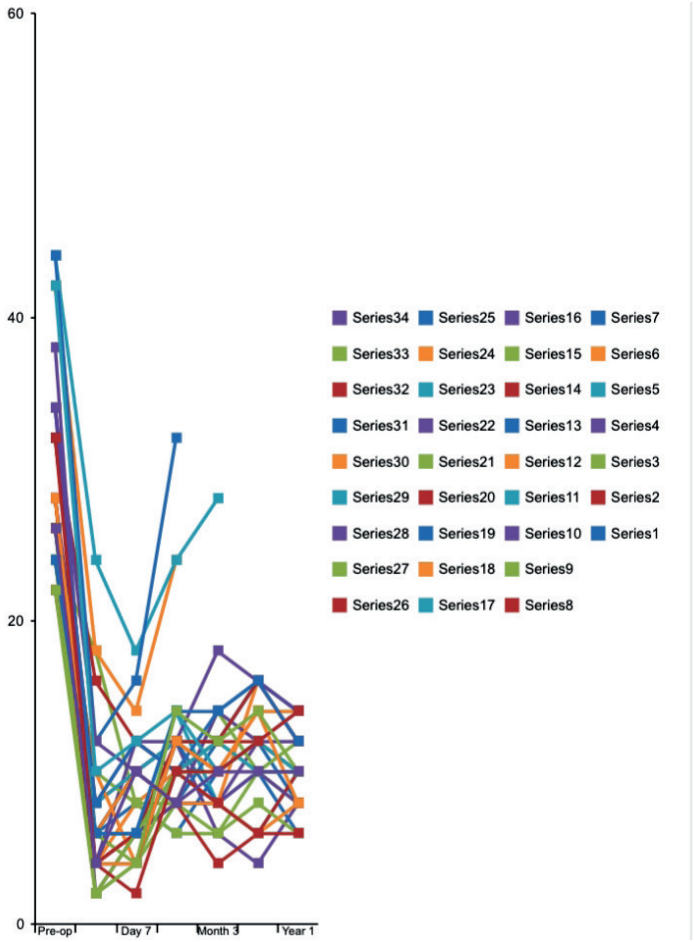

Fig. 2. Graphical representation of changes in IOP during study.

This modification has two advantages: one, it directs flow more posteriorly; and second, in the event the patient requires laser suture lysis subsequently, it is easier to lyse the anterior two tight sutures.

Postoperative review

A total of 34 patients (34 eyes) underwent trabeculectomy using this technique. Visual acuity was determined by the Snellen chart using an auto chart projector (CP-690, Nidek Corp, Japan). IOP was measured by Goldmann applanation tonometer (Carl Zeiss Meditec AG, Jena, Germany).

Patients were followed up for 1, 7, and 30 days postoperatively. Subsequently, they were reviewed according to glaucoma status, ranging from 3- to 6-monthly intervals. The first patient was operated 2 years back using this technique. However, we have included patients who completed 1 year of follow-up. The primary outcome measures analysed in this study were: 1. diffuse bleb with no leak in the immediate postoperative period; and 2. IOP between 6 and 18 mmHg. The secondary outcome measures analysed were: 1. well-functioning bleb without encapsulation/cystic changes; and 2. final IOP between 6 and 18 mmHg without medications.

Results

Descriptive statistics were used to depict baseline data and postoperative complications of the patients. Wilcoxon signed rank test was used to examine the difference between preoperative and postoperative IOP. All analyses were done using Statistical Package for the Social Sciences version 16.

Thirty-four patients were enrolled in this study. One eye of each patient underwent the procedure. We screened all patients for inclusion/exclusion criteria and performed the standard AMTT procedure as described previously. The age of the subjects ranged from 54 to 74 years, with a mean standard deviation of 64 (12). There were 10 males (29.41%) and 24 females (70.58%) in the study. Regarding the type of glaucoma, 22 (64.70%) had angle-closure glaucoma, 10 (29.41%) had open-angle glaucoma, and 2 (5.88%) had neovascular glaucoma. All patients were on four anti-glaucoma medications (a β-blocker, an α-agonist, a prostaglandin analogue, and a topical carbonic anhydrase inhibitor). We put some patients on oral carbonic anhydrase inhibitors for short periods of time while they waited for surgery.

There was a significant difference in the preoperative and postoperative median IOPs ($z = 3.928$; $p < 0.001$). The postoperative IOP (median = 12) was significantly lower than the preoperative IOP (median = 28; interquartile range = 9) (Table 1 and Fig. 3).

All 34 patients underwent AMTT and had follow-ups on day 1, day 7, day 30, 3 months, 6 months, and 3- to 6-monthly intervals thereafter. Early postoperative complications (within the first 3 months) include a flat bleb in three (8.82%) and conjunctival bleb leak in four (11.76%) patients, which occurred in the first week of the postoperative period. The only late complication (around 3 months postoperatively) noted by us was a flat bleb which developed in three (8.82%) patients (Table 1 and Fig. 3).

Table 1. Results following AMTT procedure.

Number	Preop	Day 1	Day 7	Month 1	Month 3	Month 6	Year 1
1	26	6	8	6	10	12	8
2	32	8	10	12	10	12	10
3	24	18	8	6	6	10	8
4	28	8	12	12	6	4	8
5	26	6	6	14	8	6	10
6	42	18	14	24			
7	34	6	10	12	8	10	6
8	28	4	6	8	4	6	10
9	26	2	4	8	6	8	6
10	24	4	12	10	8	12	14
11	44	24	18	24	28		
12	28	4	8	10	8	16	12
13	26	6	10	8	12	16	14
14	32	16	12	10	12	12	10
15	26	10	8	8	14	10	12
16	38	2	6	8	8	10	8
17	24	8	10	12	12	16	12
18	22	6	10	8	8	6	8
19	44	12	16	32			
20	28	4	6	10	8	6	6
21	26	6	4	10	12	10	10
22	34	12	10	8	14	12	12
23	24	6	6	10	12	10	10
24	26	10	4	12	10	14	14
25	32	8	12	10	14	16	14
26	22	4	6	12	12	16	12
27	24	2	6	10	10	12	10
28	34	4	4	12	18	16	14
29	42	10	12	14	10	12	10
30	28	4	4	12	10	14	8
31	24	6	6	14	14	16	12
32	32	4	2	10	10	12	14
33	22	2	4	14	12	14	10
34	26	4	10	8	10	10	10

Discussion

Trabeculectomy remains the gold standard to measure the success of innovations in GFS.[3,17,18] Trabeculectomy itself is being modified to make it more safe, efficient and predictable.[11] Despite all these efforts, trabeculectomy is beset with complications and failures at every stage.[5,6,19-21] In our study, 34 patients with open-angle (10), closed-angle (22), and neovascular glaucoma (2) underwent trabeculectomy due to uncontrolled IOPs with maximal medical treatment (four topical anti-glaucoma medications). Three patients had previously undergone trabeculectomies in the past, but IOP had increased,, requiring a return to four or more anti-glaucoma medications. All surgeries were performed by the author using the modifications described earlier.

We performed all surgeries in this series under sub-Tenon anaesthesia using 2% lidocaine injection. However, trabeculectomies can also be performed using lidocaine hydrochloride gel or jelly and intracameral lidocaine.[22-24]

We performed a fornix-based conjunctival flap. However, our peritomy did not reach up to the limbus. We left a cuff of conjunctiva about 0.5 mm posterior to the limbus. The two cut edges of the conjunctiva can be easily sutured and the blood vessels at both ends of the flaps promote a more rapid, more natural healing response. Excessive cautery of the episcleral vessels should be avoided to prevent contracture of the scleral flap, which may lead to uncontrolled leakage.

Trabeculectomy can be performed by either a limbus or fornix-based conjunctival flap. Limbus-based procedures are reported to have higher rates of cystic bleb formation, excessive drainage, and, according to Lemon *et al.*, more bleb leaks.[25] While limbus-based conjunctival flaps can adhere to the deeper tissues at their periphery, fornix-based flaps have a propensity to fail due to the formation of diffuse conjunctival adhesions and fibrosis spreading along the anterior part of the bleb.[26-28] We have termed this band of fibrosis as "band of steel", which is more common in darker individuals and spreads around the bleb area, leading to loss of function of the trabeculectomy. A trabeculectomy with a leaking bleb can have an adverse effect on the success rate of GFS.[7,10,29-31] Bleb leaks occur due to improper closure of the conjunctival flaps or inadvertent conjunctival buttonholes.[32-35] Late bleb leaks are usually spontaneous and occur in cystic, thin-walled blebs.[36-41] The Ibadan Study found shallow anterior chambers as the most common postoperative complication after trabeculectomy.[42]

In our study, three patients had a flat bleb and four had a bleb leak in the immediate postoperative period. All patients with the flat bleb underwent initial massage and subsequent laser suture lysis about one week after surgery. None required further surgical modification of the bleb. The patient with the leaking bleb was managed by application of a pressure-patch for two days. One patient with neovascular glaucoma underwent an anterior chamber washout

due to postoperative hyphema. Late bleb failure occurred in the two neovascular glaucoma patients and one very dark-skinned individual. On exploration and revision of the bleb, we found extensive fibrosis in the bleb area. Although revision of the bleb was done in all three cases, the two patients with neovascular glaucoma did not do well postoperatively and had to be restarted on antiglaucoma medications.

The size of the scleral flap in AMTT was kept around 4 × 4 mm. The shape and size of scleral flaps can vary between rectangular, triangular, and rhomboid. However, a study has shown that increasing the scleral flap size leads to an increase of 48.55% in aqueous egress. Also, a square flap increases aqueous drainage by 36.26% compared with a triangular flap of equivalent area. Thus, a 4 × 4 mm scleral flap used in our technique appears to be an ideal size to attain maximal aqueous outflow.[43]

In some surgical techniques, the side incisions of the scleral flap do not reach up to the limbus. This supposedly encourages posterior outflow of aqueous. However, these techniques also recommend sclerostomy incisions to be as anterior and corneal as possible to reduce bleeding and inadvertent injury or exposure of the ciliary body.[44] A scleral flap hinged posterior to the limbus does not provide adequate visualization of the surgical area anteriorly near the limbus. This increases the risk of scleral flap amputation when manipulations are performed to create a sclerostomy. Therefore, when we fashion the flap, the side incisions reach up to the limbus. This makes it easier to perform anterior sclerostomies. However, when we suture the scleral flap, the anterior two sutures are applied tightly. This encourages aqueous to flow posteriorly and is also convenient for subsequent laser suture lysis. In order to prevent the anterior chamber from collapsing, the scleral flap should be secured first with a posterior suture, after which the two anterior sutures can be applied.

In order to encourage posterior flow of aqueous, we devised another modification to the sclerostomy. After the entire sclerostomy is made as usual, the Kelly Descemet punch is brought back to the centre and tilted down and backwards to make a half-thickness cut in the posterior lip of the sclerostomy. This produces a "spout"-like configuration in the centre. Aqueous is funnelled out of this spout posteriorly, thus encouraging posterior, diffuse blebs. One should be careful while making the spout to have only a half-thickness scleral snip. This avoids any inadvertent injury to the choroid.

A failing bleb in the early postoperative period can be managed by digital massage, scleral flap suture lysis, or the removal of a releasable suture. Argon laser suture lysis can be done two days to two weeks postoperatively. However, this procedure may not be possible at times due to a thick overlying Tenon's capsule, postoperative inflammation, and subconjunctival haemorrhage. However, in our

modification, the tight sutures are applied anteriorly, facilitating lysis of these sutures compared to posterior, deeper sutures.[45,46]

Some of the popular methods recommend application of mitomycin-C after the scleral flap is made. They claim to have found scar tissue in the subscleral space upon re-exploration.[44] This is probably the "band of steel" that we have found in patients who require revision of the bleb. However, we avoid using antimetabolites after making the scleral flap. Any iatrogenic holes in the bed of the sclera, especially in cases of advanced glaucoma or myopes, may lead to increased intraocular absorption of the antimetabolite. Also, in case the scleral integrity is compromised, the antimetabolite has to be withheld.

Some techniques for conjunctival closure fashion grooves in the cornea and sutures are placed through them.[44] Such methods involve manipulating a cornea previously exposed to the antimetabolite. There is also a potential for inducing irregular astigmatism when sutures are applied over the cornea. By leaving a cuff of conjunctiva at the limbus, we are able to suture the two cut ends of the conjunctiva, providing a more secure and comfortable closure.

Some drawbacks of this study include the absence of control eyes and a relatively short follow-up of approximately one year. With this preliminary data at hand, we would like to continue evaluating the long-term results of this process. However, this modification is a simple and effective enhancement of the classic trabeculectomy technique and can be adopted by all surgeons performing GFS.

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Asian J Ophthalmol. 2019;16:242-249

Outcome of frontalis suspension surgery in pediatric ptosis

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Abstract

Purpose: *To describe the outcome of pediatric ptosis surgery using frontalis suspension technique.*

Design: *Retrospective study.*

Methods: *All patients with ptosis who underwent frontalis suspension from April 2009 to April 2014 at the Children's Hospital at Westmead were included. Medical records of patients were reviewed and analyzed.*

Results: *A total of 55 patients (74 primary procedures) were included in the study. Sixty-eight procedures (91.9%) used silicone as frontalis suspension material, three procedures used Gore-Tex, and three procedures used fascia lata. For procedures using silicone, the recurrence rate was 10.29%; 4.41% had infection and 1.47% had exposure keratopathy. All three procedures using Gore-Tex developed postoperative infection. No postoperative complication was documented in all the three procedures using fascia lata.*

Conclusion: *A change in the practice from using banked fascia lata to silicone as frontalis suspension material is seen at the Children's Hospital at Westmead. The postoperative complications and recurrence rate in procedures using silicone are relatively low. Autologous fascia lata could be considered as an alternative for older children in view of its long-term success rate and fewer complications.*

Keywords: *fascia lata, frontalis suspension, pediatric, ptosis surgery, silicone*

Introduction

Ptosis is characterized by drooping of the upper eyelid margin to an abnormally low position on the anterior surface of the eye. It is most commonly classified as congenital or acquired. Most congenital ptosis is associated with levator dystrophy, which has poor levator function. Thus, the preferred method of surgery is frontalis suspension. The frontalis suspension technique was first described

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by Hess in 1893 for the correction of ptosis and its principles remain relevant to this day.

Ptosis surgery is often delayed to a later age as congenital ptosis typically improves somewhat with time. There is also the added advantage that a more accurate assessment is often attainable in older children. Later surgery also allows further development of the orbital structures and decreases the anesthetic risk in children; however, the presence or risk of amblyopia may warrant early surgical correction in the younger age group. Age at the time of ptosis surgery may influence the type of frontalis suspension material used.

Several materials are available for frontalis suspension surgery. Autologous fascia lata is considered by many as the gold standard in frontalis suspension surgery.[1,2] Other alternatives include banked fascia lata or synthetic material such as silicone, Gore-Tex, and Ethibond.[3,4] These individual materials have their own advantages and disadvantages. Surgeons have reported a preference for using silicone slings for its flexibility and elasticity.[5,6] Gore-Tex implants have been associated with infection and granuloma formation.[7-9] We conducted a retrospective study on patients who had undergone frontalis suspension surgery at the Children's Hospital at Westmead between 2009 and 2014. We report the types of suspension material used, rate of recurrence, and postoperative complications.

Methods

This retrospective study analyzed the medical records of all patients with ptosis who underwent frontalis suspension from April 2009 to April 2014. Ethical approval was acquired from the Sydney Children's Hospitals Network Human Research Ethics Committee and conformed to the requirements of the United States Health Insurance Portability and Privacy Act. Details that might disclose the identity of the subjects under the study have been omitted. All patients had undergone an ophthalmic and orthoptic evaluation prior to surgery. All patients had undergone frontalis suspension surgery using the Fox procedure.[10]

Satisfactory functional and cosmetic success was defined as the patient having adequate lift (lids not covering visual axis in primary position) and not having ptosis recurrence nor any postoperative complications.

Results

There was a total 64 patients (87 procedures) who had undergone primary ptosis correction using the frontalis suspension technique. Nine patients (13 procedures) were excluded due to duration of follow-up being less than 6 months, leaving a total of 55 patients (74 procedures) included in the study; 38 patients were male

and 17 patients were female. The most common etiology was simple congenital ptosis (49 patients). The remaining were blepharophimosis (4 patients), Kabuki syndrome (1 patient), and Marcus Gunn jaw-winking syndrome (1 patient).

In this study, patients first presented with ptosis at a mean age of 19.3 months, ranging from 1 month to 9 years. The mean age at the time of surgery was 46.2 months. Patients with follow-up of six months or more were included in this study. The mean duration of follow-up was 30.6 months. The longest follow-up duration was 5 years (Table 1).

Table 1. Age at presentation and surgery

	Mean (months)	Standard error of mean	Range
Age at presentation	19.34	4.71	1 month-9 years
Age at time of surgery	46.17	4.75	1.5 months-13 years
Duration of follow-up	30.62	2.28	6 months-5 years

The preferred suspension material used for ptosis surgery was silicone, which accounts for 91.9% of all primary procedures (Table 2). The success rate among the primary procedures using silicone was 82.35%. Among the total of 68 primary procedures using silicone, 7 cases developed recurrence of ptosis, 3 cases had infection, 1 case had exposure keratopathy, and 1 case had sling extrusion. There were only three cases using Gore-Tex and all three cases developed infection. None of the cases using fascia lata was reported to have ptosis recurrence or postoperative complications (Table 3).

For secondary procedures, there was a total of 13 patients (14 procedures). The mean age at the time surgery was performed was 10.72 years (range from 6 to 14 years). Silicone suspension was used in 11 procedures, Gore-Tex in 2 procedures, and 1 procedure used fascia lata. Only 4 out of 13 patients who had undergone secondary procedures had a follow-up longer than 4 months.

Table 2. Type of frontalis suspension material

Types of suspension material	Total procedures	%
Silicone	68	91.9
Gore-Tex	3	4.05
Fascia lata	3 (*2 Autologous, 1 Banked*)	4.05

Table 3. Outcome and complications in primary procedures

	Silicone (n = 68)	Gore-Tex (n = 3)	Fascia lata (n = 3)
Satisfactory outcome	56 (82.35%)	0 (0%)	3 (100%)
Ptosis recurrence	7 (10.29%)	0	0
Complications			
Infection	3 (4.41%)	3 (100%)	0
Exposure keratopathy	1 (1.47%)	0	0
Sling extrusion	1 (1.47%)	0	0

Discussion

The striking result in this study was the prevalence of the use of silicone suspension at this pediatric institute. Over the 5-year period studied, more than 90% of the primary procedures performed in this center used silicone as the material in frontalis suspension surgery. Hersh *et al.* reported 63.8% of primary ptosis procedures used banked fascia lata and only 36.2% used silicone at the same center prior to 2005, highlighting a change in the practice of preferred frontalis suspension material.[3]

As noted, in contrast to Hersh *et al.*, only 3 out of 74 procedures used fascia lata during our study period. Two of the implants were autologous fascia lata, hence requiring harvesting procedure during the ptosis surgery. The patients were all older than 10 years, making it feasible to harvest the fascia lata. Autologous fascia lata has the best long-term results in conserving a good lid position postoperatively, with fewest complications.[2] Despite having a good functional outcome, autologous fascia lata also has its limitations. The child has to be old enough so that sufficient length of tissue can be harvested. The child can suffer from a hematoma formation or left with a nasty scar or keloid at the donor site.[11] The use of autologous fascia lata would also necessitate a longer anesthetic time given the harvesting of tissue.

Another option to harvesting autologous fascia lata is using banked fascia lata. As observed, only one procedure in this study used banked fascia lata. Banked fascia lata is biological material and, as such, always carries some risk of disease transmission. Previous reports have revealed cases involving transmission of viruses after transplantation of banked tissue.[12-14] Patients infected with Creutzfeldt-Jacob disease have also been reported after corneal transplant.[15,16] Banked tissues undergo a meticulous process of either freeze-drying or irradiation, or a combination of the two methods, in order to remove the genetic substance in the tissues. This is to avoid the transmission of infectious agents

in the tissues when being transplanted. Despite these preventive measures, a study has shown that freeze-dried gamma-irradiated cadaveric donor tissue still contained intact deoxyribonucleic acid.[17] These risks may be the reason banked fascia lata has been less favorably used as the choice for suspension material.

As surgery needs to be performed as early as possible in cases with possible risk of amblyopia, synthetic suspension materials need to be utilized in younger children. Silicone is one of the suspension materials of choice and is the preferred material used in this study. Silicone is readily available and easily accessed by surgeons. Silicone has been used widely in many centers as it has been tested to be effective in the treatment of ptosis.[18] Silicone was one of the earliest suspension materials described by Tillet and Tillet in 1963 using a No. 40 silicone strip.[19] All six patients described by Tillet and Tillet had good results after 19 to 24 months follow-up.[19] Silicone was found to be superior to all other materials in a study by Lamont and Tyers in regard to easily adjusting the suspension material.[20] Due to this property of easy adjustability, it is a reasonable material choice if recurrence occurs. It may also be easily revised or replaced if the intended lid position was not attained after the primary surgery due either to under- or overcorrection or recurrence of ptosis. Silicone suspension does not incorporate with surrounding collagenous tissue, making it easier to remove or adjust. Its elasticity is another advantage, making it possible for patients to close the eye against the tension of the suspension while still maintaining an acceptable lid height. This would reduce the risk of exposure keratopathy. Several other studies have reported recurrence and complication rates when using silicone in ptosis surgery (Table 4). The recurrence rate in our study was comparable to previous reports, while the rate of infection and exposure keratopathy was comparatively low. The recurrence rate in previous studies seems to vary widely. Different study design and definition of terms may cause this variation. However, all studies did report cases of infection, which is not surprising given a foreign material is being implanted. Comparison for fascia lata and Gore-Tex was not done, as the numbers of procedures in our study were too small.

Gore-Tex (polytetrafluoroethylene suture) was used in 3 out of 74 procedures during this study period. It is a heterologous material that has been used in brow suspension surgery since 1986.[22] All three cases in our study were complicated with infection and granuloma. In 2001, Steinkogler reported that 5 out of 11 (45.5%) needed removal of Gore-Tex for suspected infection.[27] Another study also reported a 40% complication rate in procedures using Gore-Tex.[9] The complications reported include ptosis recurrence and granuloma formation. This high percentage of infection and granuloma formation may be attributed to the porous feature of Gore-Tex, which may allow an influx of pathogens leading to infection.

Table 4. Comparison of complication rates using silicone with previous studies

	Our study	Bansal and Sharma[21]	Khan *et al.*[22]	Ali *et al.*[23]	Horng *et al.*[24]	Morris *et al.*[25]	Hersh *et al.*[3]	Simon *et al.*[26]
Type of study	R	R	P	P	R	R	R	R
Number of procedures (n)	68	38	15	35	49	110	46	34
Recurrence (%)	10.3	2.63	7	2.8	0	–[a]	13	44
Infection/ granuloma (%)	4.41	7.89	7	2.8	2.04	1.81	15.2	7.41
Exposure keratopathy (%)	1.47	–[a]	–[a]	–[a]	18.0	3.63	–[a]	–[a]
Sling extrusion/ exposure (%)	1.47	7.89	7	–[a]	4.08	–[a]	15.2	3.73
Lagophthalmos (%)	–[a]	13.1	–[a]	–[a]	–[a]	–[a]	–[a]	–[a]
Under correction (%)	–[a]	10.52	26	–[a]	–[a]	9	–[a]	–[a]
Chronic eyelid edema (%)	–[a]	2.63	–[a]	–[a]	–[a]	–[a]	–[a]	–[a]

P: Prospective study; R: retrospective study;
[a]No record in the results of the studies

At the Children's Hospital in Westmead, there has been a move away from stored fascia lata to the use of silicone as the choice of material for ptosis surgery. The recurrence rate with silicone is slightly lower (10.29% vs. 13%) and rate of infections/ granuloma is significantly lower (4.1%) compared to compared to 15.2% in the Hersh *et al.*[3] study.

Conclusions

Silicone is the preferred choice of material used for frontalis suspension surgery for ptosis at the Children's Hospital at Westmead. The complication and recurrence rates are relatively low. Silicone allows for easy removal and adjustability where indicated. Autologous fascia lata could be considered as an alternative for older children in view of its long-term success rate and few complications.

Acknowledgments

The authors thank the participating ophthalmologist at the Children's Hospital at Westmead (Westmead, Australia) in assisting with the data collection.

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Asian J Ophthalmol. 2019;16:250-259

Validation of the WINROP screening algorithm among preterm infants in East Malaysia

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Abstract

Objective: *To prospectively validate the WINROP (Weight, Insulin-like growth factor 1, Neonatal, Retinopathy of Prematurity) screening algorithm (www.winrop.com) based on longitudinal measurements of neonatal body weights in predicting the development of severe retinopathy of prematurity (ROP) among preterm infants admitted to the neonatal intensive care unit of a tertiary care center in East Malaysia.*

Methods: *All premature infants of less than 32 weeks gestational age (GA) were included in this cohort. Their body weight was measured weekly from birth to 36 weeks postmenstrual age and entered into the computer-based surveillance system: WINROP. Infants were then classified by the system into high- or low-risk alarm group. The retinopathy findings were recorded according to Early Treatment for ROP criteria. However, the screening and management of infants were done according to the recommendations of the Continuous Practice Guidelines, Ministry of Health, Malaysia. The team members involved in screening and those recording the findings were kept blinded from each other.*

Results: *A total of 151 infants with median GA at birth of 30 weeks (interquartile range [IQR] ± 2.1) and mean birth weight of 1,264 g (standard deviation ± 271) were analyzed. High-risk alarm was signaled in 85 (56.3%) infants and 9 (6.6%) infants developed type 1 ROP. One infant in the low-risk alarm group developed type 1 ROP requiring laser retinal photocoagulation. The median time lag from the high-risk alarm signal to the development of type 1 ROP was 10.4 (IQR ± 8.4) weeks.*

Conclusion: *In this cohort, the WINROP algorithm had a sensitivity of 90%, with negative predictive value of 98.5% (95% confidence interval) for detecting infants with type 1 ROP and was able to predict infants with ROP earlier than their due screening date. This study shows that a modified version of the WINROP algorithm aimed at specific populations may improve the outcome of this technique.*

Keywords: *infant, insulin-like growth factor 1, premature, retina, retinopathy of prematurity (ROP)*

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Introduction

Retinopathy of prematurity (ROP) remains a common cause for pediatric visual impairment and blindness worldwide. The Cryotherapy for ROP study reported that 65.8% of infants with birth weight less than 1,251 g developed ROP.[1] In a similar group, the Early Treatment for ROP (ETROP) study had given an incidence of ROP at 68%.[2] In a study from Malaysia, Choo *et al.* reported the incidence of ROP in this country to be 58.6% in extremely low birth weight infants.[3] In the ETROP study, ~8% of infants with ROP required treatment.[2] ROP remains an important cause for preventable blindness in children. A study by Rahi and Cable reported ROP to be responsible for almost 3% of all childhood blindness.[4] This number could be higher in developing countries. These data confirm the existence of a huge burden of ROP in vulnerable populations and the need to develop better screening strategies to manage this condition.

Traditionally, screening recommendations for ROP have emphasized strict follow-up visits to diagnose the condition. However, these protocols suffer from some shortcomings, including the stressful nature of the examination for infants, carers, and practitioners; the economic burden on health services; maintaining standby neonatal intensive care unit (NICU) services, with the need for experts to identify and treat the condition if required.[5,6] It is imperative to find better screening techniques and protocols to overcome these deficiencies, especially in underserved areas. One such online-based surveillance system that has gained attention is the WINROP. The acronym WINROP (Weight, Insulin-like growth factor 1, Neonate, ROP) indicates the correlation between early postnatal weight gain and insulin-like growth factor 1 (IGF-1) in the development of severe ROP. A number of studies performed, mainly in developed countries, have shown the high sensitivity and specificity of this system in raising alarms, which direct the practitioner to a need for intervention.[7,8] In a further simplification of the WINROP system, only the weight of the preterm infant is monitored.[9-11] This refinement would further facilitate the WINROP method. However, this modification needs to be validated extensively and widely across different population groups in order to confirm its effectiveness.[12-14]

We conducted a longitudinal cohort study on 151 preterm infants admitted to the NICU of a tertiary care facility in East Malaysia. This study assessed the modified WINROP method in monitoring the postnatal weight gain and capturing the data into the online surveillance system. Alarms were raised when any intervention was required. Our results show that this modified WINROP algorithm has a sensitivity of 90% with negative predictive value of 98.5% (95% confidence interval [CI]) in detecting infants with type 1 ROP. Thus, this modality can be an effective means of screening infants for ROP.

Methods

Patients

A prospective cohort study was performed between May 2015 and March 2016 on premature infants born at a gestational age (GA) of less than 32 weeks, seen at a tertiary care hospital in East Malaysia. All infants in the study were admitted to the NICU, written informed consent for inclusion in the study was obtained from the parents, daily weight was measured, and the infants screened for ROP. Premature infants who had incomplete weight measurement until 36 weeks postmenstrual age, nonphysiological weight gain, or retinal disease other than ROP were excluded from this study.

The GA of participating infants was determined by obstetricians and neonatologists based on last menstrual date of the infant's mother, early antenatal ultrasonography, and/or neonatal physical assessment using the New Ballard Score.[15] The body weight of premature infants was measured from the day of birth until discharge from hospital using a validated infant weighing scale. The data collected included GA at birth, body weight, weekly postnatal weight measurements conducted until 36 weeks postmenstrual age, sex, parity, race, ROP examination results, and incidence of bronchopulmonary dysplasia (BPD), intraventricular hemorrhage, necrotizing enterocolitis, or neonatal sepsis.

ROP screening and treatment

All the participating infants were examined according to the Clinical Practice Guidelines by the Ministry of Health Malaysia for ROP screening.[16] The first ROP examination was performed between fourth and sixth weeks postnatal age, or for very premature infants, at 31 to 33 weeks of GA and repeated every 2 weeks or more according to the severity of ROP. The examination was continued until full vascularization of the peripheral retina, regression of ROP, occurrence of type 1 ROP, or the need for treatment was achieved. The ROP examinations were performed by a qualified pediatric ophthalmologist using the standard binocular indirect ophthalmoscope with a 20 D or 28 D condensing lens. Prior to the examination, the pupil was dilated using cyclopentolate 0.5% and phenylephrine 2.5% eye drops.

The ROP findings were classified according to the International Classification of Retinopathy of Prematurity, revisited 2005 (stages 1-5).[17] The highest stage of ROP, the lowest zone, presence of prethreshold or threshold disease, and the need for treatment were recorded. Prethreshold ROP was further subclassified according to the ETROP criteria into type 1 or type 2 ROP.[2]

Type 1 ROP is defined as any zone I ROP with plus disease, zone I stage 3 ROP without plus disease, or zone II stage 2 or 3 ROP with plus disease. Type 2 ROP is defined as zone I stage 1 or 2 ROP without plus disease or zone II stage 3 ROP without plus disease. If the infant developed type 1 ROP during the study,

standard treatment with laser photocoagulation was given.

WINROP screening

The WINROP algorithm was developed using the method of online statistical surveillance system (www.winrop.com) that permits the user to enter body weight, GA, date of birth, and successive weight measurements; allows tracking of multiple infants; and provides a user-friendly indication of low- or high-risk status for developing sight-threatening ROP. The requirements for using the WINROP algorithm system are:

1. GA less than 32 weeks at birth;
2. weekly weight measurement;
3. physiological weight gain;
4. absence of other pathological retinal vascular disease.

The WINROP algorithm is based on expected weight gain data obtained from premature infants with no ROP or stage 1 ROP, and then calculating the difference from the observed values.[7] The differences or deviations between the expected weight gain and the actual weight gain are accumulated weekly. When these cumulative deviations surpass a threshold signal level, an alarm is signaled, indicating that the premature infant is at risk for developing severe ROP. Thus, the WINROP outcome is either no alarm or alarm.

In our study, the weekly body weight of participating premature infants was measured by an observer blinded from the ROP and WINROP outcome, then entered into the WINROP online website by another person who was also unaware of the ROP outcome. The WINROP algorithm system calculates the risk weekly to predict infants who are at risk of developing severe ROP. Based on the WINROP analysis, the participating infants were categorized into two groups: no (also called low-risk) alarm group, who are less likely to develop type 1 ROP, and high-risk alarm group, who are at risk of developing type 1 ROP. The screening and management of the infants were done according to the Continuous Practice Guidelines formulated by the Ministry of Health, Malaysia. The alarm status was recorded by the main author; however, the screening protocol was kept unchanged and followed the guidelines. As this was a double blinded study, the team members involved in screening and the persons involved in data entry or alarm acquisition remained unaware of the outcomes of each other. Ethical approval for this study was obtained from the ethics committee of University Kebangsaan Malaysia.

Statistical analysis

The sensitivity and specificity of WINROP screening to identify premature infants who developed type 1 ROP were analyzed with Statistical Package for the Social Sciences. The negative and positive predicted values were calculated using the

sensitivity, specificity, and prevalence of type 1 ROP for the participating premature infants. We calculated 95% CI for estimated binary proportions (sensitivity and specificity).

Results

Patients

A total of 151 infants admitted in the NICU of a tertiary care hospital participated in this study and were screened for ROP. In this cohort, male and female

Table 1. Patient demographic data

Birth characteristics	No. (%)
GA, median (IQR), weeks	30 (±2.1)[a]
BW, mean (SD), g	1,264 (±271)
Sex	
Male	77 (51)
Female	74 (49)
Birth multiplicity	
Single	130 (86)
Twin	21 (14)

BW: birth weight
[a]Skewed to the left

Table 2. Prematurity-associated comorbidities

Characteristic	Infants, no.			
	No ROP	Non-PT ROP	Type 1 ROP	Total infants
BPD	83	9	10	102
Intraventricular hemorrhage	20	6	4	30
Necrotizing enterocolitis	4	0	0	4
Neonatal sepsis	80	9	5	94

PT: prethreshold

patients were almost equal in number, with median GA at birth of 30 weeks (interquartile range [IQR] ± 2.1) and mean body weight of 1,264 g (standard deviation [SD] ± 271). Singleton births were recorded in 86% infants and the remaining were twins. The birth characteristics of the study population are shown in Table 1.

There was a statistically significant association between BPD and type 1 ROP ($p = 0.031$) as all infants with type 1 ROP were diagnosed with BPD. There were no significant differences in intraventricular hemorrhage, necrotizing enterocolitis, and neonatal sepsis with the severity of ROP (Table 2).

ROP and WINROP outcome

Type 1 ROP developed in 10 infants (6.6%), with a median GA at birth of 27.8 weeks (IQR ± 2.7) and mean body weight of 1,047 g (SD ± 272). The diagnosis of type 1 ROP was made at median GA of 39.7 weeks (range, 37.6-44.6 weeks). Infants in this group were treated with laser retinal photocoagulation within 72 hours of the diagnosis. Three of these required repeated laser treatments and none of them progressed to retinal detachment. Non-prethreshold ROP developed in 12 infants (7.9%), with median GA at birth being 27.7 weeks (IQR ± 1.9) and mean body weight of 1,029 g (SD ± 137). Most of the infants in the non-prethreshold group were in stage 1 and 2 at zone II ROP, which regressed spontaneously without treatment. No ROP occurred in 85% of the premature infants. The median GA at birth was 30.1 weeks (IQR ± 1.8) and mean body weight was 1,303 g (SD ± 263) (Table 3).

Table 3. Alarm signal in relation to ROP categories and birth characteristics

		Alarm status		All infants
		Low risk	High risk	
Infants, no. (%)		66 (43.7)	85 (56.3)	151
ROP categories, no.	No ROP	64	65	129
	Non-PT ROP	1	11	12
	Type 1 ROP	1	9	10
Birth characteristics	GA, median (IQR) weeks	31.0 (±1.1)[a]	29.1 (±2.0)[a]	30 (±2.1)[a]
	BW, mean (SD) g	1,518 (±157)	1,067 (±152)	1,264 (±271)

BW: birth weight; PT: prethreshold
[a]Skewed to the left

Table 4. Sensitivity, specificity, PPV, NPV in predicting type 1 ROP using the WINROP algorithm

Alarm status	ROP categories, no.		Predictive values
	Type 1 (n = 10)	Non-type 1 (n = 141)	
High risk (n = 85)	9	76	PPV = 10.6%, 95% CI: 6, 19
Low risk (n = 66)	1	65	NPV = 98.5%, 95% CI: 92, 99
	Sensitivity 90%, 95% CI: 60, 98[a]	Specificity 46%, 95% CI: 38, 54[a]	

NPV: negative predictive value; PPV: positive predictive value

A high-risk alarm was signaled in 56.3% of infants, of which 9 infants developed type 1 ROP and 11 infants developed non-prethreshold ROP. Type 1 ROP was treated with laser retinal photocoagulation, while non-prethreshold ROP regressed and resolved spontaneously. Most of the type 1 ROP infants were diagnosed before 40 weeks of GA, except two infants who developed type 1 ROP after 45 weeks of GA and were treated. A low-risk alarm developed mostly in no-ROP premature infants. One infant in the low-risk alarm group who developed type 1 ROP was born at 30.6 weeks GA and birth weight was 1,700 g with severe BPD, requiring prolonged intubation for more than 3 weeks. ROP was identified at 36 weeks of GA and treated with laser photocoagulation. Another infant in the non-prethreshold group had a high-risk alarm and developed stage 1 ROP, which then regressed spontaneously. The median GA at birth and body weight were lower in the high-risk alarm group than in the low-risk alarm group (Table 3).

The median time from birth to high-risk alarm signaled was 2 weeks (IQR ± 2.0) and from high-risk alarm signaled to development of type 1 ROP was 10.4 weeks (IQR ± 8.4).

Test characteristics

In this prospective cohort, the sensitivity of the WINROP algorithm in predicting severe ROP was 90% (95% CI, 60%-98%; 9 of 10 infants) and the specificity was 46% (95% CI, 38%-54%; 65 of 141 infants). The positive predictive and negative predictive values in this study group were 10.6% and 98.5%, respectively (Table 4).

Discussion

Worldwide, there is an uptrend in the number of infants being diagnosed with ROP, especially so in the developed and higher strata developing areas.[18,19]

This has been directly attributed to better survival rates of premature infants as a consequence of advances in neonatal care and better access to NICUs. In underdeveloped areas, poor neonatal services are responsible for higher infant mortality rates among preterm babies, which may lead to lower overall ROP rates. In Malaysia, the Ministry of Health has set out specific guidelines regarding screening of premature infants.[16] All babies who are less than 32 weeks GA or with a birth weight of less than 1,500 g or infants with an unstable clinical course who are at high risk (as determined by the neonatologist or pediatrician) need to be screened until the retina is fully vascularized, or there is regression of ROP or need for treatment. In our study, on average, an infant was subjected to the screening procedure at least 5 to 6 times if there was no ROP and more frequently in cases where ROP was detected. This produces severe stress on the fragile preterm infants, as well as on the healthcare system.[20] A study by Laws *et al*. has documented a rise in systolic and diastolic blood pressure as well as a fall in oxygen saturation in infants during ROP screening.[5]

Early diagnosis and management of ROP by lasers and anti-vascular endothelial growth factor agents has reduced the incidence of blindness by 25% in infants diagnosed with late-stage ROP. However, these treated infants continue to have poor visual acuity following treatment, while ocular and visual development is significantly impaired.[21] About 70% of infants with ROP develop myopia during the first year after birth.[22] Astigmatic refractive errors are seen in 40% of eyes having a history of ROP, while strabismus affects 20% infants diagnosed with ROP.[21] These pathologies need to be addressed by an earlier diagnosis of ROP.

The WINROP algorithm is an ROP screening protocol based on weekly postnatal weight measurements and assessment of IGF-1 levels to predict the development of severe ROP in premature infants.[7] The system uses a cumulative deviation statistical approach. Every week the infant's actual weight is compared to an expected growth curve of infants who developed no or mild ROP. The differences or deviations between the expected weight and the actual weight are accumulated from week to week. When these cumulative deviations surpass a threshold, an alarm is signaled, indicating the preterm infant is at risk for developing sight-threatening complications of ROP. In a further modification of the procedure, only the weight gains are taken into consideration.[8] By avoiding the weekly blood sampling to assess IGF-1, this modification makes the procedure simpler, safer, and more economical.

The sensitivity of the WINROP system has shown variations among countries and populations, being high in developed countries and slightly lower in developing countries and Asian populations.[8-14] In this study, the modified WINROP algorithm correctly identified 9 of 10 (90%) infants who had developed type 1 ROP that required treatment. The sensitivity of the WINROP algorithm was found to be as high as in the Korean study (90%)[13] and higher than the Chinese study (87.5%)[14]

when evaluated in Asian countries. Every country has different demographics and differences in terms of birth weight and postnatal weight gain according to their GA. Asian populations (Malaysia) are small and light in body weight as compared to European populations. Thus, in this study the sensitivity was high/comparable to other studies; however, the specificity is much lower. In this cohort, among infants who developed type 1 ROP, the high-risk alarm was signaled at a median of 2 weeks after birth and 10 weeks before the diagnosis of type 1 ROP. The high sensitivity and early identification of infants at high risk of developing type 1 ROP before the scheduled screening showed that it can be used as an adjunct for conventional ROP screening protocols.

Conclusion

Our study validates the successful implementation of the modified WINROP algorithm in a population of preterm infants seen in East Malaysia. This protocol can prove to be a useful tool to modify the current ROP screening guidelines, wherein an infant with no alarm can be examined less often, while an infant with a high-risk alarm signal can be screened as per guidelines. This would save these fragile infants from unnecessary examinations and direct the efforts of the staff toward the sicker infants who require more attention.

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Asian J Ophthalmol. 2019;16:260-267

Original Article

Comparative study of ocular manifestations of HIV infection at a tertiary care hospital in Maharashtra, India

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Abstract

Purpose: *We conducted the study to observe the change in infection patterns with the introduction of highly active antiretroviral therapy (HAART) and correlation of CD4 count with various ocular manifestations of acquired immune deficiency syndrome (AIDS).*

Design*: This was a prospective observational cohort study.*

Methods*: The study was conducted at a tertiary care teaching institute with established antiretroviral therapy (ART) centre. A total of 240 eyes of 120 ART-naive patients were enrolled. Ocular manifestations of these patients were observed and followed up for six months for any change with HAART.*

Results: *Out of 240 eyes, 24 showed ocular involvement (10%), of which human immunodeficiency virus (HIV) microangiopathy and molluscum contagiosum were most common. Out of the four cases of HIV microangiopathy, two cases demonstrated complete resolution after six months of ART. Only one of three cases of cytomegalovirus (CMV) retinitis showed healing after six months of ART.*

Conclusions: *Vision-threatening CMV retinitis and herpes zoster ophthalmicus can improve if specific treatment is initiated promptly. There is direct correlation between CD4 count, ocular manifestation, and prognosis of the patients; 33.33% of patients showed improvement in ophthalmic manifestations after HAART during a follow-up period of 6 months.*

Keywords: *antiretroviral therapy, CD4 lymphocyte count, CMV retinitis, herpes zoster ophthalmicus, HIV infection, HIV microangiopathy*

Introduction

India is on the verge of being the country with the largest number of individuals living with human immunodeficiency virus (HIV)-acquired immune deficiency syndrome (AIDS). The total number of people living with HIV (PLHIV) in India was estimated at 2.117 million (1.711-2.649 million) in the year 2015.[1] Ocular lesions are also on the rise as the number of HIV-infected individuals is increasing.

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Ocular lesions were first reported in India in 1995 at Sankara Nethralaya, Chennai. The lifetime cumulative risk of developing at least one abnormal ocular lesion for a PLHIV ranges from 52% to 100% in various studies.[2] The epidemiological pattern of the disease in developed countries is different from that in developing countries. With the development of highly active antiretroviral therapy (HAART) in 1998, we witnessed a delay in illness and death, as well as a change in the pattern of ocular manifestations. The incidence of opportunistic ocular-infections causing retinitis has dramatically decreased, and clinicians should be aware of changes in the clinical manifestations of HIV. Pune and Mumbai are cosmopolitan cities with rising number of HIV-infected patients. At Pune, we run a well-equipped antiretroviral therapy (ART) plus centre, which has helped us in managing patients effectively.[4]

Materials and methods

The study was conducted at a tertiary eye care teaching institute from December 2008 to April 2011. Ethical approval was obtained from the ethics committee of our institute. Detailed evaluation of any ocular morbidity was conducted in 240 eyes of 120 HIV-naive patients who attended the ART centre of the institute after obtaining written consent from them. All patients underwent detailed history-taking which included World Health Organization clinical stage, CD4 count, and ocular symptoms at presentation.

A complete ophthalmological examination was performed including visual acuity examination, direct and indirect ophthalmoscopy and slit lamp microscopy, fundus fluorescein angiography, fundus photography, and B scan.

Inclusion criteria

1. Drug-naive patients diagnosed as having HIV infection by enzyme-linked immunosorbent assay test at the Integrated Counselling and Testing Centre.
2. Patients who are ART eligible as per National AIDS Control Organization criteria.

Exclusion criteria

1. Patients with pre-existing diabetic or hypertensive retinopathy.
2. Patients initiated on ART from private centres or patients who were exposed to ART drugs at any point of time.
3. Patients on ART who were lost to follow-up during the study.

Patients were followed up for six months on a monthly basis. CD4 count and ocular manifestations were compared using paired t-test and chi-square test.

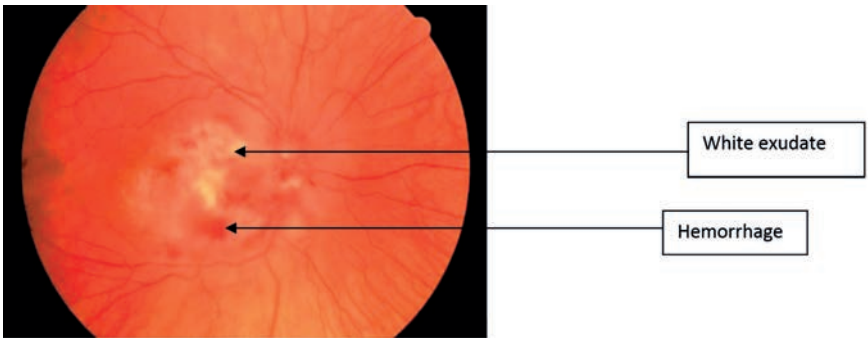
Observations and results

The age of the population included in the study ranged ffrom 2 to 70 years. Most patients fell (62.5%) within 21 to 40 years of age. Males predominated in the 120 patients, of which 24 had ocular involvement. The mean CD4 count pre-HAART was 140; post-HAART was 221.

We observed that low CD4 count patients (<100) presented more commonly with severe vision-threatening manifestations in the pre-HAART group (cytomegalovirus [CMV] retinitis, HIV retinopathy, herpes zoster ophthalmicus [HZO]). Some ocular manifestations are shown in Figures 1A, B and 2.

Molluscum contagiosum and HIV microangiopathy were the most common presentations. Patients who had received ART for more than two months showed a reduction in infection rates, although statistically insignificant.

A.



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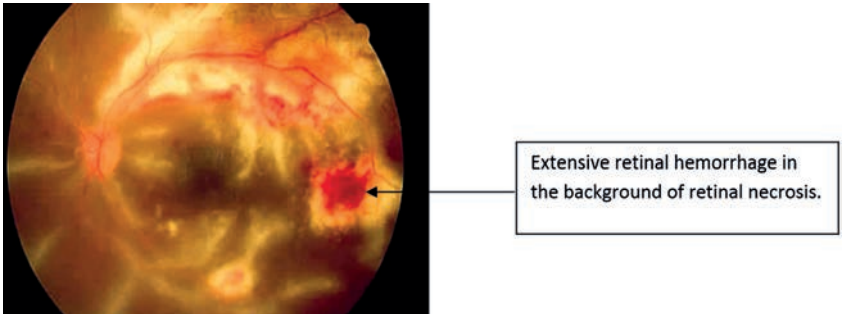

Fig. 1. Fundus photograph in case of CMV retinitis.

Table 1. Comparison of ocular manifestations in AIDS

Manifestation	Pre-ART (n = 120)	Follow-up (n = 105)
HIV microangiopathy	5 (4.17%)	3 (2.85%)
Molluscum contagiosum	4 (3.33%)	2 (1.90%)
CMV retinitis	3 (2.5%)	2 (1.90%)
Keratoconjunctivitis sicca	3 (2.5%)	2 (1.90%)
HZO	2 (1.67%)	1 (0.95%)
Orbital cellulitis	2 (1.67%)	0
Fungal ulcer	1 (0.83%)	1 (0.95%)
Blepharitis	1 (0.83%)	0
Conjunctivitis	1 (0.83%)	1 (0.95%)
Neuro-ophthalmic signs	1 (0.83%)	0
Choroiditis	1 (0.83%)	0
Vitritis	0	1 (0.95%)
Immune recovery uveitis	0	1 (0.95%)
Drug reaction	0	1 (0.95%)
Stevens-Johnson syndrome	0	1 (0.95%)
Any ophthalmic manifestation	24 (20%)	16 (15.23%)

Association between CD4 count and ocular manifestation at presentation

Tables 1 and 2 summarize our results. Molluscum contagiosum was observed in four cases and all had CD4 ranging between 100 and 250. HIV retinopathy and HZO were noted in patients with CD4 below 100. CMV retinitis was evident in cases with CD4 < 50. CD4 count improved after initiation of ART. In half the cases of HIV microangiopathy, fundoscopic changes were normalized.

Discussion

Our study described the ocular manifestations in patients with HIV-AIDS and the change in the pattern of the disease with HAART. When the gender distribution of study cases is taken into account, a male preponderance was noted. In their study in Western India, Shah *et al.* have also reported a greater number of male patients

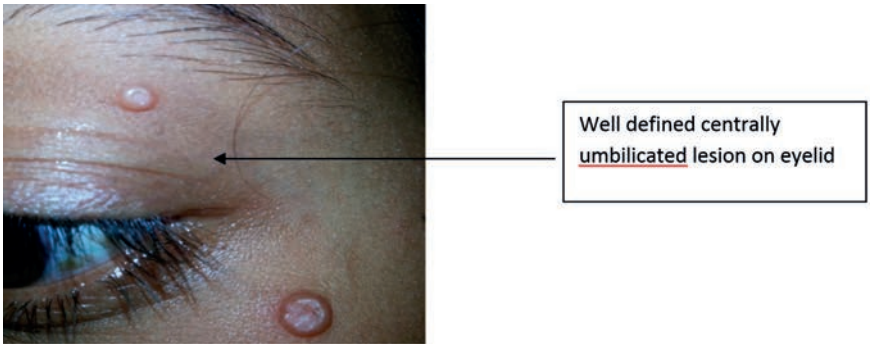

Fig. 2. Molluscum contagiosum.

Table 2. Pre- and post-ART manifestations.

Sl. No.	At the time of screening		On follow-up	
	CD4	Ophthalmic manifestation	CD4	Ophthalmic manifestation
1.	69	HIV microangiopathy	244	HIV microangiopathy
2.	22	HZO Dendritic ulcer	66	Keratitis
3.	34	CMV retinitis	56	Healed
4.	82	HIV microangiopathy	99	Normal
5.	60	HIV microangiopathy	123	Normal
6.	58	HIV microangiopathy	68	HIV microangiopathy
7.	141	Normal	313	Immune reconstitution uveitis
8.	64	Keratoconjunctivitis sicca	190	Keratoconjunctivitis sicca
9.	44	Keratoconjunctivitis sicca + CMV retinitis	Death	Keratoconjunctivitis sicca + CMV retinitis
10.	184	HIV microangiopathy	196	HIV microangiopathy
11.	115	Orbital cellulitis		Death
12.	130	Fungal ulcer	304	Healing fungal ulcer
13.	139	Keratoconjunctivitis sicca	296	Keratoconjunctivitis sicca
14.	76	HZO	–	Death
15.	33	CMV retinitis	40	CMV retinitis

with ocular infection. The difference between male and female number of cases could be due to increased prevalence of HIV infection in males. Secondly, females are deprived of screening modalities due to socioeconomic factors.

We recorded the maximum age of study patients to be 70 years and minimum age to be 2 years. The mean age was 33.4 years and median age was 35 years. Most cases (87.5%) fell in the group between 20 and 50 years of age. Of the total 120 cases, 73 (60.8%) were male and 47 (39.2%) were female.

Biswas *et al.* concluded that the cumulative risk of at least one abnormal ocular lesion developing in HIV-infected patients is 52-100%. It was also pointed out that 40-45% of HIV-infected patients in India have at least one ophthalmic manifestation when examined by the ophthalmologist. Cunningham and Margolis reported that 70-80% of HIV-infected patients had ophthalmic disease at some time during their lifetime. Table 3 compares the prevalence of ocular manifestations in our study with various other studies.

The prevalence of ocular manifestations is certainly on a declining trend owing to the rise in patients on ART and widespread availability of antiretroviral drugs through public health systems. Molluscum contagiosum and HIV microangiopathy were the most common ocular findings in the anterior segment, while CMV retinitis was the most common finding in the posterior segment. HIV microangiopathy showed significant response to HAART.

The mean CD4 count in the pre-HAART group was 140,whereas in the post-HAART group it was 224, which was statistically highly significant ($p < 0.001$ by paired t-test). It proves beyond doubt that HAART is playing a major role by increasing the CD4 count, and thus, life expectancy. All three cases of CMV retinitis were observed in patients with CD4 count < 50. Herpes zoster and HIV retinopathy occurred at CD4 count of less than 100. Only one case of immune reconstitution uveitis was noted in a patient from the post-ART group. It responded well to glucocorticoid therapy. In this patient, there was a rise in CD4 count from 141 to 313. Ocular lesions were observed in 24 patients in the pre-HAART group and 16 in the post-HAART group. In patients with ocular lesions, the median CD4 was 70 before initiation of HAART and 156.5 after initiation of HAART. This finding was highly significant statistically ($p = 0.006$ by paired t-test), emphasizing the pivotal role of HAART in reducing ocular morbidity and improving the quality of life.

Table 3. Prevalence of ocular manifestations in the present study with other studies

Manifestation	Holland *et al.*	Khadem *et al.*	Jabs *et al.*	Lim *et al.*	Kestelyn *et al.*	Our study
Sample size	30	08	200	118	20	120
Ocular involvement	63%	50%	25%	37%	55%	20%

In CMV infection, early retinitis was seen as small, white perivascular retinal infiltrates or dot-blot haemorrhages. The classic lesion is a hemorrhagic necrotizing retinitis that follows the retinal vasculature. Fluffy retinal infiltrates and necrosis are usually associated with scattered hemorrhages ("scrambled eggs and ketchup" appearance) (Fig. 1A and B).

Twenty-four of 120 patients in the pre-ART group had ocular manifestations, while 16 of 105 patients in the post-ART group had ocular manifestations. In the post-ART group, the ocular manifestations decreased and the types of manifestations were different, although not clinically significant. CMV retinitis and keratoconjunctivitis sicca, which have permanent sequelae, were counted in both groups, as this is a follow-up study.[12,13] Thus, prevention of ocular scar formation is of great relevance. ART initiation has been pivotal in the overall reduction of opportunistic infections.[14,15]

Conclusions

The prevalence of ocular manifestations decreased in the post-HAART group. Molluscum contagiosum and HIV microangiopathy in the anterior segment and CMV retinitis in the posterior segment were the most common presentations in the pre-HAART group, while Stevens-Johnson syndrome and immune recovery uveitis were specific to the post-HAART group. On comparing ocular manifestations in the pre- and post-HAART group, it was observed that the severity of ocular disease significantly declined in the post-HAART group. To conclude, availability of HAART treatment, screening from various specialties and experts through cross-reference after enrolment are necessary to prevent disastrous complications of the disease. As far as ocular manifestations are concerned, early diagnosis and follow-up will help the patient have a better visual prognosis and prevent vision-threatening complications.

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Prevalence of dengue-related fundus and macular optical coherence tomography findings among inpatients in a regional referral hospital

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Abstract

Purpose: *To investigate the prevalence of fundus and macular optical coherence tomography (OCT) findings, and the spectrum of dengue-related fundus presentation in a Malaysian tertiary hospital. The associations between platelet count and haematocrit level with fundus and macular OCT findings were also investigated.*

Design: *Cross-sectional study.*

Methods: *The study was conducted at Hospital Raja Permaisuri Bainun, Ipoh, from June to August 2015. Patients who consented to participate underwent a comprehensive ocular examination. Examination included a best-corrected distance (6 m) and near visual acuities, standard black-on-white Amsler chart testing, pupillary light reflex, fundus examination, followed by dilated fundus photographs and OCT of the macula.*

Results: *A total of 134 patients were included in the study. The prevalence of positive fundus finding and macular OCT finding was 35% (95% confidence interval [CI]: 27%, 43%) and 13% (95% CI: 8%, 19%), respectively; 62 eyes of 47 patients had positive fundus findings, whereas 30 eyes of 18 patients had positive macular OCT findings. Scotoma ($p < 0.001$), near vision disturbance ($p = 0.04$), and abnormal Amsler findings ($p < 0.001$) were significantly associated with presence of macular OCT findings compared to absence of macular OCT findings. In the total of 268 eyes, the two most common fundus findings were vessel tortuosity (53 [20%]) and yellow subretinal dot (28 [10%]). Out of 30 eyes, diffuse retinal thickening was the most frequent OCT finding (22 [73%]), followed by 4 (13%) with foveolitis, 3 (10%) with cystoid macular oedema and 1 (3%) with submacular fluid. Platelet count and haematocrit were not associated with abnormal fundus or macular OCT manifestation in patients suffering from dengue fever.*

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Conclusion: *Our study revealed that the prevalence of clinical fundus and macular OCT findings among dengue inpatients was higher when compared to other countries, especially during dengue outbreaks. Furthermore, the spectrum of fundus and macular OCT findings in our population can be varied.*

Keywords: *dengue, fundus, optical coherence tomography*

Introduction

Dengue virus (DEN) is a common *Aedes*-borne flavivirus of humans in Malaysia. There are four antigenically related serotypes present in Malaysia, which include DEN-1, 2, 3, and 4.[1] The World Health Organization (WHO) estimates 50 to 100 million dengue infections occurring annually across 100 countries including Asia, Pacific regions, Americas, Africa, and Caribbean.[1]

Dengue is endemic in Malaysia, and the incidence has more than doubled from 2013 to 2014, with an increment over 150%.[2] The cumulative number of reported dengue cases in 2015 alone had reached almost 120,000.[2] Perak is the fourth largest state in Malaysia, and the cumulative incidence of dengue was 8,157 cases from January to October 2015. In comparison to 2014, it was half of the numbers reported within the same period.[3] Our study hospital, Hospital Raja Permaisuri Bainun, is the referral hospital in Perak.

For the past few decades, there have been numerous reports describing ocular manifestations associated with dengue fever. These findings ranged from mild subconjunctival haemorrhage to significant visual morbidities.[4-11] However, the prevalence of dengue-related ocular findings is not well studied and there are no local data available. A study by Teoh *et al*.[12] has shown that optical coherence tomography (OCT) is a useful tool in assessing dengue maculopathy. Three patterns of maculopathy are identified—diffuse retinal thickening, cystoid macular oedema and foveolitis. Approximately 18% of patients with diffuse retinal thickening are asymptomatic. To the best of our knowledge, there is no reported study on the prevalence of macular OCT findings among dengue patients.

The interval between presentation with ocular symptoms and the onset of dengue fever is a mean of 7 days (range of 1-28 days).[8] However, a study by Gupta *et al*. has reported a delayed onset of post-dengue uveitis 3 to 5 months after dengue infection.[9] The precise pathophysiology of dengue ophthalmic complications is not known. Studies have suggested the possibility of immune-mediated process.[10] The management of dengue-related ocular complications is variable, ranging from observation to immunosuppression as there is no consensus for treatment or guideline-based therapy.

This study aims to investigate the prevalence of fundus and macular OCT findings, and the spectrum of dengue-related fundus presentation in a referral

hospital in Malaysia. As dengue infection is associated with derangement in platelet count and haematocrit, the association between the platelet counts (and haematocrit) and the fundus findings (and macular OCT findings) is investigated.

Methods

This was a cross-sectional study conducted at Hospital Raja Permaisuri Bainun, Ipoh, from June to August 2015. A total of 134 patients were included in the study based on dengue prevalence of 7.5%,[13] with 95% CI of 5% precision.[14] The primary investigator was responsible for the recruitment process and ocular examination. Daily screening of all newly admitted dengue patients (within 24 hours of admission) was carried out at bedside.

All dengue patients who were admitted with a clinical diagnosis of dengue fever[15,16] (confirmation via NS1/dengue serology), age ≥ 12 years, able to sit for ocular examination and investigation, and a presence of clear media allowing fundus examination were included in the study. Patients who were clinically unstable, unwilling to give consent, with other febrile illnesses, with pre-existing ocular diseases or with a history of intraocular surgery within the last 3 months were excluded.

The criteria for admission based on Malaysian Dengue Clinical Practice Guidelines[16] include the presence of alarming symptoms and signs, namely abdominal pain, persistent vomiting, clinical fluid accumulation, restlessness, tender enlarged liver or laboratory results showing increment in haematocrit level with concurrent decrease in platelet count, bleeding manifestations, inability to tolerate oral fluid, urine output reduction or seizures. Other admission criteria are patients with signs of dehydration, shock, bleeding or any organ failure. Patients were also being admitted under special circumstances such as elderly or for social factors that limit follow-up. Informed consent was obtained from all the participants. The study received ethical approval from the Ministry of Health Malaysia (NMRR-15-117-23895), and adhered to the tenets of the Declaration of Helsinki.

All enrolled patients were first subjected to a comprehensive ocular examination of best-corrected distance (6 m) and near visual acuities, standard black-on-white Amsler chart testing, pupillary light reflex, fundus examination using slit-lamp biomicroscope (Topcon SL D7), followed by dilated fundus photographs and OCT of the macula (Cirrus HD-OCT; Zeiss). The fundus and OCT findings were re-checked by another ophthalmologist for agreement on the findings.

Patients were further categorized into either normal or abnormal based on the presence or absence of dengue-related fundus or macular OCT findings. Patients with normal fundus or macular OCT findings were taught self-monitoring with a

near visual acuity chart and Amsler chart, and were advised to report should there be any ocular symptoms within 1 month of dengue infection. Platelet count and haematocrit level were recorded. Subjects with abnormal fundus or macular OCT findings were observed or managed according to our standard clinical practice.

This study used the classification and phases of dengue as proposed by the WHO.[15] According to the suggested WHO classification 2009, dengue is classified based on the level of severity as dengue with or without warning signs and severe dengue. The criteria of severe dengue included severe plasma leakage, severe haemorrhage and severe organ impairment. The clinical course of dengue infection consists of three phases which are febrile, critical and recovery phase.

The degree of thrombocytopenia was divided into $<50 \times 10^9$/l (severe) and $\geq 50 \times 10^9$/l (moderate and mild) for data interpretation.[17] All data were entered into Statistical Package for the Social Sciences version 20.0 for univariate and multivariate analysis; $p < 0.05$ was the cut-off point for statistical significance. Distance visual acuity was recorded in logarithm of the minimum angle of resolution (logMAR) for data analysis.

Results

During the study period between June and August 2015, a total of 245 (record taken from ward census) dengue patients were admitted. However, 103 patients were excluded based on exclusion criteria. Another eight patients were admitted at odd hours and discharged before screening could be done (admitted <24 hours).

Out of 245 patients, a total of 134 (55%) patients participated in this study, and fundus and OCT findings were recorded from both eyes. There were 75 (56%) male and 59 (44%) female patients. Their ages ranged from 12 to 82 years (median age of 27.5 years). Sixty-three per cent of participants were <35 years old. Malays and Chinese comprised three quarters of the participants, which mirrors the local population. The mean interval between onset of illness and admission was 6.86 days. Seventy-two per cent were admitted as dengue infection with warning signs, while 9.7% had severe dengue infection. More than half were in recovery phase. One quarter of the participants were found with at least one comorbidity. Table 1 illustrates the demographics of the subjects.

Among 134 patients, the prevalence of positive fundus findings was 35% (95% CI: 27%, 43%) and positive OCT findings was 13% (95% CI: 8%, 19%). In other words, out of 134 patients, 47 subjects had positive fundus findings, whereas 18 subjects were found to have positive macular OCT findings. Only one of the patients with positive OCT findings had comorbidity in the form of bronchial asthma.

Table 2 compares the eyes with and without OCT finding. Total 30 eyes were found to have OCT findings. Among the eyes with positive macular OCT findings, the main symptom was blurring of vision (40%), followed by scotoma (30%), near

Table 1. Characteristics of the study population (n = 134)

Characteristic	
Age (years), median (min, max)	27.50 (12, 82)
Gender, n (%)	
Male	75 (56.0)
Female	59 (44.0)
Ethnicity, n (%)	
Malays	57 (42.5)
Chinese	45 (33.6)
Indians	26 (19.4)
Others	6 (4.5)
Day of illness, mean (SD)	6.86 (1.76)
Classification of dengue, n (%)	
Without warning sign	24 (17.9)
With warning signs	97 (72.4)
Severe dengue	13 (9.7)
Phase of dengue fever, n (%)	
Febrile	8 (6.0)
Critical	52 (38.8)
Recovery	74 (55.2)
Comorbidity, n (%)	
Diabetes	6 (4.5)
Hypertension	10 (7.5)
Diabetes and hypertension	9 (6.7)
Bronchial asthma	6 (4.5)
None	103 (76.9)
Platelet count ($\times 10^9$/l), median (min, max)	60.00 (7,355)
Haematocrit (%), mean (±SD)	42.86 (4.69)

SD: standard deviation

Table 2. The characteristic of eyes with OCT findings (n = 30)

Characteristic	Eyes with OCT findings (n = 30)	Eyes without OCT finding (n = 238)	p value
Visual symptoms, per eye, n (%)[a]			
Blurring of vision	12 (40)	81 (34.0)	0.52[b]
Scotoma	9 (30)	0 (0.0)	<0.001[c]
Near vision disturbance	8 (26.7)	28 (11.8)	0.04[c]
Metamorphopsia	2 (6.7)	1 (0.4)	–
Asymptomatic	14 (46.7)	151 (63.4)	0.08[b]
Macular findings[a]	17 (57)	0 (0.0)	–
Dull foveal reflex	13 (43.3)		
Macular haemorrhage	8 (26.7)		
Macular oedema	4 (13.3)		
Normal (subclinical)	13 (43.3)		
Distance VA			
Worse than logMAR 0.15, n (%)	17 (56.7)	93 (39.1)	0.07[b]
Near VA			
N6 or worse, n (%)	6 (20)	44 (18.5)	0.84[b]
Amsler findings, n (%)			
Presence	10 (33)	0 (0.0)	<0.001[c]
Central	5 (16.7)		
Paracentral	5 (16.7)		

VA: visual acuity
[a]One eye can have more than one type of visual symptoms/macular findings
[b]Pearson Chi-square
[c]Fisher's exact test

vision disturbance (27%) and metamorphopsia (6.7%). Eyes with dengue macular OCT findings were more likely to have scotoma ($p < 0.001$) and near vision disturbance ($p = 0.04$). However, 14 (47%) of affected eyes were asymptomatic or unnoticed symptoms because of mild visual disturbance. Amsler findings had further detailed the types of scotoma, of which paracentral and central scotoma

were equally common. Our study revealed that none of the patients with negative macular OCT findings had scotoma ($p < 0.001$) and abnormal Amsler findings ($p < 0.001$). Moreover, near and distance visual acuities were compared between the two groups based on the study done by Su *et al*.[18] Our study found there was no statistical difference in visual acuities between the two groups. Meanwhile, as high as 13 (43%) eyes with macular OCT findings had been labelled clinically as normal. However, dull foveal reflex (43%) had been shown to be the most frequent macular abnormality, followed by macular haemorrhage (27%) and macular oedema (13%). In our study, none of these subclinical macular OCT finding patients developed clinically significant maculopathy.

In the total of 268 eyes, 62 eyes were found to have one or more fundus findings. Vessel tortuosity and yellow subretinal dot were the two most common clinical fundus findings occurring in 20% and 10% of eyes, respectively. Vessel tortuosity commonly happened bilaterally compared to yellow subretinal dot which tends to occur unilaterally. Other fundus findings were <5% of eyes, and the spectrum of fundus findings are shown in Table 3.

Diffuse retinal thickening was the commonest OCT abnormality in the study (Table 4). Out of these 30 eyes, 73% of macular OCT findings were diffuse retinal thickening. Other findings included foveolitis (13%), cystoid macular oedema (10%) and submacular fluid (3%). Twelve patients were found to have bilateral macular OCT findings and 6 participants with unilateral findings. Out of these

Table 3. Types of fundus findings

Types	Number of eyes	% (n = 268)	Unilateral	Bilateral
Vessel tortuosity	53	19.8	3	25
Yellow subretinal dot	28	10.4	12	8
Dull foveal reflex	12	4.5	4	4
Macular haemorrhage	8	3.0	2	3
Macular oedema	7	2.6	1	3
Retinal vasculitis	7	2.6	1	3
Disc swelling and hyperaemia	4	1.5	0	2
Retinal haemorrhage	1	0.4	1	0
Cotton wool spot	1	0.4	1	0

One eye can have more than one type of fundus findings

12 patients with bilateral positive macular OCT findings, 9 had similar types of macular OCT findings in each eye.

In terms of univariate analysis, there was no significant association between the presence of fundus abnormalities with patients' demographic (age, gender, ethnicity, day of illness, classification or phase of dengue and comorbidity), platelet count and haematocrit level (Table 5). With regard to

Table 4. Types of OCT findings

Types	Number of eyes, n = 30 (%)	% (n = 268)	Unilateral	Bilateral
Diffuse retinal thickening	22 (73.3)	8.2	6	8
Foveolitis	4 (13.3)	1.5	2	1
Cystoid macular oedema	3 (10.0)	1.1	3	0
Submacular fluid	1 (3.3)	0.4	1	0

Table 5. Summary of demographics and laboratory test results of fundus and OCT macula with abnormal features

No	Characteristic	Fundus features present (n = 47)	p value	OCT features present (n = 18)	p value
1	*Age (years)*				
	Median (min, max)	25.00 (12, 64)	0.06[a]	21.50 (12, 36)	0.001[a]
2	*Gender, n (%)*				
	Male	29 (61.7)	0.33[b]	12 (66.7)	0.33[b]
	Female	18 (38.3)		6 (33.3)	
3	*Ethnicity, n (%)*				
	Malays	22 (46.8)	0.56[b]	5 (27.8)	0.04[c]
	Chinese	13 (27.7)		11 (61.1)	
	Indians and others	12 (25.5)		2 (11.1)	
4	*Day of illness*				
	Median (min, max)	7 (2, 12)	0.80[a]	7 (4, 9)	0.04[a]

No	Characteristic	Fundus features present (n = 47)	p value	OCT features present (n = 18)	p value
5	*Classification of dengue, n (%)*				
	Without warning sign	11 (23.4)	0.22[b]	6 (33.3)	0.09[c]
	With warning signs and severe dengue	36 (76.6)		12 (66.7)	
6	*Phase of dengue fever, n (%)*				
	Febrile and critical	26 (55.3)	0.07[b]	7 (38.9)	0.59[b]
	Recovery	21 (44.7)		11 (61.1)	
7	*Comorbidity, n (%)*				
	Present	9 (19.1)	0.42[b]	1 (5.6)	0.07[c]
	Absent	38 (80.9)		17 (94.4)	
8	*Platelet count ($\times 10^9$/l), n (%)*				
	<50	22 (46.8)	0.32[b]	8 (44.4)	0.75[b]
	50 and above	25 (53.2)		10 (55.6)	
9	*Haematocrit, n (%)*				
	<40	14 (29.8)	0.58[b]	6 (33.3)	0.57[c]
	40 and above	33 (70.2)		12 (66.7)	

[a]Mann-Whitney U test
[b]Pearson Chi-square
[c]Fisher's exact test

the commonest presentations of fundus findings, both vessel tortuosity and yellow subretinal dot denied association with platelet count or haematocrit. The same parameters were evaluated for OCT macula in univariate analysis (Table 5). Our study showed that patients with abnormal macular OCT findings were significant younger (p = 0.001), Chinese ethnicity predominant (p = 0.04) and day of illness ranged from day 4 to day 9 (p = 0.04). Platelet

count and haematocrit level had no role in the presence of dengue-related macular OCT features.

Similarly, there was no significant association seen between the presence of fundus findings with patients' demographics, platelet count and haematocrit level in both single and multiple logistic regressions (Tables 6 and 7). However, multivariate logistic regression showed Chinese ethnicity (odds ratio [OR] 3.48; 95% CI: 1.05, 11.54; p = 0.04), dengue without warning sign (OR 5.08; 95% CI: 1.35, 19.11; p = 0.02) and absence of comorbidity (OR 8.54; 95% CI: 0.98, 74.30; p = 0.05)

Table 6. Single logistic regression (SLR) of fundus findings

Factors	Fundus findings (n = 47)	No fundus finding (n = 87)	SLR OR (95% CI)	p value
Platelet count ($\times 10^9$/l)				
<50	22 (46.8)	33 (37.9)	1.44 (0.70, 2.95)	0.32
50 and above	25 (53.2)	54 (62.1)	1.00	
Haematocrit (%)				
<40	14 (29.8)	22 (25.3)	1.25 (0.57, 2.76)	0.58
40 and above	33 (70.2)	65 (74.7)	1.00	

Table 7. Multiple logistic regression (MLR) of fundus findings

Factors	Fundus findings (n = 47)	No fundus finding (n = 87)	MLR OR (95% CI)	p value
Platelet count ($\times 10^9$/l)				
<50	22 (46.8)	33 (37.9)	0.67 (0.32, 1.39)	0.28
50 and above	25 (53.2)	54 (62.1)	1.00	
Haematocrit (%)				
<40	14 (29.8)	22 (25.3)	1.33 (0.60, 2.97)	0.48
40 and above	33 (70.2)	65 (74.7)	1.00	

(Tables 8 and 9) were significant confounders in the presence of abnormal macular OCT findings. In our study, 28 of our patients had cataract but none of them had undergone any intraocular surgery. None of the patient with normal fundus or macular OCT finding (or subclinical macular OCT finding) was reassessed due to new eye complaint.

Table 8. Single logistic regression (SLR) of macular OCT findings

Factors	OCT findings (n = 18)	No OCT finding (n = 116)	SLR OR (95% CI)	p value
Platelet count ($\times 10^9$/l)				
<50	8 (44.4)	47 (40.5)	1.17 (0.43, 3.20)	0.75
50 and above	10 (55.6)	69 (59.5)	1.00	
Haematocrit (%)				
<40	6 (33.3)	30 (25.9)	1.43 (0.49, 4.16)	0.51
40 and above	12 (66.7)	86 (74.1)	1.00	
Ethnicity, n (%)				
Malays	5 (27.8)	52 (44.8)	1.00	0.04
Chinese	11 (61.1)	34 (29.3)	3.37 (1.07, 10.54)	0.04
Indians and others	2 (11.1)	30 (25.9)	0.69 (0.13, 3.80)	0.67
Classification of dengue, n (%)				
Without warning sign	6 (33.3)	18 (15.5)	2.72 (0.91, 8.19)	0.08
With warning signs and severe dengue	12 (66.7)	98 (84.5)	1.00	
Comorbidity				
Present	1 (5.6)	30 (25.9)	1.00	0.09
Absent	17 (94.4)	86 (74.1)	5.93 (0.76, 46.49)	

Table 9 Multiple logistic regression (MLR) of macular OCT findings after adjusting for other confounders.

Factors	OCT findings (n = 18)	No OCT finding (n = 116)	MLR OR (95% CI)	p value
Platelet count ($\times 10^9$/l)				
<50	8 (44.4)	47 (40.5)	1.94 (0.61, 6.19)	0.27
50 and above	10 (55.6)	69 (59.5)	1.00	
Haematocrit (%)				
<40	6 (33.3)	30 (25.9)	2.43 (0.71, 8.37)	0.16
40 and above	12 (66.7)	86 (74.1)	1.00	
Ethnicity, n (%)				
Malays	5 (27.8)	52 (44.8)	1.00	0.04
Chinese	11 (61.1)	34 (29.3)	3.48 (1.05, 11.54)	0.04
Indians and others	2 (11.1)	30 (25.9)	0.61 (0.10, 3.79)	0.60
Classification of dengue, n (%)				
Without warning sign	6 (33.3)	18 (15.5)	5.08 (1.35, 19.11)	0.02
With warning signs and severe dengue	12 (66.7)	98 (84.5)	1.00	
Comorbidity				
Present	1 (5.6)	30 (25.9)	1.00	0.05
Absent	17 (94.4)	86 (74.1)	8.54 (0.98, 74.30)	

Discussion

Out of 134 patients, the prevalence of positive fundus findings is 35% (62 eyes of 47 patients) and of OCT findings is 13% (30 eyes of 18 patients). Vessel tortuosity (53 eyes, 28 patients) and yellow subretinal dot (28 eyes, 20 patients) are the two most common fundus findings. Diffuse retinal thickening is the most

frequent OCT finding. It was found in 73% out of 30 eyes with OCT findings. There is no association between platelet count and haematocrit level, with presence of abnormal fundus or macular OCT findings.

To date, this is the first study to assess the prevalence of macular OCT findings among dengue patients. Our patients were recruited strictly based on inclusion and exclusion criteria. Slit-lamp and OCT machines used were standardized in the study. In addition, the fundus and OCT findings were re-checked by a consultant ophthalmologist to ensure the accuracy of the findings.

There are several limitations in this study which need to be addressed. Dengue affects all patients regardless of age group across Malaysia. However, this study was conducted at a single centre, and excluded outpatients, which may limit some of the findings. Moreover, patients may have unchecked or undiagnosed clinical or macular OCT findings prior to dengue fever. The immobility of the assessment tools requires sophisticated transport procedures. It is therefore difficult to conduct similar assessment on unstable or critically ill patients.

The prevalence of fundus findings in this study is 35%. It is higher compared to a study done by Kapoor *et al*.[13] The difference could be due to the inclusion of yellow subretinal dot as a manifestation of dengue-related complication, in the absence of any other causes. Yellow subretinal dot has been listed as one of the fundus findings of dengue as suggested by other studies.[18,19] Furthermore, absence of macular finding in the study done by Kapoor *et al*. could be another contributing factor of the lower prevalence.[13]

OCT finding in this study was detected in 13% of patients (30 eyes of 18 patients). However, there were 8% (17 eyes of 11 patients) of patients who had clinically abnormal macular findings. In other words, 5% (13 eyes of 7 patients) of the patients with OCT findings had no detectable clinical findings. These findings strongly suggest OCT is more sensitive in detecting dengue-related maculopathy.

A study done in Singapore by Su *et al*. in the year 2005 found 10% of dengue patients had clinical maculopathy,[18] while Chee in Singapore in year 2007[20] and Kapoor *et al.* in India[13] did not find any macular-related finding. The difference is most likely attributed by the different subtype of the DEN affecting different populations. In Singapore, the DEN-1 was predominant in the community in year 2005, whereas DEN-2 was predominant in year 2007. No individual dengue serotyping was performed. During our study period, DEN-1 had been the dominant serotype (60%).[2] It was similar to the study in Singapore in year 2005 in which the predominant (71.2%) dengue serotype was type 1.[20]

Similar to other studies,[12,21,22] our study found that vessel tortuosity was the most frequent fundus findings which was 20% (53 eyes) while diffuse retinal thickening (73%, 22 eyes) was the commonest macular OCT findings, followed by foveolitis (13%, 4 eyes) and cystoid macular oedema (10%, 3 eyes). However,

distinct from other studies,[11,19] macular haemorrhage, retinal vasculitis and retinal haemorrhage were unusual fundus findings in our study which only contributed 3.0% (8 eyes), 2.6% (7 eyes) and 0.4% (1 eye), respectively. One of the patients had macular OCT finding of submacular fluid which was never reported in previous studies. A study shows increased vascular permeability was observed in DEN-1, whereas more systemic haemorrhage was associated with DEN-2.[23] Based on the results, we postulate that DEN-1-infected patients have higher risk of maculopathy because of increased vascular permeability, whereas patients with DEN-2 has more risk of retinal haemorrhage.

Consistent with a study done by Su *et al*.,[18] our study found that there was a significant association between subjects having scotoma ($p < 0.001$) and abnormalities on Amsler grid testing ($p < 0.001$) with presence of OCT findings. However, we did not find significant difference of near or distance visual acuity between those with and without dengue maculopathy. This could be due to early cataract, under- or uncorrected refractive error in patients without dengue maculopathy.

In clinical management of dengue infection, blood investigations, traditionally full blood count, have been used as a screening and monitoring test for dengue infection. Among the available parameters, platelet count and haematocrit are frequently used to assist in dengue management. The risk factors of ocular complications following dengue infection have been studied. Some evidences showed that the severity of retinal abnormalities is related to the severity of thrombocytopenia.[13,21,24] However, our study showed there was no significant association detected between fundus findings with platelet count and haematocrit. The reason could be due to less retinal and macular haemorrhage in our fundus findings. In this study, we also did not find any significant association between the patients' demographics with fundus findings.

Similar to the other studies,[18,20] our study found that patients with dengue-related macular OCT findings were significantly younger than those without OCT findings ($p < 0.001$). Moreover, platelet and haematocrit had no impact on the presence of clinical dengue- related macular finding. Although the precise pathophysiology of dengue ophthalmic complications is still not elucidated, this study suggests that the possibility of younger age group has more robust immune-mediated process.[10,18,19] In addition, the delayed onset of dengue maculopathy in days 4 to 9 in our study favours the possibility of immune response in development of dengue maculopathy.

In multivariate logistic regression analysis, dengue without warning sign, Chinese ethnicity and absence of comorbidity were found to be the significant confounders in this study as far as OCT findings are concerned. The pathophysiology behind this association remains unknown. We believe that it is related to variable immune-mediated mechanism in patients with comorbid issues like

diabetes mellitus, hypertension and bronchial asthma or even among different ethnicities or different severity of dengue. However, none of the factors above showed any association with clinical fundus finding.

Results from our study show that it is not uncommon to have fundus or OCT findings in our population. Furthermore, the spectrum of fundus and macular OCT findings in our population can be varied. Platelet count and haematocrit level have little value as the predictors in dengue maculopathy. Instead, Amsler grid testing is still a useful and important test in the screening of dengue maculopathy. It may not be time and cost effective for eye screening in all dengue patients. However, fundus examination should be done in dengue patients with scotoma, near visual disturbance or abnormal Amsler finding.

We propose a larger multicentre study, looking at all dengue patients both admitted and those seen as outpatients, to provide further understanding of ocular manifestation of dengue fever. Furthermore, association between different serotype of *Aedes*-borne flavivirus and fundus and/or OCT finding should be investigated.

Conclusion

In conclusion, our study reveals that the prevalence of clinical fundus and macular OCT findings among dengue inpatients was higher compared to other countries especially during dengue outbreaks. Furthermore, the spectrum of fundus and macular OCT findings in our population can be varied.

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Asian J Ophthalmol. 2019;16:284-292

Original Article

Contrast sensitivity before and after small incision lenticule extraction and femtosecond laser in situ keratomileusis

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Abstract

Introduction: *Contrast sensitivity function after laser ablation of the cornea in refractive surgery is an important tool for measuring quality of visual function. The effect of small incision lenticule extraction (SMILE) and femtosecond laser in situ keratomileusis (FS-LASIK) on visual function can be compared by measuring spatial contrast sensitivity.*

Purpose: *This study was to compare contrast sensitivity function in patients undergoing refractive surgery for myopia at Tilganga Institute of Ophthalmology.*

Methods: *In a retrospective study, 15 subjects who underwent refractive surgeries comprising 9 cases of SMILE and 6 cases of FS-LASIK at Tilganga Eye Hospital were enrolled in the study. A major assessment included best corrected monocular contrast sensitivity with functional vision analyzer at spatial frequencies of 1.5, 3, 6, 12, and 18 cycles/deg in photopic condition (85 cd/m2) before, 3 months, and 1 year after the surgery. The average functional acuity contrast test scores for each spatial frequency were recorded. Differences between preoperative and postoperative contrast sensitivity at each spatial frequency were analyzed through parametric paired Student's t-test.*

Results: *Contrast sensitivity of postoperative FS-LASIK and SMILE did not differ from preoperative values at a photopic level. However, at high spatial frequency (12 and 18 cycles/deg), contrast sensitivity function improved significantly ($p < 0.05$) in eyes after FS-LASIK. Eyes after SMILE surgery did not show any reduction in contrast sensitivity at all the spatial frequencies.*

Conclusion: *Under photopic conditions, the contrast sensitivity function is unaffected by SMILE or FS-LASIK.*

Keywords: *contrast sensitivity, FS-LASIK, myopia, SMILE*

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Introduction

Excimer laser refractive surgery aims to reproduce the preoperative optical performance while making the eye emmetropic. Though technology and refractive surgeons have made great strides toward establishing emmetropia postoperatively, they have not been able to duplicate the optical performance previous to surgery. Some studies have reported visual problems such as haze, halos, stray light images, or glare in patients following refractive surgery,[1-9] complications that cause significant decreases in visual performance. Efforts have been made to achieve better results by modifying some characteristics of the surgery such as transition zones, multistep ablations, and new techniques like femtosecond laser in situ keratomileusis (FS-LASIK) and small incision lenticule extraction (SMILE).

LASIK has evolved from a variety of techniques in refractive surgery. LASIK combines a technique of creating a hinged corneal flap from the automated lamellar keratectomy with excimer laser ablation from the photorefractive keratectomy (PRK). In early days, a microkeratome was used to create corneal flaps. But, nowadays, it has been replaced by femtosecond laser that creates precise and desired corneal flaps. Since Food and Drug Administration approval of an ultrafast laser in 2000, the femtosecond laser has transfigured the creation of flaps for LASIK.[10-13] The pulse duration of the femtosecond laser is in the 10^{-15} second range. The 1,053 nm wavelength of light used by the laser is not absorbed by optically transparent tissues. Moreover, it can be focused anywhere within the cornea where the energy can be raised to a threshold such that a plasma is generated.[14] The corneal flap is kept aside and the excimer laser is applied to reshape the surface of the cornea by removing anterior stromal tissue. The word excimer is an abbreviation of the term "excited dimer." The excimer laser produces a beam of ultraviolet energy at various wavelengths depending upon the gas elements used. The 193 nm ultraviolet light from the argon fluoride laser, which has the least corneal transmission, causes less adjacent tissue damage and creates a smoother ablation than longer wavelength lasers.[15] At a wavelength of 193 nm, high-energy photons break organic molecular bonds of the superficial corneal tissue in a process called ablative photodecomposition.[16,17] Further improvement in lasers occurs with eye-tracking systems that allow precise corneal ablation during eye movement.[18]

SMILE involves the use of a femtosecond laser to create a corneal lenticule that is extracted whole through a small incision without the use of an excimer laser. In 2007, an intrastromal lenticule method was reintroduced as an alternative to LASIK called femtosecond lenticule extraction (FLEx) and was intended for patients with extreme myopia. After improvements to scan modes and energy parameters, improved visual recovery times were noted (stability and predictability of the refractive outcome, improvement in visual acuity with lesser

complications), with refractive results similar to LASIK.[19] Following the implementation of FLEx, a procedure called SMILE was developed, which involves passing a dissector thorough a small 2 to 3 mm incision to separate the lenticular interfaces and allow extraction of the lenticule without a need to create a flap.[20]

Contrast sensitivity is a very important measure of visual function, especially in situations of low light, fog, or glare, when the contrast between objects and their background often is reduced. It provides us information about the visibility of objects that vary in size, contrast, and orientation. Loss of contrast sensitivity can occur at high, low, and broad spatial frequencies. Various ocular and systemic diseases can affect contrast sensitivity functions in different ways and at different frequencies. Changes in contrast sensitivity can also be observed in the refractive surgeries that could be related to an increase in higher-order aberrations such as coma and trefoil. When there is a loss of contrast sensitivity, light entering the eye does not focus uniformly on to the retina. Instead, some of the light scatters and the vision in that eye can appear washed out and/or foggy. Loss of contrast sensitivity can range from not noticeable to extremely annoying.[21]

Montés-Micó *et al.*[22-25] reported that visual function after refractive surgery can be documented by measuring spatial contrast sensitivity. It assesses the combined visual impact of any light scattering, optical aberration, or defocus that may occur following refractive surgery.[6,8-9,26] However, in order to explore the visual performance in patients before and after refractive surgery, mesopic contrast sensitivity function should be evaluated.[26] These authors found significant reduction in contrast sensitivity under mesopic conditions following PRK and LASIK, even though the photopic contrast sensitivity function was normal.

FS-LASIK and SMILE are now available in Nepal. Though FS-LASIK and SMILE provide normal uncorrected visual acuity, the visual performance in different illuminations is largely unknown in our context. As the contrast sensitivity function is one of the major determinants of visual performance, the present study was conducted to compare contrast sensitivity function among patients before and after SMILE and FS-LASIK.

Materials and methods

This study was a retrospective, longitudinal, and comparative analysis of 15 subjects who underwent SMILE (nine subjects) and FS-LASIK (six subjects) for correction of myopia and myopic astigmatism at Tilganga Institute of Ophthalmology, Kathmandu, in July and August 2014. All subjects were programmed for SMILE and LASIK procedure. The procedure that gave the maximum correction with minimum amount of tissue loss was selected as an operating procedure for that individual subject. The mean age of subjects undergoing FS-LASIK was 22.0 (SD 3.8) years, with the age ranging between 18 and 27 years. The mean age of

subjects selected for SMILE was 24.8 (SD 4.6) years, with the age ranging between 19 and 30 years.

All the subjects who were enrolled in the study had stable refraction, keratometry, and pachymetry at least for 12 months and did not have dry eye, any preoperative medication other than those prescribed, active diseases of ocular surface, and adnexa. No patient had ocular morbidities that could affect contrast sensitivity such as glaucoma, corneal and neuro-ophthalmic diseases, or cataracts. Those patients who were lost to follow-up during 3 and 12 months were excluded. All patients received a detailed explanation of the procedure involved in the study and provided informed consent. The approval of the implementation of the study was sought from the ethical review committee of Tilganga Institute of Ophthalmology, Kathmandu. The study protocol adhered to the provision of the Declaration of Helsinki for research involving human subjects.

Intervention

All patients' eyes were cleaned with sterile cotton and ofloxacin (0.3%) eye drops were applied 10 minutes before the procedure. Patients were laid supine on the operating table and proparacaine 0.5% eye drops was applied for topical anesthesia. Visual axis was documented in both eyes. Docking or ocular alignment was done as per the visual axis and suction was applied. Carl Zeiss VisuMax femtosecond laser (Carl Zeiss Meditec, Jena, Germany) was applied for lenticule or flap creation and for superficial corneal incision. Both nasal and temporal 2 mm incisions were made superiorly. Using the dissector, the lenticule was separated and taken out with forceps in the SMILE procedure, while the flap was separated and lifted, exposing the anterior stroma for ablation in LASIK. In LASIK, Carl Zeiss MEL 80 was used for photoablation and the flap was replaced back. A slit-lamp examination was performed in the operating room to check for any interface particles and the wound site. Postoperatively, patients were observed for an hour and discharged with proper medication instructions (prednisolone eye drops 1% four times a day, tobramycin eye drops 0.3% four times a day, ofloxacin eye drops 0.3% four times a day, sodium carboxymethylcellulose 0.5% every hour).

Assessment

Assessment included measurement of visual acuity in internally illuminated Bailey Lovie logMAR chart at 4 m distance, objective refractive status with Topcon Auto Kerato-Refractometer (KR-8900), subjective refraction to find out subjective acceptance of refractive error, best spectacle corrected visual acuity before surgery, and uncorrected visual acuity after surgery. Subjects' preoperative variables (corneal power, corneal astigmatism, and corneal thickness) were

obtained through corneal topography (Atlas 9000) and Oculus Pentacam 70700 (SN 3951 5001). Corneal thickness was measured with OptoVue pachymetry (RTVue-100 Fourier domain OCT) version 6.9.

Contrast sensitivity function was measured with functional vision analyzer (Vision Tester 6500P; Stereo Optical Company Inc., Chicago, IL). In this test, the grating patches on rows A to E correspond to spatial frequencies of 1.5, 3, 6, 12, and 18 cycles/deg. The patient scanned the patches from left to right and reported the last pattern recognized in each row and this response was recorded. The testing instrument was fixed at photopic condition (85 cd/m^2). The contrast sensitivity function was measured at various spatial frequencies presurgery with best optical correction and postsurgery unaided at 3 and 12 months. The average functional acuity contrast test scores for each spatial frequency were recorded and the contrast sensitivity function graph was plotted.

All data were evaluated using Statistical Package for the Social Sciences (version 16.0). Differences between preoperative and postoperative contrast sensitivity at each spatial frequency were analyzed through parametric paired Student's t-test. The p-value was considered significant at 0.05 for 95% confidence interval.

Results

The mean age of the subjects undergoing refractive surgery was 23.7 ± 4.4 years (range: 18-32 years) including 11 males and 4 females. Distribution of preoperative and postoperative refractive error is given in Table 1. The mean spherical equivalent myopia (MSEM) was −4.68 ± 1.74 DS in the right eye, −4.88 ± 1.71 DS in the left eye, and −4.78 ± 1.72 DS in both eyes preoperatively. MSEM was −3.2 ± 0.8 (range −2.00 DS to −4.50 DS) for FS-LASIK and −5.9 ± 1.2 (range −4.00 DS to −7.50 DS) for SMILE. Postoperative residual refractive error that was recorded in 3 and 12 months was clinically insignificant and slightly at the hypermetropic side. All of the patients after refractive surgery had refractive error less than +0.75 DS of hyperopia postoperatively. Emmetropia was noted in 4 eyes (13.33%), whereas residual refractive error of +0.12 DS, +0.25 DS, +0.50 DS, and +0.75 DS was noted in 13 (43.33%), 4 (13.33%), 8 (26.66%), and 1 (3.33%) eyes, respectively, postoperatively. The postoperative refractive error was stable over the period of 12 months. Preoperative best spectacle corrected visual acuity was in the range of 20/20 to 20/16 in all the subjects. Postoperative visual acuity was 20/20 or better in 17 subjects (56.7%), 20/20 in 12 subjects (40.0%), and 20/25 in 1 subject (3.3%).

The mean corneal thickness of 30 eyes so included in the study was 528.07 ± 18.49 microns, which after corneal refractive surgery became 444.43 ± 23.34 microns. The average change in corneal thickness after LASIK was 69.58 ± 16.23 microns, whereas after SMILE it was 93 ± 25.32 microns.

Table 1. Distribution of mean spherical equivalent refractive error

Characteristics	Spherical equivalent refractive error		
	Right eye	Left eye	Both eyes
Preoperative	−4.68 ± 1.74 DS	4.88 ± 1.71 DS	4.78 ± 1.72 DS
3 months postoperative	+0.29 ± 0.20 DS	+0.27 ± 0.23 DS	+0.28 ± 0.21 DS
12 months postoperative	+0.20 ± 0.19 DS	+0.21 ± 0.17 DS	+0.21 ± 0.18 DS

Contrast sensitivity function after refractive surgeries

Figure 1 represents contrast sensitivity functions after refractive surgeries. Overall, contrast sensitivity function was found to be equally improved in 3 months and 1 year after the surgeries at spatial frequencies of 3, 12, and 18 cycles per minute (Fig. 1A and Table 2). Contrast sensitivity after LASIK surgery was noted to be equally improved in 3 months and 1 year at spatial frequencies of 12 and 18 cycles per minute. Though the graph sloped down in 1 year follow-up at spatial frequency of 6 cycles/minute, the contrast sensitivity function was insignificantly better than preoperative values (Fig. 1B and Table 2). Though contrast sensitivity function was improved after SMILE, this improvement was statistically insignificant at all the spatial frequencies (Fig. 1C and Table 2).

Discussion

The present study showed that both SMILE and FS-LASIK were predictable for the correction of myopia and myopic astigmatism and had better outcome of visual acuity. Myopic regression was seen in none of the cases included in this study for 12 months.

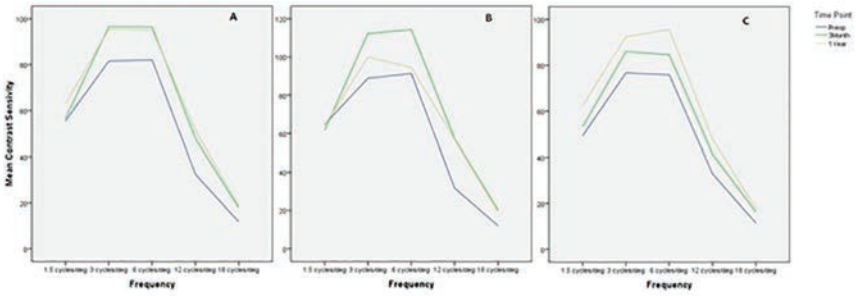

Fig. 1. Preoperative and postoperative contrast sensitivity in FS-LASIK and SMILE. (A: Overall; B: FS-LASIK; C: SMILE).

Table 2. Difference between preoperative and postoperative contrast sensitivity function at each spatial frequency

Spatial frequency (cycles/min)	Overall		FS-LASIK		SMILE	
	3 months	1 year	3 months	1 year	3 months	1 year
1.5	0.1816	0.8149	0.7249	0.9435	0.5474	0.0987
3.0	0.0149[a]	0.0264[a]	0.0572	0.2404	0.1478	0.06779
6.0	0.0853	0.1868	0.1114	0.8113	0.4073	0.1684
12.0	0.0113[a]	0.0021[a]	0.0309[a]	0.0149[a]	0.1880	0.0602
18.0	0.0494[a]	0.0056[a]	0.0450[a]	0.0175[a]	0.2924	0.0746

[a]Significantly different at $p \leq 0.05$ by a paired t-test

There was statistically insignificant increment in contrast sensitivity function after refractive surgery in our study. Preoperative contrast sensitivity was assessed in all subjects with refractive correction in trial lenses. Montés-Micó *et al*. reported no significant change in the level of contrast sensitivity under photopic conditions and dramatic reduction in contrast sensitivity under mesopic conditions.[25] We assessed contrast sensitivity in photopic conditions only. Under photopic conditions, contrast sensitivity of postoperative FS-LASIK patients did not differ from normal. In fact, the study showed improved contrast sensitivity function at high spatial frequencies (12 and 18 cycles/deg) after FS-LASIK. This outcome concurs with that reported by Pérez-Santonja and colleagues[26] and Montés-Micó and Charman, who found no statistically significant decrease in photopic contrast sensitivity at any spatial frequency 3 and 6 months after FS-LASIK.[24]

During early refractive surgery techniques and laser technologies, the quality of vision as measured by contrast sensitivity was typically lower after surgery. The introduction of customized wavefront LASIK greatly improved the accuracy of the laser surgery techniques, resulting in tremendous improvements in the quality of vision.[27] The Tuan *et al*. study showed an improvement in contrast sensitivity in a significant percentage of patients following custom LASIK.[28]

Similarly, contrast sensitivity function did not differ postoperatively after SMILE surgery under photopic conditions in our study. Prior studies also suggest that visual function does not alter even after laser refractive correction when evaluated at photopic state.[25]

While comparing the contrast sensitivity between FS-LASIK and SMILE, there was not much of a difference at low spatial frequencies prior to the surgery. However, at high spatial frequencies, contrast function seemed to improve

significantly after FS-LASIK compared to SMILE. The probable reason could be a smoother interface achieved after photoablation of the tissue with excimer laser in FS-LASIK.

This study only compared contrast sensitivity under photopic conditions among the subjects undergoing FS-LASIK and SMILE. So the application of the study is limited as no mesopic and scotopic conditions were maintained and compared. Generalization is also nominal, the sample size being very small. Important information such as topographic measurement data and tear function tests is missing in the study as it is being a retrospective study. Further prospective study is warranted considering all these variables and measuring them especially under mesopic and scotopic conditions.

Contrast sensitivity function is an important tool to measure visual function, which may be altered after multitude of refractive surgeries. Under photopic conditions, the contrast sensitivity function remains the same or becomes slightly better after refractive surgery.

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Asian J Ophthalmol. 2019;16:293-297

Extraocular muscle enlargement: rare presentation of plasmablastic lymphoma

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Abstract
Plasmablastic lymphoma (PBL) is a very rare and highly aggressive variant of non-Hodgkin lymphoma. It is usually seen in the oral cavity of human immunodeficiency virus (HIV)-affected individuals. Very few cases of PBL are reported in the orbit till date. Morphologically and immunologically, it can mimic plasma cell myeloma. It is highly fatal and poses diagnostic and therapeutic challenges to the treating clinician. This scenario makes reporting of such rare tumors more relevant. We report a rare case of PBL of the orbit in a 49-year-old HIV-positive lady who presented with acute onset of painful proptosis and loss of vision in her left eye.

Keywords: *extraocular muscle enlargement, HIV, NHL, plasmablastic lymphoma*

Introduction

Orbital lymphoma is a type of non-Hodgkin lymphoma (NHL) that can involve the conjunctiva, lacrimal gland, eyelid, or extraocular muscles.[1] It can be a primary lymphoma when it arises from the orbital tissues itself or a secondary lymphoma when there is a metastatic spread from an extraorbital site. Orbital lymphomas are very rare and form about 1% of all NHL and 55% of all primary orbital tumors.[2,3] It is more commonly seen in immunocompromised patients. But there are case reports of orbital lymphoma in human immunodeficiency virus (HIV)-negative otherwise healthy individuals also.[3] Majority of the cases are extranodal marginal zone B-cell lymphomas of mucosa-associated lymphoid tissue type.[3] Here, we are reporting a very rare, fatal variant of orbital lymphoma plasmablastic type, which is usually seen in the oral cavity of HIV-positive individuals.[4]

Case description

A 49-year-old immunocompromised female patient presented with an acute onset of painful proptosis of the left eye associated with loss of vision of 7 days duration. There was no history of trauma and fever. She was diagnosed to be HIV positive 5 years ago but was not on any antiretroviral therapy at the time of presentation.

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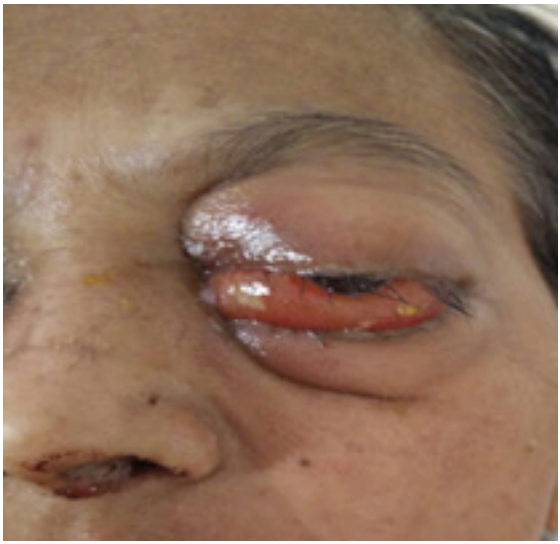


Fig. 1. Left eye proptosis with lid edema, conjunctival chemosis.

On examination, the best corrected visual acuity was 6/6p Snellen's in the right eye and counting finger 1 m in the left eye. Right eye examination was normal. Left eye showed proptosis of 9 mm on Hertel exophthalmometry. There was lid edema, conjunctival congestion, chemosis, and exposure keratitis (Fig. 1). Extraocular movements were restricted in all directions. Pupil showed relative afferent pupillary defect. Fundus showed pale disc with hemorrhages and cotton wool spots superior to disc.

A provisional diagnosis of orbital cellulitis was made. Patient was started on intravenous antibiotics, amoxicillin with clavulanic acid combination (1.2 g thrice daily), gentamicin (80 mg twice daily), and tinidazole (800 mg once daily). Her hemoglobin was 6.9 g/dl, erythrocyte sedimentation rate was 109 mm/hour (Ves-Matic cube method), CD4/CD8 ratio was 0.11 (normal value 2); absolute CD4 count was 91.74 cells/µl (normal value 500-1,200 cells/µl), lactate dehydrogenase (LDH) was highly raised: 959 IU/l (normal value 105-333 IU/l). Reports came positive for HIV-1. Computed tomography (CT) scan of the orbit showed enlargement of all the extraocular muscles of the left eye, with swollen bulky medial rectus abutting optic nerve at the orbital apex. Right medial rectus was also enlarged. There was no evidence of mass lesion or bony destruction (Fig. 2). Thyroid function test was done in view of enlarged muscles on CT and was normal. Chest x-ray was normal. Ultrasound abdomen did not

show any hepatosplenomegaly or enlarged lymph nodes. Bone marrow study was normal.

Transnasal endoscopic incision biopsy of the enlarged medial rectus of the left eye was done. Histopathology showed monomorphic population of medium sized to large abnormal lymphoid cells with round nuclei, some with 2-5 nucleoli and irregular nuclear membrane, others with eccentric nuclei with single nucleoli, moderate cytoplasm with perinuclear hof imparting a plasmacytoid appearance along with brisk mitosis, interspersed mature lymphocytes, apoptotic bodies, and numerous triple body macrophages containing karyorrhectic debris focally imparting a starry sky appearance (Fig. 3). Immunohistochemically, tumor cells were CK, CD79a, CD20, CD3 negative and CD138 positive.

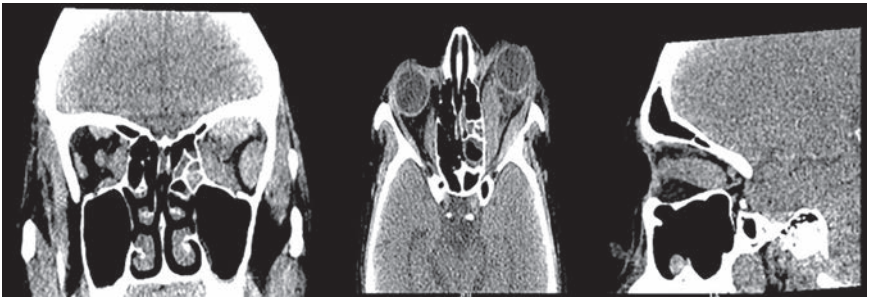
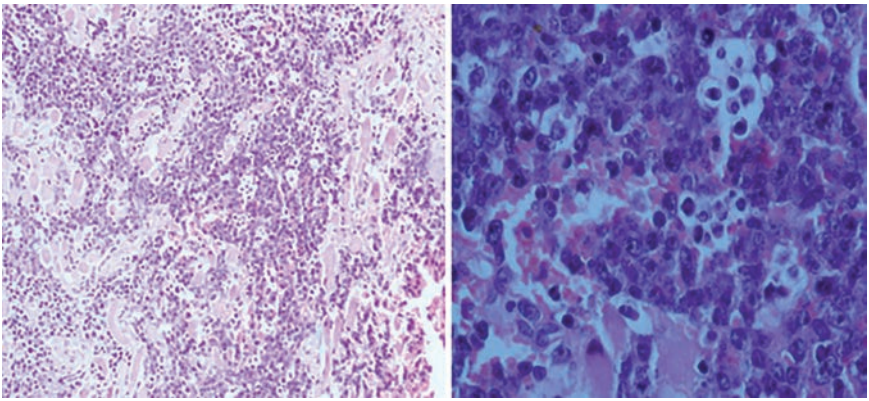


Fig. 2. CT images of orbit showing bulky extraocular muscles of left eye and enlarged medial rectus of right eye with no mass lesion.



Infiltration of tumor cells into and between skeletal muscle

Medium sized to large abnormal lymphoid cells

Fig. 3. Histopathology images.

These features confirmed the diagnosis of high-grade NHL plasmablastic type. Patient was referred to medical oncology. She was restarted on antiretroviral therapy; however, she refused further chemotherapy.

Discussion

Plasmablastic lymphoma (PBL) is considered as a distinct subtype of diffuse large B-cell lymphoma, which is seen more commonly in patients with HIV infection.[1] In 2008, Valenzuela *et al*. reported a case of PBL in a HIV-positive female, wherein the patient had lesions in the oral cavity following which she developed orbital manifestations,[5] and also by Barkhuysen *et al*., in which the presentation of PBL exactly mimicked orbital cellulitis.[6] Ocular involvement of PBL is very rare, with very few cases having been reported in literature till now.[2] Majority of the patients with PBL present with diminution of vision and/or proptosis of the affected eye. Conjunctival chemosis, lid swelling, ptosis, and loss of sensation along the trigeminal nerve are other findings described. Mild to severe globe motility restriction is a consistent finding on examination.[2] Our patient too had these features. Clinically, orbital inflammation is the most common differential diagnosis. This reflects the challenge posed to the physician in coming to a proper diagnosis and specifies the importance of histopathological analysis of the involved tissue.

In most of the cases of PBL reported in literature, patients had mass lesion in the orbit on CT. Our patient had massive enlargement of all the extraocular muscles of the left eye and medial rectus of the right eye. None of the cases of PBL reported in literature had such a presentation. Discrete lymphomatous lesions of the extraocular muscles are rare. They are often low-grade malignancies that respond well to radiotherapy and have a good prognosis.[7] However, our patient had the aggressive type of NHL. Clinically, there was no involvement of the right eye though CT scan showed enlargement of right medial rectus. At the time of presentation, metastatic involvement of liver, bone marrow, or lymph nodes is not uncommon, showing the highly aggressive nature of PBL. Our patient did not show any evidence of systemic involvement. In view of bilateral orbital involvement without any systemic spread, she was considered to be Ann Arbor stage II_E.

Diagnosis of PBL is confirmed by histopathology and immunohistochemical studies, which show large immunoblasts or plasma cells that express plasma cell markers (CD138, CD38, CD79a) and lack B-cell markers (CD19, CD20).[8] In our patient, CD138 was positive. The main challenge in the diagnosis of PBL is its morphologic and immunologic resemblance to plasma cell myeloma.[9] Differentiation is mainly with the help of immunohistochemical markers. Though Epstein-Barr virus (EBV) infection was invariably noticed in most of the cases reported in literature,[2,5] we could not perform any tests for EBV as this facility was not available in our lab.

The International Prognostic Index scoring system is the most commonly used risk stratification tool for aggressive lymphomas, and it includes age, performance status, LDH levels, number of extranodal sites involved, and clinical stage to prognostic survival.[8] According to this, we categorized our patient under high-intermediate risk group.

Though orbital involvement in PBL is very rare, its incidence is on the rise in HIV-positive individuals. This is because of the increased awareness about PBL in clinicians and the pathologists.[8] Initial clinical presentation can resemble orbital inflammation. But when this type of presentation coincides with an immunocompromised status, the clinician should always keep PBL as one of the differential diagnosis. Ocular adnexal lymphoma with discrete involvement of extraocular muscles is rare. Our patient had unusual features of extraocular muscle enlargement as found in CT, which has not been reported in the literature for PBL till date.

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Asian J Ophthalmol. 2019;16:298-301

Two cases of spontaneous closure of full-thickness macular hole

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Abstract
We report two cases of spontaneous closure of full-thickness macular hole (FTMH). The first was in a patient with relieved traction from tractional macular detachment with spontaneous closure after diagnosis at 16 months. The second case is FTMH that developed after vitrectomy from rhegmatogenous retina detachment with spontaneous closure after diagnosis at 9 months. Spontaneous closure of FTMH is rare and the main treatment is vitrectomy.

Keywords: *full-thickness macular hole, spontaneous closure*

Case 1

A 56-year-old Chinese man with right proliferative diabetic retinopathy and retinitis proliferans with traction affecting the macula developed full-thickness macular hole (FTMH) while he was undergoing panretinal photocoagulation. His visual acuity decreased from 6/18 to 6/36. The macular traction was, however, relieved (captured via optical coherence tomography [OCT]). He was noted to have spontaneous closure of FTMH prior to surgery with visual acuity of 6/24 (Figs. 1 and 2).

Case 2

A 43-year-old Malay man presented with right macula-off rhegmatogenous retinal detachment. Vitrectomy and gas tamponade were performed, and intraoperatively there was no macular hole (MH). His vision improved from counting fingers to 6/36, but 4 months after surgery there was a drop in vision to 1/60. A FTMH was noted and confirmed via OCT. He refused surgery and 9 months after the diagnosis of FTMH, his vision improved to 6/36 and OCT showed spontaneous closure of FTMH with remnant of subfoveal fluid. Four months later, the amount of fluid further decreased and his vision improved to 6/24.

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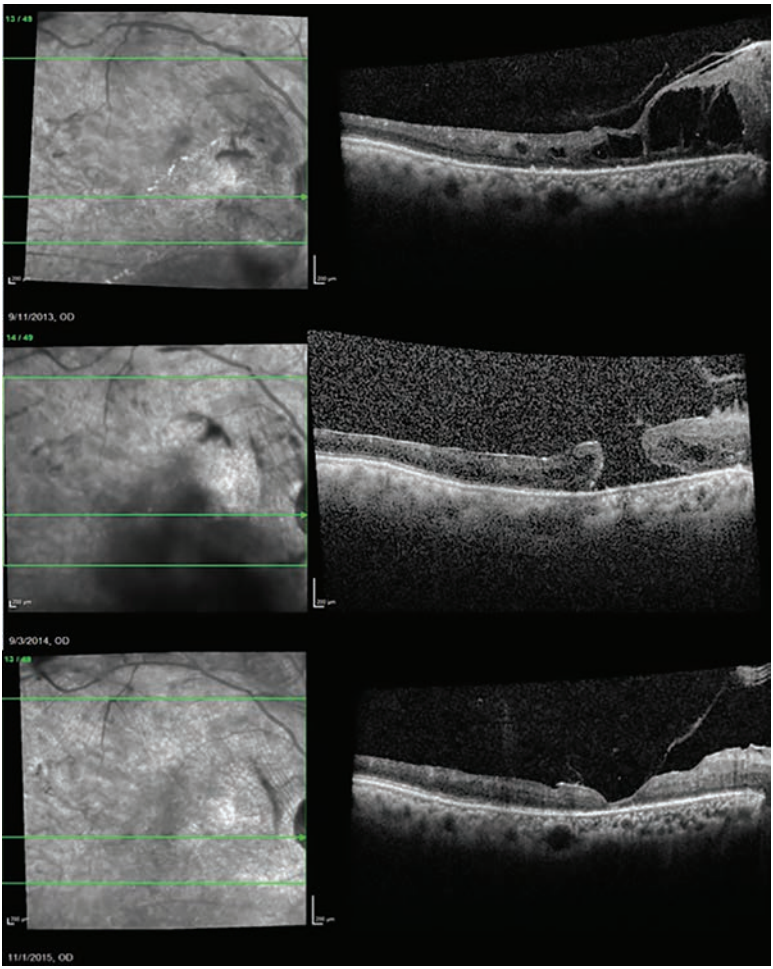

Fig. 1. Serial OCT showing the development of FTMH and subsequent spontaneous closure of FTMH.

Discussion

FTMH is a retinal break involving the fovea. It is classified as stage 3 based on the modified Gass classification system.[1] Spontaneous closure of FTMH is rare, with reported rates between 4% and 6%.[2]

There are two major theories that explain the formation of MH: the anteroposterior vitreofoveal traction and the tangential vitreous traction.[1,3] The former theory

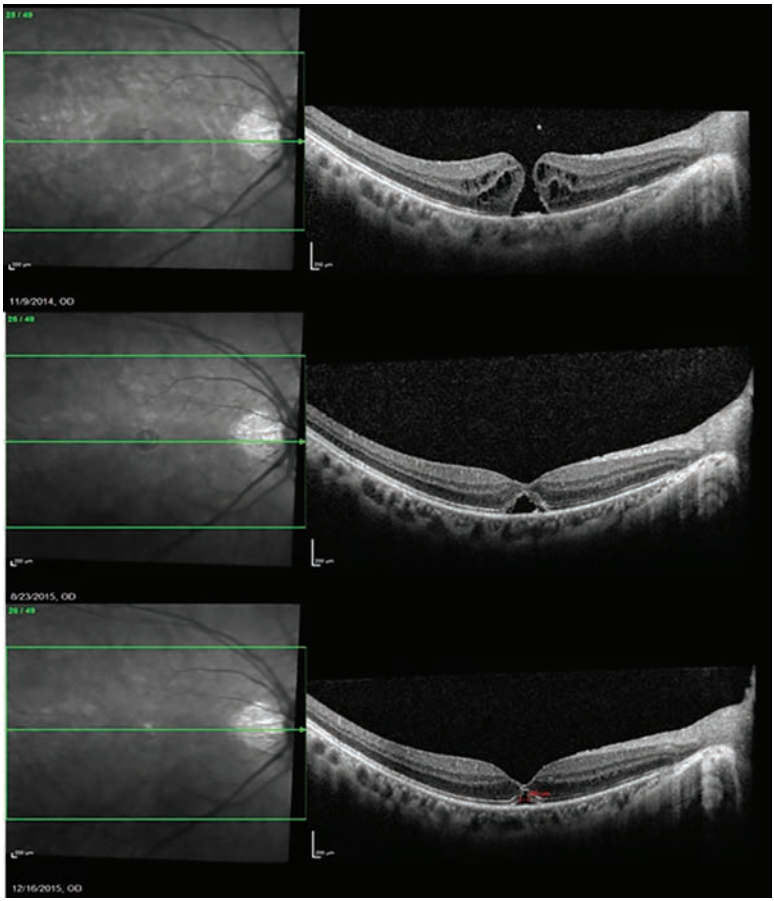

Fig. 2. Serial OCT showing the progression of spontaneous closure of FTMH.

results from a posterior vitreous detachment (PVD) with subsequent foveal cyst formation, whereas the latter is due to condensation and tangential contraction of the prefoveolar vitreous cortex, leading to spontaneous vitreofoveal separation. The mechanism of FTMH formation in both the above-mentioned cases is different. Case 1 developed a FTMH secondary to anteroposterior vitreous traction affecting the macula. However, Case 2 had a FTMH after pars plana vitrectomy, most likely secondary to tangential vitreous traction.

The exact mechanism behind spontaneous closure of FTMH is unclear; however, a few theories have been postulated. Takahashi *et al*. suggested that the bridging

of the protruding retinal tissue over the MH led to closure.[4] Meanwhile, Suzuki *et al*. suggested that the process of resolving FTMH could be related to the degeneration of the inner retinal layers due to either atrophy or coalescence of cystoid edema.[5] Ishida *et al.* mentioned that a PVD with release of vitreomacular traction plays an important role for spontaneous closure of the MH.[6]

The current gold standard to diagnose MH is via OCT, which is widely available. Besides providing an excellent aid in the monitoring of FTMH, it also serves as a guide in the management of the condition. Vitrectomy remains the mainstay of treatment for MH as it has a favorable outcome, with improvement of visual function in addition to a low recurrence rate.

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Asian J Ophthalmol. 2019;16:302-306

A peculiar case of corneal autograft in a patient with bilateral advanced glaucoma

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Abstract
The technique of autograft employs the use of a clear corneal graft from an otherwise blind eye that is transplanted to the fellow eye, which has a visual potential in the same patient. A patient with advanced glaucoma in both eyes presented to us with pseudophakic bullous keratopathy with Ahmed glaucoma valve in the right eye, and cataract and patent peripheral iridotomy with no perception of light in the left eye. The autograft and allograft corneas for bilateral penetrating keratoplasty (PK) were obtained from the contralateral eye and a cadaver eye, respectively. Central corneal button was used for PK. One year after the surgery, the graft host junction was well apposed with no vascularization, corneal surface was clear, sutures were intact, and best corrected visual acuity improved in right eye to 1 logMAR. Bilateral simultaneous PK with autograft in one eye and allograft in the other was done to decrease the chances of rejection.

Keywords: *autograft, keratoplasty*

Introduction

The technique of autograft employs the use of a clear corneal graft from an otherwise blind eye that is transplanted to the fellow eye, which has a visual potential in the same patient. The common indications for the procedure of autografts are aphakic bullous keratopathy, pseudophakic bullous keratopathy (PBK), and healed herpetic keratitis.[1,2] The donor eye must have a clear cornea and must be blind, possibly due to posterior segment pathology, which in this case is advanced glaucoma. A homologous donor transplantation in the blind eye is done in order to provide cosmesis. The main advantage of autograft is that there is no risk of immune graft rejection.

In this case, the patient's left eye was blind with no perception of light, while the right eye had PBK. Simultaneous bilateral penetrating keratoplasty (PK) was planned for her with the right eye cornea receiving an autograft and the left eye cornea receiving an allograft.

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Case report

A 75-year-old female came to our hospital with advanced glaucoma in both eyes and on antiglaucoma medication, Misopt (dorzolamide 2%, timolol 0.5%) (Microlabs, India) eye drops two times a day since four years. She gave a history of cataract surgery and glaucoma surgery five years and three years back, respectively. On ophthalmic examination, best corrected visual acuity (BCVA) in the right eye was 1.7 logMAR, while the left eye had no perception of light. On slit-lamp examination, the right eye was status post Ahmed glaucoma valve implant with PBK, while the left eye had cataract with a clear cornea. Intraocular pressure (IOP) in the right eye was 16 mmHg and 14 mmHg in the left eye on applanation tonometry. Posterior segment examination of the right eye was not possible due to dense corneal oedema, while the left eye fundus was hazy due to dense cataract. B-scan ultrasonography revealed posterior vitreous detachment in both eyes and advanced optic nerve head cupping in the left eye. Specular microscopy of the left eye revealed a cell count of 3,029 cells/mm^2, coefficient of variance of 38, and central corneal thickness of 535 µ. A healthy donor cornea with specular count of 3,100 cells/mm^2 was chosen for the left eye. Preoperatively, anaesthetic clearance was obtained and informed consent was taken from the patient, and all surgical risks were explained to the patient, including graft rejection. Patient was started on intravenous mannitol 20 g/100 ml half an hour before surgery. Simultaneous bilateral PK was performed, with the right eye cornea trephined and transplanted with the blind eye (left eye) cornea, while the latter was transplanted with donor tissue. Viscoat (sodium chondroitin sulphate and sodium hyaluronate; Alcon, Fort Worth, TX) was injected into the anterior chamber, after which trephination of the left cornea was done. Donor corneas were oversized by 0.5 mm with respect to the recipient. Graft host junction was well apposed with interrupted 10-0 nylon suture bandaged after placing the contact lens. Postoperative regimen given was topical steroid prednisolone acetate (Alcon), Vigamox (moxifloxacin 0.5%; Alcon) and Homide (homatropine 1%; Warren, India) in both eyes. Patient was advised to continue antiglaucoma medication (Misopt eye drops) in both eyes until further instruction. Follow-up examinations were performed on day 1, 1 week, 1 month, 3 months, 6 months, 9 months, and 12 months. IOP measurement using the Tono-Pen was performed during each visit. No intraoperative complications occurred. Postoperatively, the graft host junction was well opposed with no vascularization and sutures were intact in both eyes (Figs. 1 and 2). There was no sign of infection, graft failure, or slippage of tissue. The BCVA improved to 1 logMAR by 1 week and N10 for near visual acuity. IOP remained normal at 16 mmHg. Topical steroids were gradually tapered in the right eye to only twice a day by the end of the third month, while steroids were maintained at four times a day at the end of the third month in the left eye. Homide was stopped after two weeks. BCVA was

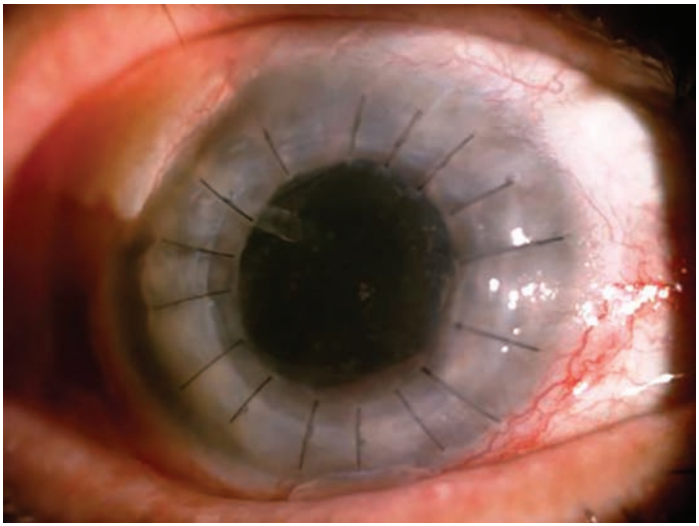

Fig. 1. Autograft with clear cornea with tube *in situ*.

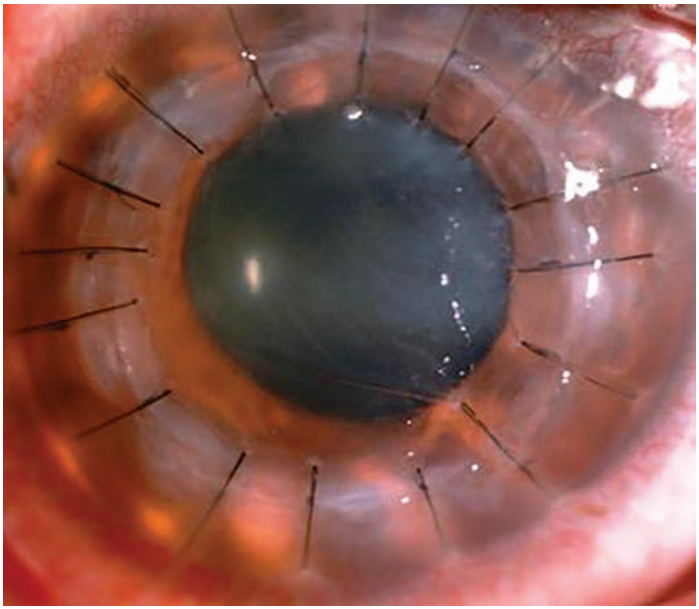

Fig. 2. The other eye with clear graft.

maintained at 1 logMAR with clear graft. In the left eye, the graft remained clear at the end of one year after surgery. A dilated fundus examination in the right eye revealed optic disc cupping of 0.85:1. Patient is on constant follow-up with us.

Discussion

It has long been recognized that bilateral simultaneous PK significantly increases the risk of corneal graft rejection, and it can be due to the pre-existing corneal disease. With recent advances in surgical techniques like phacoemulsification, simultaneous bilateral cataract surgeries are commonly done worldwide. The use of topical anaesthesia and minimal tissue damage in these new techniques have aided in early visual recovery and reduced the incidence of postoperative infections and complications in patients undergoing simultaneous cataract surgeries. But simultaneous bilateral PK has not gained much acceptance due to increased risk of graft rejections and postoperative complications, leading to visual morbidity. Strict operation theatre asepsis and efficient sterilization techniques can aid in preventing these complications. As per our knowledge, there has not been any report on bilateral simultaneous PK in the Indian scenario, which makes our case unique: the blind eye (left eye) cornea was transplanted to the seeing eye (right eye) diagnosed with PBK, while the former received a donor cornea. This patient is a case of advanced glaucoma in both eyes with right-eye PBK, both of which are known risk factors for allograft failure.[2,3] Stewart *et al*. retrospectively analyzed transplants in eyes with and without glaucoma.[4] The three-year graft survival was 86% in eyes without pre-existing glaucoma and 72% in eyes with pre-existing glaucoma. The risk of failure was dependent on the indications of PK.[5] Patients undergoing PK for PBK or Fuchs' dystrophy with pre-existing glaucoma had significantly increased risks of graft failure (1.5 and 1.9 with topical and 2.0 and 3.1 with oral antiglaucoma medication, respectively) compared to those without pre-existing glaucoma. Graft failure after successful keratoplasty most often results from inflammatory reactions that represent immune-mediated corneal allograft rejection[6]; therefore, the use of autograft, would solve the problem of immunologically mediated damage in corneal transplantation, the procedure first being described by Plange in 1908. Since there has not been much evidence on autograft rejection in glaucomatous or PBK eyes, this procedure was innovative in its own kind with less chances of rejection; however, a larger sample size with a longer follow-up would substantiate the efficacy better.

Conclusion

This is a unique case of bilateral simultaneous PK with an autograft used from the fellow eye to prevent any chance of graft rejection and failure in the only seeing eye. Three months postoperative follow-up showed good surgical outcome and graft survival.

Acknowledgements

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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Asian J Ophthalmol. 2019;16:307-318

Implantation of Artificial*Iris*, a CustomFlex® iris prosthesis, in a trauma patient with an Artisan lens

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Abstract

Purpose: *To evaluate probable complications of ArtificialIris implantation with iris-fixated intraocular lens.*

Method: *Development of photophobia, glare, and psychological strain during face-to-face communication in a 23-year-old man with a widespread traumatic iris defect terminate to make a decision for performing implantation an ArtificialIris (HumanOptics, Erlangen, Germany) under the remnant iris without removing the patient's existing Artisan lens.*

Results: *Without any intraoperative or postoperative complications, the patient's visual acuity increased by one line, the endothelial cell loss was comparable with the cell loss associated with standard cataract surgery, and the anterior chamber depth and anterior chamber anatomy did not change. At the final follow-up examination, the mean intraocular pressure (IOP) did not differ from baseline, and we achieved high level of patient satisfaction and subjective vision improvement. We discuss the particular importance of considering the patient's expectations, the appropriate measurements, ways to perfect color evaluation, and the types of ArtificialIris products.*

Conclusion: *The implantation of the ArtificialIris in patients with aphakic iris-supported lenses (i.e., preexisting Artisan lenses) is a feasible approach and a useful option for patients with thin irises and iris hypoplasia who are at risk of subluxation or the dislocation of the PCIOL as well as those with sclerally fixed PCIOLs.*

Keywords: *ArtificialIris, Artisan, CustomFlex, trauma*

Introduction

Symptoms such as aberration disorders, contrast sensitivity restriction, dysphotopsia, depth of focus limitations, and ghosting phenomenon experiences (which can be remembered by: AbCDefGh*) can occur in eyes with normal irises; however, these adverse effects are particularly noticeable in patients with iris and pupil

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defects. The magnitude of higher order aberrations (HOAs) is closely related to the pupil and pupil size and to depth of focus.[1,2] In addition to congenital aniridia, which can entail amblyopia,[3] large iris defects and persistent mydriasis after ocular trauma are among the major indications for surgical interventions. Congenital diseases (e.g., coloboma and aniridia), iatrogenic causes (e.g., eye surgery in cases with intraoperative floppy iris syndrome),[4] iris tumor excision, and iridocorneal endothelial syndrome[5] are less common causes. Many patients with large and multiple iris defects are not satisfied with conservative management techniques, such as sunglasses, tinted contact lenses,[6] lamellar intrastromal corneal tattoos,[7] or specific suture techniques[8] (e.g., iridoraphy or iridopexy side-to-side iris sutures). The Artificial*Iris* is foldable in its rolled state, and it can be inserted through a 3.0-mm incision. The previous generation of iris prostheses that have been used with and without penetrating keratoplasty[9] are difficult to apply, can require large incisions, and might not have a realistic appearance.[10] Few iris reconstruction studies have been published using the intended new type of silicon iris implant. This implant was developed in 1998 by Prof. Dr. Hans-Reinhard Koch and Dr. Karlheinz Schmidt. Conformité Européenne approved Artificial*Iris* in 2011, and it is currently undergoing the Food and Drug Administration approval process in the United States. This novel artificial iris is a handmade device for various surgical options.[10-12] This implant is made of a foldable, highly biocompatible, and medical-grade silicone material. The anterior surface mimics the natural appearance of the iris with regard to its color composition (via embedded nontoxic pigments), and the iris structure is created from a Makrolon mold. The posterior surface, with its black pigmentation, completely prevents light transmission. Artificial*Iris* is designed without an optic to allow the surgeon to select the most appropriate intraocular lens (IOL) or optic for the patient. All Artificial*Iris* are 360°, 12.8-mm diameter disks with fixed pupils of 3.25 mm[13,14] Artificial*Iris* (HumanOptics, Erlangen, Germany) is known as the CustomFlex® iris prosthesis in the United States. It comes in two types: an Artificial*Iris* with a suturable fiber with high mechanical stability preferred for partial implant surgery[12] and an Artificial*Iris* without fiber for easier handling and greater pliability in cases in which suturing is not indicated.[12]

To the best of our knowledge and based on a comprehensive literature search of PubMed, the ISI Web of Science, Google Scholar, and Scopus, no other studies exist on this topic except one study of concomitant iris defects and Artisan lens implantation.[15] This study is the first report of Artificial*Iris* (HumanOptics) implantation in a trauma patient with an existing Artisan lens. In this regard, traumatized eyes with highly diverse posttraumatic conditions might benefit from this device because of its outstanding outcomes. We present this case to report the results of this procedure.

Case report

In February 2014, a 23-year-old man presented with photophobia and a history of eye trauma (penetration) 10 years earlier. "I can't communicate with my friends or participate in social activities because people stare at my disfigured eye," he said (Figs. 1 and 2). He was upset about his appearance and was unable to maintain eye contact comfortably, even with me. He was not satisfied with conservative management techniques (spectacles or contact lenses) or suturing the natural iris (via iridoraphy, iridopexy, or side-to-side iris sutures). The patient was advised to ignore his condition and focus on more positive things (exercise, listening to music and other similar activities). The patient signed and received a copy of the written informed consent document that explained probable treatment complications, such as glaucoma, corneal decomposition and consecutive surgeries. A customized Artificial*Iris* was ordered based on the patient's face, focusing on the color of his normal eye. In this case, an Artificial*Iris* with a fiber meshwork was ordered for its reliability. A second Artificial*Iris* was also requested as a backup.

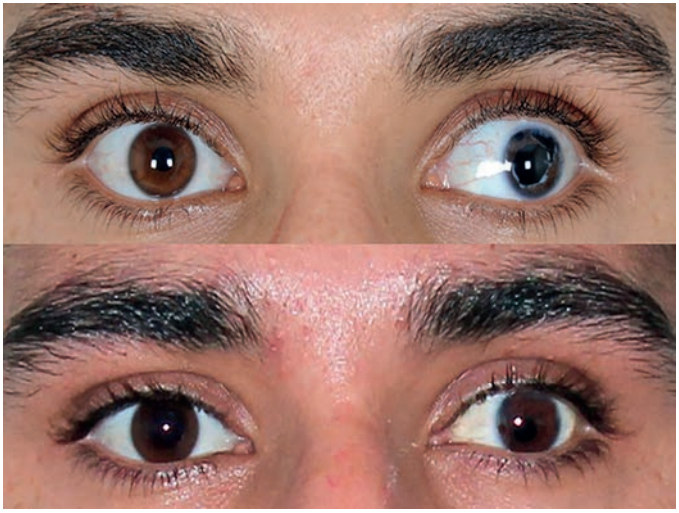

Fig. 1. Photographs of the 23-year-old patient who sustained severe penetrating trauma of the left eye with a consecutive loss of the lens and iris and multiple eye surgeries, before (up) and after (down) ArtificialIris implantation (HumanOptics, Erlangen, Germany) without previous Artisan lens exchange. The pupil is well centered and the color matches the fellow right eye. Even though the match between the two eyes may not be perfect in every case, from cocktail party distance it is very difficult to see any difference between the two eyes.

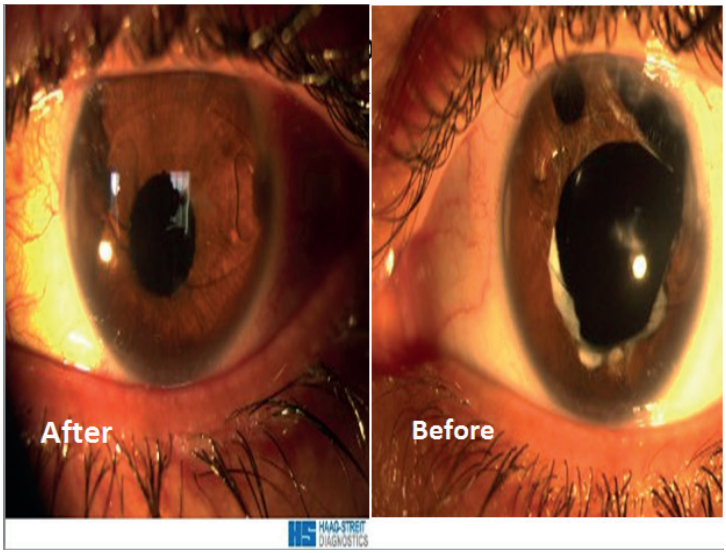

Fig. 2. Photo slit image before and after surgery.

The patient underwent anterior segment reconstruction with the implantation of the Artificial*Iris* at the university eye hospital in 2016. The medical records were evaluated for changes in visual acuity as a functional parameter, for IOP values to assess secondary glaucoma, and for endothelial cell density (ECD).[16] The angle grading upon gonioscopic exam[17] was used as a quantitative parameter for the evaluation condition. Slit-lamp photography and anterior segment optical coherence tomography (OCT)[16] images were reviewed when available.

The candidate was examined before and after surgery when the wound healing was complete. Best-corrected visual acuity was assessed using a Snellen chart. IOP was measured using a standard Goldmann applanation tonometer and a Canon TX-10 non-contact tonometer (Canon USA Inc., One Canon Plaza, Lake Success, NY, USA). The gonioscopic examination of the anterior chamber angle (ACA) was performed in the dark using a Goldmann 3 mirror lens at a high magnification (X16), and all of the quadrants were graded in the primary position at 4:35° to 45 using the Shaffer grading system.

White-to-white (W-W) was detected using calipers (Table 1) and an OrbscanIIZ (Bausch & Lomb, New York, NY, USA). Sulcus-to-sulcus distance was measured using an ultrasound biomicroscope (UBM Quantel Medical, Aviso S).[18] Endothelial cell biomicroscopy was used to calculate ECD (CellChek XL: Canon Medical

Table 1. Patient characteristics and surgical considerations

<table>
<tr><th colspan="2">Patient history, examination</th><th colspan="2">Official recommendations</th><th>Surgical considerations</th></tr>
<tr><td colspan="2">23-year-old man with a history of primary repair—lensectomy, pars plana vitrectomy after trauma, secondary IOL, iris sutures, no history of systemic diseases with realistic expectations.</td><td colspan="2">Sulcus-to-sulcus measurement with ultrasound biomicroscopy (Quantel Medical, Aviso S) or OCT direct intraoperative measurement of white-to-white with caliper and OrbscanIIZ (Bausch & Lomb, New York, NY, USA).</td><td>New technique for resizing:
the device sized relative to the shorter meridian and iris remnant intraoperatively.</td></tr>
<tr><td>Preoperative</td><td>Postoperative</td><td>White to white</td><td>Sulcus to sulcus</td><td rowspan="6">3.5 mm scleral tunnel incision
≤12.0 mm size of ArtificialIris
Sulcus implantation behind iris remnant and Artisan
Folding; no rolling or injection of ArtificialIris</td></tr>
<tr><td>VA: 20/80</td><td>VA: 20/63</td><td>Caliper: 11.8
Orbscan 11.8</td><td>UBM: 12.15</td></tr>
<tr><td>IOP: 15 mmHg</td><td>IOP: 16 mmHg</td><td colspan="2" rowspan="2">Rule of thumb: For horizontal white-to-white (caliper) measurements add a value of +0.5 mm (Prof. Dr. H.-R. Koch).</td></tr>
<tr><td>ECD: 2,249</td><td>ECD: 2,209</td></tr>
<tr><td>Hexagonality (%): 56.3</td><td>Hexagonality (%): 55.6</td><td rowspan="2">Routine trephine sizes for sulcus implantation: 12.0mm, 11.5 mm, 11.0 mm</td><td rowspan="2">Routine trephine sizes for in-the-bag implantation: 10.0 mm, 9.5 mm, 9.0 mm (Snyder)</td></tr>
<tr><td>Coefficient of variation (%): 36.8</td><td>Coefficient of variation (%): 37.5</td></tr>
</table>

ECD: endothelial cell density; IOP: intraocular pressure; VA: visual acuity

Inc., Irvine, CA, USA).[16] All of the parameters were assessed before surgery as well as 1 day, 3 days, 1 week, 1 month, 2 months, 3 months, and monthly thereafter. The ACA characteristics were defined via spectral-domain OCT (SD-OCT) using a Cirrus OCT device (Carl Zeiss Meditec, Inc.) in an objective manner.[17] The patient rated his satisfaction with the overall results on a scale from 1 to 10 (1 = none, 10 = maximum satisfaction).[19]

Surgery was performed using general anesthesia through a 3.5-mm scleral tunnel incision at the 12 o'clock position. The anterior chamber was filled with 1% sodium hyaluronate (Provisc), which was completely removed at the end of the surgery. Because the packaged Artificial*Iris* was 12.8 mm, cutting and resizing were performed to provide a ≤12-mm Artificial*Iris* with regard to the W-W and S-S preoperative evaluation and intraoperative eye measurement.

Some of the border was made slightly smaller (11 mm)[20,21] than the measurements above for glaucoma prevention.

We cut and resized the Artificial*Iris* in additional places where the remnants of the iris formed a circular border. Support was provided for the Artificial*Iris* in the posterior segment, and the Artificial*Iris* was implanted under the remnant iris without removing the existing Artisan lens. Suturing of the device was not performed because of the sufficient support.

The superior and inferior leaflets were simultaneously unfolded using two hooks (folding was used in place of rolling or injection). We used bimanual instrumentation to ensure that endothelial contact was not made while another Neuhann chopper was placed through a second side port between the cornea and implant to prevent touching. Unfolding occurred posteriorly (not toward the endothelium). After implantation, the colored side faced up. The proper pupil centration of the Artificial*Iris* in the sulcus was evaluated via horizontal movements with the forceps. The centration was aesthetically pleasing, without any decentration or dislocation.

After the irrigation/aspiration of the anterior chamber and the stable positioning of the Artisan® IOL was ensured, the scleral tunnel incision was sutured with a nonabsorbable Nylon 10-0 thread. Postoperatively, 0.3% ciprofloxacin and 0.1% betamethasone eye drops were used four times/day for 1 week; then, ciprofloxacin use was discontinued, and betamethasone use was tapered during follow up. To reduce the risk of postoperative inflammation, 1 mg/kg/day of oral steroids were used for the first 3 weeks and then tapered. During the follow-up period, the patient's visual acuity increased by one line, the anterior segment depth and anterior segment anatomy did not change significantly, the endothelial cell loss was comparable with the cell loss in standard cataract surgery, and the IOP increased to 25 mmHg. The increase in IOP was only temporary and returned to normal during the follow-up examinations without medication. This case study shows the effectiveness of the small pupil in relieving the symptomatology

associated with increased HOAs, including light sensitivity and ghosting. Furthermore, we achieved a high level of patient satisfaction and subjective vision improvement. The cosmesis empowered the patient, and he is eagerly looking forward to continuing his studies again.

We did not observe threatening endothelial damage (Table 1), retinal detachment, secondary glaucoma, bleeding, corneal edema, or dislocations associated with the device. Since the operation, the patient has contacted us in different ways, thanking us and claiming that this surgery was the best thing that has happened in his life: "I had not directly looked into people's eyes for years" he said. Our colleagues even introduced us to three more patients who are currently being scheduled.

Discussion

To best of our knowledge, this study is the first report of an Artificial*Iris* (HumanOptics) implantation in a trauma patient with an Artisan® lens using a new method. Conformité Européenne approved use of Artificial*Iris* in 2011, and it is currently undergoing the Food and Drug Administration approval process in the United States.[16] The implantation of the Artificial*Iris*, particularly after iris-fixated IOL implantation with probable postoperative complications, such as intraocular inflammation, glaucoma,[21] corneal edema and endothelial cell loss,[22] in traumatic cases, might provoke a lack of enthusiasm for these surgical procedures. Contradictory reports exist regarding certain cosmetic types[23] of anterior chamber Artificial*Iris* implantation in phakic eyes.[24] In addition, some patients are unhappy with the necessary indications[10] for aesthetic impairment (i.e., AbCDefGh). Thus, we were motivated to make progress in this area of medicine. A recent case series concerning Artificial*Iris* reported high levels of patient satisfaction and postoperative vision improvement.[10,13,16,21,25] The Artificial*Iris* should not be confused with other devices available under the trademark NewIris (Kahn Medical Devices Corp.) or other cosmetic implants.[23]

In our case, visual acuity and anterior segment depth did not change, the endothelial cell loss was comparable with the cell loss that occurs in standard cataract surgery, and the IOP increased to 25 mmHg (which was only temporary and returned to normal during the follow-up examinations). We also achieved a high level of patient satisfaction and subjective vision improvement. In Mayer et al.'s prospective study, the mean anterior chamber depth increased after combined cataract surgery and Artificial*Iris* implantation. This finding was related to the combined thickness of the Artificial*Iris*, the artificial lens, and the residual iris being less than that of the natural lens.[16,18]

The factors that contribute to the occurrence of glaucoma associated with Artificial*Iris* implantation might include patients with preexisting glaucoma or

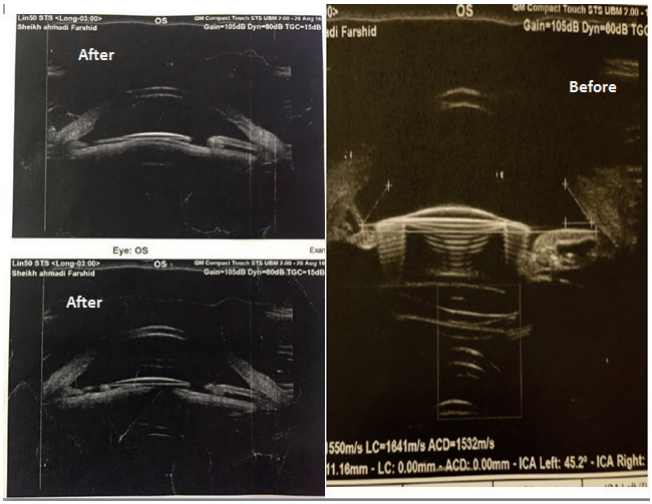

Fig. 3. UBM image before and after surgery.

a tendency toward glaucoma[25] and techniques or materials that cause chronic irritation due to partially cut prostheses with mesh.[21] Regular pre- and postoperative measurements of IOP are required for Artificial*Iris* implantation. Because the trabecular meshwork plays an important role in aqueous outflow, the assessment of its anatomy in the at-risk population might provide am insight into one of the potential contributors to elevated IOP and the probability of glaucoma development. In this regard, although gonioscopic examination is the gold standard, it is a subjective procedure. For controversial cases, such as Artificial*Iris* implantation for patients (with or without preexisting glaucoma) who are at risk for postoperative glaucoma,[21,25] gonioscopy is useful but in short supply. In contrast, objective evaluations might have better practical implications. The following methods might help and predict the size of the Artificial*Iris* with a better ACA definition: SD-OCT has a high sensitivity and low specificity for detecting angles compared with gonioscopy, and it does not require the placement of a scleral cup or corneal probe; ultrasound biomicroscopy (UBM) allows for the investigation of the mechanisms that underlie angle closure; and the peripheral iris cannot be visualized via a Pentacam[16,17] (Fig. 3).

Rickman considered hyperpigmentation of the iris remnant as a sign of the chronic irritation of the surrounding tissues via the sharp borders of the cut Artificial*Iris*.[21] Using the full prosthesis without a mesh and a size smaller than

originally planned is recommended to reduce the risk of complications, such as glaucoma.[20,21] In this complex case of a perforating trauma with a corneal scar, an Artisan lens and a history of nine surgeries (including primary repair, secondary IOL implantation, deep vitrectomies, and so on), a suturable Artificial*Iris* with fiber seemed more reliable than Artificial*Iris* without mesh.[10,20,21,24,25] In contrast, to provide an appropriately sized (approximately 12-mm or less) Artificial*Iris* according to the OCT, W-W, and S-S preoperative evaluations[16] and intraoperative measurements using a ruler,[26] cutting and resizing are recommended because the Artificial*Iris* is sized at 12.8 mm. Even smaller (11 mm) irises have also been recommended[20,21] for glaucoma prevention.

To achieve these goals, we resized the Artificial*Iris* where remnant iris was present. In other words, we sized the device relative to the shorter of the intraoperative meridians and gained better aesthetic results, which encouraged us to resize the Artificial*Iris* in the places with remnants with circular borders. This exclusive handmade device is friendly to surgeons' hands, and it facilitates various surgical methods; the Artificial*Iris* can be suture fixated[10,20] if necessary, sutured side to side to the remaining iris tissue,[27] sutureless[14] or use knotless sutures.[28] In eyes with remaining capsules, the Artificial*Iris* can be placed using the Rosenthal method in the sulcus or with a capsular tension ring[26] and staining (Trypan blue or indocyanine green in cases of congenital aniridia with a fragile capsule)[29,30] in the bag. In these cases, no suturing is needed, and a more flexible variant of the Artificial*Iris* without the tissue layer can be used. As an alternative, we could have removed the patient's Artisan lens and stitched the new PCIOL to the scleral wall first; in the second step, the Artificial*Iris* would have been inserted on top of the IOL and fixated with sutures to achieve a four-point fixation. Four-point fixation can be achieved using haptics with the Artificial*Iris* alone. The IOL could also have been sutured to the Artificial*Iris* first and then implanted together as a complex unit, necessitating a larger incision. These methods were not used because of the existence of sufficient support for the Artisan lens and the likely higher risk of complications during IOL exchange.

As is known, when combined with careful patient selection and the appropriate surgical technique, the posterior implantation of the Artificial*Iris* in aphakic and pseudophakic eyes can improve vision, the AbCDefGh* conditions, and positively affect quality of life while also providing satisfactory aesthetic results. Surgeons might sometimes be tempted to perform the seemingly convenient and less time-consuming method of implanting a foldable Artificial*Iris* via small-incision surgery; however, this method is not always an appropriate approach. In this report we found that the implantation of the Artificial*Iris* in patients with aphakic iris-supported lenses (i.e., preexisting Artisan lenses)

is a feasible approach and a useful option for patients with thin irises and iris hypoplasia who are at risk of subluxation or the dislocation of the PCIOL as well as those with sclerally fixed PCIOLs.

Patient expectations (i.e., detailed informed consent explaining the risk of complications such as glaucoma and corneal decompensation), preoperative evaluations (objective and subjective), and postoperative examinations (EEE) are important to patient satisfaction, particularly in these specific cases.

In traumatic cases with unpredictable conditions, re-performing the intraoperative measurements and modifying the device based on the meridians might be possible. The surgeon might decide to use the Artificial*Iris*, most likely without mesh, with fewer complications; hence, having another type of Artificial*Iris* at hand as a backup adds to the convenience of the procedure and increases the likelihood of successful results.

Patient consent

In addition to following the tenets of the Declaration of Helsinki in the current study, I obtained a written informed consent from the case for probable complication of this implantation and also publication of its results.

Acknowledgments

We acknowledge the professional manuscript services of American journal experts. We thank Dr. Feaz Niazi, Associate Professor at SBUM. We would also like to acknowledge Dr. Nima Jalali and Sana Niazi for their kind help. Finally, we thank Dr. Reza Ghaffari, Associate Professor of Ophthalmology at Tehran University of Medical Sciences.

Funding

No funding or grant support.

Conflict of interest

None of the authors have financial or proprietary interests in any of the materials or methods mentioned.

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Asian J Ophthalmol. 2019;16:319-322

Eyelash in lacrimal punctum: demonstrating a negative pressure in the lacrimal sac

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Abstract
Eyelashes are normally arranged in two or three rows on the upper and lower eyelids. They are more numerous on the upper eyelid, with approximately 150 eyelashes being present on the upper and 75 on the lower eyelid. Eyelashes, like body hair, are shed regularly every 100 to 150 days.[1] Usually, the shed eyelashes do not cause any symptoms.

However, the cilia may sometimes get misplaced and end up in the lacrimal puncta, meibomian gland orifice, subconjunctival space, and corneal stroma. An eyelash that gets misplaced into the punctum has the potential to cause additional problems. Once the eyelash enters the punctum, the barbs on the hair prevent it from being expelled.[2]

Keywords: *canaliculus, cilium, punctum*

Case report

A 41-year-old female patient presented with watery eyes, foreign body sensation, and mild erythema on the nasal bulbar conjunctiva in the left eye for last two days. She had persistent discomfort and pain in her left eye. The visual acuity in both eyes was 20/20. The intraocular pressure in both eyes was normal. A slit-lamp examination revealed a protruding eyelash from the upper punctum, with the root of the eyelash into the canaliculus (Figs. 1 and 2). The conjunctiva was congested on the nasal side. Fluorescein staining revealed punctate lesions on the nasal part of cornea adjacent to the limbus. The eyelash was easily removed from the punctum with forceps. Almost 3.5 mm of the cilium had entered the upper punctum. She was treated with topical moxifloxacin 0.5%. Corneal lesions healed within three days.

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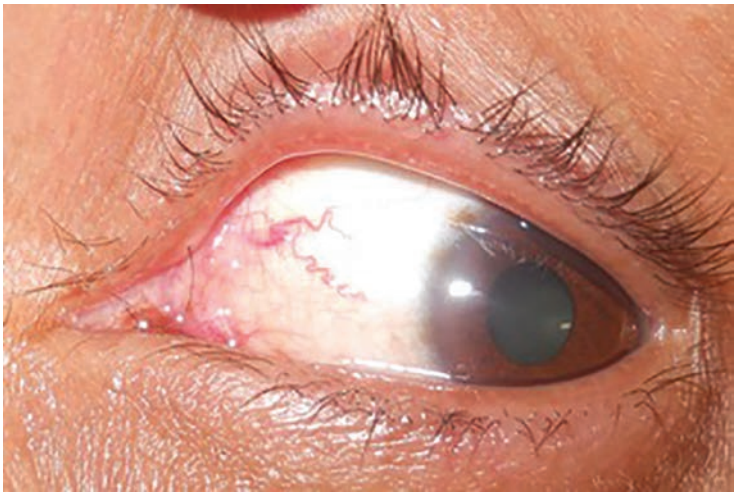

Fig. 1. Outer segment of the left eye with protruding cilium from the upper punctum.

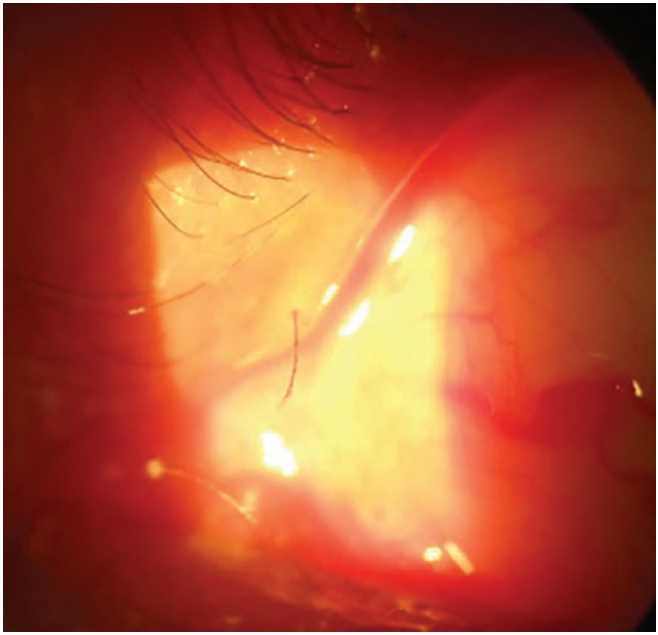

Fig. 2. Slit-lamp photograph showing nasal bulbar erythema with cilium protruding from the upper punctum.

Discussion

The presence of eyelash in a lacrimal punctum is said to be a not infrequent occurrence, although many authoritative textbooks do not mention it.[3] Boase[3] stated that, anatomically, the cilium has no business lodging itself in this peculiar position. The average length of the vertical portion of the canaliculus is 1.8 to 2.25 mm. There is a physiological constriction just above the punctum where the canaliculus is 0.1 mm wide, much less than the average cilium. The eyelash would have fallen out when the patient rubbed her eyes, and its root lying in front of the punctum would have been sucked into the canaliculus, thus demonstrating a negative pressure in the lacrimal sac as postulated by several theories of the conduction of tears.[4] Once an eyelash is shed into the external ocular surface, it can cause foreign body sensation, leading to reflex tearing that will carry it away to the lacus lacrimalis where it can be propelled by lids or sucked into the canaliculus in the blink cycle.[5]

Unusual location of cilia after falling out of their follicles may cause diagnostic difficulty. Gutteridge[6] and Agarwal *et al*.[7] reported cases of cilium lodging in the orifice of the meibomian gland. Jain *et al*.[8] reported a trimmed eyelash embedded in the meibomian gland orifice, which simulated the symptoms of endophthalmitis after an uneventful phacoemulsification, and it was suggested that trimming of eyelashes should be avoided preoperatively. Eyelashes are reported to enter the upper punctum more frequently than the lower punctum. Werb[9] and Meel and Vashisht[2] reported cases of eyelash impacted in the upper lacrimal punctum. Yeo[10] reported a female patient who presented with a cut hair end lodged in the upper punctum. Her history revealed that she had a haircut earlier that day after which her symptoms started. Nagashima and Kido[11] studied 88 cases of impaction of eyelash in the lacrimal punctum, and they found that cilia in the upper punctum were three times more frequent than cilia in the lower punctum.

To conclude, in patients with nonspecific eye symptoms like irritation, watering, mild erythema of nasal bulbar conjunctiva, etc., a misplaced eyelash may be the cause, which can be easily overlooked and treated inappropriately. Therefore, it is important to examine the eyelid margin carefully in such cases.

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Asian J Ophthalmol. 2019;16:323-328

Optimized imaging of the suprachoroidal space with swept-source OCT

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Abstract

Purpose: *To compare enhanced depth imaging (EDI) and non-EDI swept source optical coherence tomography (SS-OCT) in their ability to capture the suprachoroidal space (SCS).*

Materials and methods: *Twenty volunteers with a minimum age of 18 years without any ocular pathology and refractive error below ± 2 diopters underwent SS-OCT foveal scanning, with and without EDI. Masked averaged B-scan lines were analyzed for presence of the SCS. When the SCS was seen, the percentage of the scan on which this structure could be unequivocally observed was measured. Scores obtained from the images taken with or without EDI were then compared.*

Results: *Thirty-seven eyes were analysed, since three eyes of three different patients were eliminated, as the outer border of the choroid was insufficiently delineated with both modalities. The SCS was not detected at all on 14 pictures (37.8%) obtained by non-EDI SS-OCT and 9 pictures (24.3%) obtained by EDI SS-OCT. When the SCS was detected with both modalities, it was observable on 27.2±24.2% of the scan without EDI and 40.4±30.3 of the scan with EDI ($p < .001$)*

Conclusions: *EDI SS-OCT enables a more frequent and extensive visualization of the suprachoroidal space than non-EDI SS-OCT. This new approach could be considered as the most accurate modality to currently visualize the SCS in vivo.*

Keywords*: choroid, EDI, suprachoroidal layer, swept-source OCT*

Introduction

The suprachoroidal space (SCS) is receiving increasing attention as its potential role in the diagnosis and treatment of various retinal conditions is being recognized.[1]

Enhanced depth imaging (EDI), a modification of the regular acquisition technique, was originally described for spectral-domain optical coherence tomography (SD-OCT) in order to improve visualization of deeper structures within the choroid.[2] EDI improved visualization of the choroidoscleral interface.

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There are, however, limitations in the ability of EDI SD-OCT to capture details of the outer choroidal border.[3,4]On the other hand, the SCS has been captured in health and disease by using swept-source OCT (SS-OCT).[5]

In this research, we aim to compare non-EDI and EDI-OCT in their ability to capture the SCS in healthy subjects and thereby attempt to improve the visualization of such an important structure. For this, we propose to evaluate the proportion of eyes in which the SCS is identified, applying the EDI acquisition protocol. When the SCS is seen, we aim to quantify on what percentage of the macular scan it is patent and draw a comparison between both imaging approaches.

Materials and methods

Ethics approval for this prospective, interventional case series was obtained from the Ethics Committee at Shaare Zedek Medical Center.

Participants and imaging protocol

Healthy volunteers with a minimum age of 18 years and refractive error below ±2 D, without any ocular pathology, were prospectively recruited at the Department of Ophthalmology, Shaare Zedek Medical Center, Jerusalem. Without pupil dilatation, they were imaged with DRI OCT-1 Atlantis (Topcon Medical Systems Inc., Oakland, NJ; software version 9.10; 1,050 nm central wavelength) in random order by a single, experienced operator. For each eye, averaged B-scan lines at the fovea were obtained by two techniques, with the hyperreflectivity at the bottom of the foveal pit as an indicator of correct scan position. Non-EDI pictures were first taken according to the instructions of the manufacturer. Then, EDI scans were obtained, the device being pushed close enough to the eye to create an inverted image near the top of the display. Enough separation from the top of the display was used to avoid image ambiguity from image folding with respect to zero depth.

Image evaluation

All pictures were transferred to the image software. Those obtained by EDI, presented originally with the choroid up and the retina down, were inverted, so masking of the acquisition technique could be guaranteed. For each image, a retina specialist noticed if a hyporeflective band corresponding to the described location of the SCS was identified. When the SCS was seen, the percentage of the scan (from Bruch's membrane opening at the temporal border of the optic nerve head to the temporal edge of the scan) on which this structure could be unequivocally observed was measured. Scores obtained from the images taken with or without EDI were then compared.

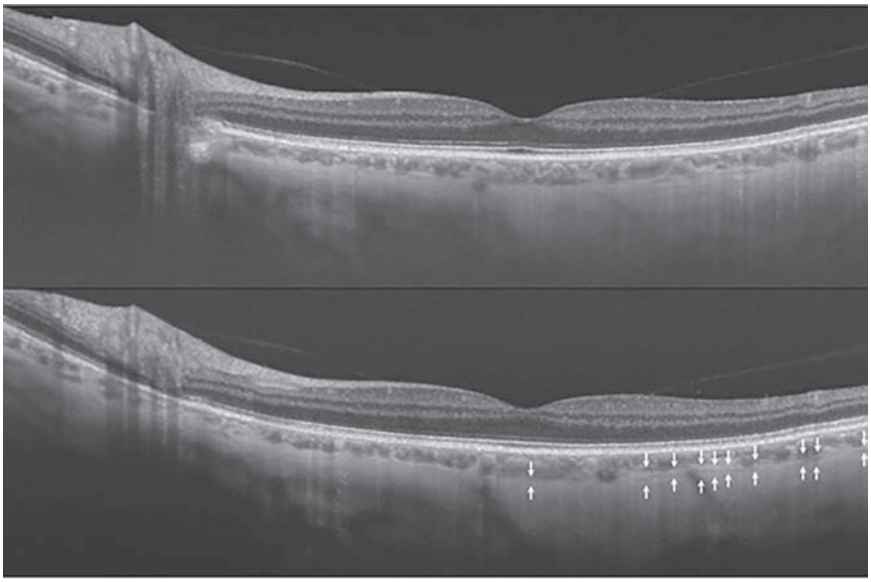

Fig. 1. EDI-OCT enabling visualization of the SCS. Using SS-OCT without EDI, the SCS was not detected. EDI allows following the SCS on the temporal macula.

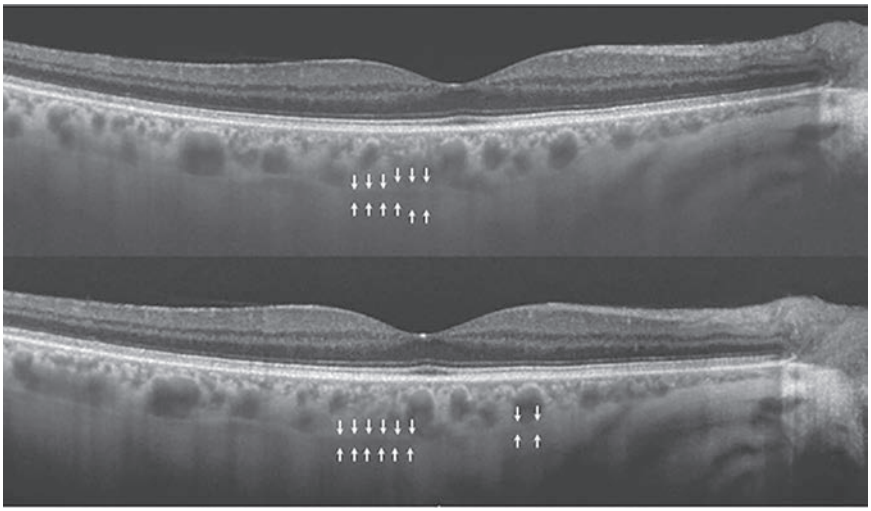

Fig. 2. Mild improvement in visualization of the SCS with EDI. While the SCS was captured with non-EDI SS-OCT, applying EDI enabled to detect it to a greater extent.

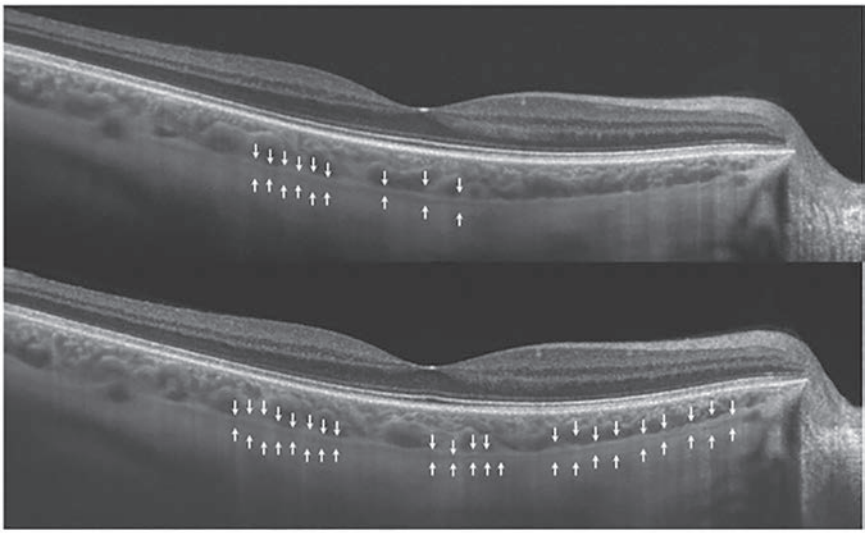

Fig. 3. Considerable improvement in visualization of the SCS with EDI. The SCS could be followed over some part of the scan length without EDI. However, by applying the EDI technique, it was visualized until the opening of Bruch's membrane.

Results

Forty eyes of 20 volunteers were included. The mean age (±standard deviation) was 37.7 ± 8.5 years. EDI images were easily obtained for all eyes. There was no significant difference in the number of averaged eyes between the non-EDI (93.4 ± 6.5) and EDI series (91.9 ± 9.6; $p = 0.4$). Three eyes of three different patients were eliminated, as the outer border of the choroid was insufficiently delineated with both modalities. SCS was not detected in 14 pictures (37.8%) obtained by non-EDI SS-OCT and 9 pictures (24.3%) obtained by EDI SS-OCT. In the five eyes in which SCS was captured by EDI SS-OCT only, SCS could be followed over 10 ± 1.6% of the scan (range: 5%-15%).

When SCS was detected with both modalities, it was observable on 27.2 ± 24.2% of the scan without EDI (range: 5%-70%) and 40.4 ± 30.3% of the scan with EDI (range: 5%-90%). The difference in proportion of observable SCS was found to be statistically significant ($p < 0.001$).

Discussion

Applied to SS-OCT, EDI increases the proportion of eyes in which the SCS is detectable (from 62.2% to 75.7%) (Fig. 1).

EDI also enables to see larger parts of the SCS than non-EDI SS-OCT (13.2% more of the total scan length) (Figs. 2 and 3).

In the young population we studied, SS-OCT obtained better results than previously reported studies with EDI SD-OCT.[6-8] In our series, the SCS was identified in 62.2% of the eyes, EDI increasing the detection rate to 75.7%.

Michalewska *et al.* assessing the suprachoroidal layer and space using non-EDI SS-OCT were able to visualize the SCS in 20% of eyes with neovascular age-related macular degeneration (AMD), 50% of eyes with dry AMD, and 50% of those with full-thickness macular holes.[5] Remarkably, they identified the SCS in only one healthy and one highly myopic eye (5% of each group), a rate lower than EDI SD-OCT.[5-8]

With EDI SS-OCT, we were able to observe the SCS more frequently than what was reported by researchers using EDI SD-OCT or non-EDI SS-OCT.

It is likely that in the near future, the SCS will become a routine component in the diagnosis, monitoring, and treatment of retinal diseases, and it is likely that new discoveries regarding its potential uses will be made in the near future.[1]

Our results, based on a small number of patients, should be validated by larger studies, with other SS-OCT devices and involvement of various observers, in order to analyze the SCS not only in health but also in disease.

In conclusion, this study indicates that the EDI technique applied to SS-OCT enhances visualization of the SCS. Currently, this approach is probably the most accurate to detect and study the SCS.

Conflict of interest

The authors report no conflict of interest.

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Asian J Ophthalmol. 2019;16:329-346

Original Article

Risk factors for anxiety and depression in patients diagnosed with glaucoma at the Philippine General Hospital

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Abstract

Objective: *The main objective of this study is to identify the risk factors associated with anxiety and depression among Filipino patients with glaucoma at a tertiary hospital in Manila. The study also aims to determine the sociodemographic profile of patients diagnosed with glaucoma based on age, sex, and social history. Additionally, the study seeks to determine the prevalence of anxiety and depression among Filipino glaucoma patients.*

Methods: *This is a single-center, cross-sectional study. The levels of anxiety and depression in 82 glaucoma patients, seen in a tertiary hospital in Manila, were evaluated using the Filipino version of the Hospital Anxiety and Depression Scale (HADS-P) questionnaire, which consists of two subscales, representing HADS-anxiety (HADS-A) and HADS-depression (HADS-D). The sociodemographic profile of the glaucoma patients was identified using percentages and frequency distribution. The prevalence of anxiety and depression among the participants was determined using percentages. To identify the risk factors for anxiety and depression, Pearson correlation and linear regression analysis were performed with the HADS-A and HADS-D subscores as dependent variables and demographic and clinical features as independent variables.*

Results: *After analyzing the data available, it was noted that HADS-A score ≥11 was present in 15% of cases, indicating anxiety among the glaucoma patients. Borderline cases of anxiety were observed in 20% (HADS-A score of 8-10), and 65% were normal, with HADS-A scores of ≤ 7. Clinically diagnosed (HADS-D score of ≥11) cases of depression were 1%, borderline cases (HADS-D 8-10) were 12%, and patients with normal HADS-D score were 87%. The linear regression analysis revealed the following results: a significant relationship between the HADS-A subscore and age ($B = -0.07$, $p = 0.0129$); a significant relationship between the logarithm of minimum angular resolution (logMAR) best corrected visual acuity (BCVA) of the worse eye and HADS-A subscore ($B = 0.424$, $p = 0.086$); and the mean deviation of the worse eye and HADS-A subscore ($B = 0.078$, $p = 0.025$). The linear regression analysis revealed the following statistically significant relationships: HADS-D subscores and age ($B = -0.06$, $p = 0.0125$); logMAR BCVA of the worse eye and HADS-D subscore ($B = 0.541$, $p = 0.006$); mean deviation of*

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the worse eye and HADS-D subscore (B = 0.070, p = 0.016); and mean deviation of the better eye and HADS-D subscore (B = 0.097, p = 0.032).

Conclusion: *This study shows that the prevalence of anxiety is higher than that of depression in patients with glaucoma. It can also be concluded that younger age is a risk factor for both anxiety and depression. The patient's visual acuity in the worse eye and visual field severity are also risk factors for both anxiety and depression. It is therefore essential for physicians to be aware of the risk factors for anxiety and depression in patients with glaucoma and to provide glaucoma patients with appropriate psychological care, in addition to ophthalmological care, to prevent the development of these psychological conditions.*

Keywords: *anxiety, depression, glaucoma, Hospital Anxiety and Depression Scale, psychological disturbance*

Introduction

Glaucoma is one of the most common chronic eye diseases where blindness is a potential outcome. Due to its asymptomatic, chronic nature and potential to result in blindness, it can often impose a psychological burden on patients.[1,2] Anxiety and depression are two common forms of psychological disturbance, and previous studies have shown that patients with glaucoma have a greater likelihood of having these conditions.[3,4] In a study by Mabuchi *et al.* comparing patients with primary open angle-glaucoma (POAG) with sex- and age-matched reference subjects, using the Hospital Anxiety and Depression Scale (HADS), it was shown that the prevalence of anxiety or depression was higher in POAG patients than in the reference subjects, which supports the view that glaucoma is related to anxiety and depression and detrimentally affects the quality of life of glaucoma patients.[3,5] Anxiety is characterized by excessive, uncontrollable, and often irrational worry, that is, apprehensive expectation about events or activities. On the other hand, depression is a state of low mood and aversion to activity that can affect thoughts, behavior, feelings, and sense of well-being, as defined by the *Diagnostic and Statistical Manual of Mental Disorders V*.[6]

Younger age, female gender, and having a moderate or heavy economic burden are risk factors for anxiety, while being older and having increased severity and duration of glaucoma are risk factors for depression, as noted by the studies of Tastan[7] and Mabuchi *et al*.[8] Glaucoma also negatively affects psychosocial functioning. Chan and associates noted that early-stage glaucoma with mild visual field (VF) loss adversely affects anxiety, self-image, and confidence in health care. As visual acuity worsens in advanced glaucoma, anxiety further increases and self-image deteriorates.[5] Providing glaucoma patients with appropriate psychological care is therefore essential to improving their quality of life and drug compliance. In order to detect, prevent, and treat the emotional problems that

can develop in glaucoma patients, it is important to understand the risk factors for these psychological disturbances.

There were several psychometric tools used in the studies mentioned, namely, HADS questionnaire, 25-item National Eye Institute Visual Functioning Questionnaire, and the 36-item Glaucoma Quality of Life questionnaire. The HADS questionnaire was used in the studies of Mabuchi *et al*.,[8] Zhou *et al.*,[9] and Kong *et al*.[10] It was developed by Zigmond and Snaith[11] to identify and quantify the two most common forms of psychological disturbance in medically ill patients—anxiety and depression. The original HADS was translated into Chinese Mandarin and Japanese and has been validated in many studies.[11,12] The HADS has also been translated into Filipino (HADS-P) and has been used in three local studies in a tertiary hospital in Manila. In 2004, it was used to screen for anxiety and depression in Filipino epileptics,[13] and in 2012 and 2013 it was used to ascertain the prevalence and causes of anxiety and depression among Filipino chronic obstructive pulmonary disease patients.[14,15] The third national survey on blindness, conducted in the Philippines in 2002, ranked glaucoma as the third most common cause of bilateral blindness in the country and the fifth most common cause of low vision. The survey projected that a total of 71,821 Filipinos have glaucoma, 18,620 of whom are bilaterally blind.[16] However, no local studies have been conducted to determine the presence of anxiety and depression among Filipino glaucoma patients.

The main objective of this study is to identify the risk factors associated with anxiety and depression among Filipino patients with glaucoma seen in a tertiary hospital in Manila. It also aims to determine the sociodemographic profile of patients diagnosed with glaucoma, based on age, sex, and social history. In addition, the study seeks to determine the prevalence of anxiety and depression among Filipino glaucoma patients.

Methodology

This is a single-center, cross-sectional study. Patients with clinically diagnosed glaucoma, including those with POAG, exfoliation glaucoma, primary angle-closure glaucoma (PACG), and secondary glaucoma (SG), seen from June 2015 to September 2015 at the glaucoma clinic of the Department of Ophthalmology and Visual Sciences, Philippine General Hospital, were recruited for the study. The inclusion criteria were: Filipino-speaking adult patients (18 years and above) with clinically diagnosed glaucoma, based on typical glaucomatous cupping of the optic disc, with compatible VF defects detected by automated static perimeter (Humphrey VF analyzer 30-2, 24-2, and/or Octopus G1 program) in one or both eyes. Only reliable VFs, determined by false-positive results, false-negative results, or fixation losses not exceeding 33%, were used. The exclusion criteria were: patients with any other coexisting ocular condition that could impair

visual function and cause VF defects, for example, a visually significant cataract, retinal or neural pathology; patients with diagnosed psychiatric illnesses prior to diagnosis of glaucoma; patients who underwent incisional ocular surgery or laser treatment within the previous month; patients currently using antipsychotic or other medicines that might cause psychological disturbance; and patients demonstrating disability in a VF test due to cognitive impairment. Those who had recently experienced grief due to severe illness, death, or any other cause in the immediate family within the previous six months were also excluded. The formula used to compute the sample size was the one appropriate for a descriptive questionnaire-type cross-sectional study:

$$\text{ss} = \frac{Z^2 \times (p) \times (1-p)}{c^2},$$

where ss is the sample size, Z is the Z value (90% confidence level), p is the percentage picking a choice, expressed as a decimal (0.5 used for sample size needed), and c is the confidence interval, expressed as a decimal (0.1 = ±10).

A sample size of 82 patients will result in a 90% confidence level with ±10 confidence interval, with 9.05% margin of error. Prior to enrollment, each participant was given a patient's information sheet explaining the study. Informed consent was also obtained.

Patients underwent a standard ophthalmologic examination (measurement of the uncorrected and corrected Snellen visual acuity, refraction, Goldmann applanation tonometry, a slit lamp biomicroscopic examination, gonioscopic examination, and optic nerve evaluation). Newly diagnosed glaucoma patients were subjected to a VF analysis with automated perimetry (Humphrey Field Analyser, Carl Zeiss Meditec AG, jena, Germany) using a 30-2 (HFA 30-2) or a 24-2 (HFA 24-2) threshold program, or the SITA standard strategy of the Octopus G1 program. The preexisting follow-up glaucoma patients recruited to the study used their old VF results and the mean deviation (MD) in the last HFA 30-2 or HFA 24-2 or Octopus G1 program taken within six months of enrolment in this study was used to evaluate VF loss. Once the patients were referred to the study, another examination was conducted to complete the data collection form. Sociodemographic characteristics such as age, sex, social history (educational background, marital status, living companions), medical history (previous medical history and family medical history), and ocular history (duration of glaucoma, history of glaucoma medication use, history of glaucoma laser procedure, and history of glaucoma surgery) were obtained.

The HADS questionnaire, developed by Zigmond and Snaith, was used to pinpoint anxiety and depression. In patients who are unwell, these are the two most common forms of psychological disturbances. The HADS focuses solely on

psychological symptoms, while omitting physical symptoms, which could be attributed to the physical illness. It is a 14-item, self-assessment questionnaire, comprising seven items each for the anxiety subscale and depression subscale. The minimum total score of each of the seven-item subscales is 0 and the maximum is 21. Higher scores indicate a higher level of depression and anxiety.

The HADS has been translated into several languages. The Filipino version (HADS-P) has been validated and is used in this study. The participants were requested to answer the questionnaire (see Appendix A) by themselves. The questionnaire was explained to them and assistance was provided where needed. In cases where participants were unable to read due to poor eyesight, their companion was asked to read the questionnaire to the patients and their answers were then recorded. The HADS-P was tested for validity and reliability, with a recommendation of 11 as the optimal cut-off score when screening for depression and anxiety in Filipino patients. A clinical diagnosis of anxiety or depression is likely if either of the two subclasses produces a total score of 11 or more. A score of 8 to 10 is considered borderline and a score of 7 or less is considered normal.[17]

Descriptive analysis was compiled for sociodemographic data and for the psychological profile. Mean ± standard deviation with a minimum and maximum range of values was used for continuous data and frequency, with a percentage distribution for categorical data. To determine the prevalence of anxiety and depression among the participants, the frequency and percentages of both were calculated. To identify the associating factors for psychological disturbances (anxiety and depression) in patients with glaucoma, a Pearson correlation and linear regression analysis were used with the HADS-A and HADS-D subscores as dependent variables, and demographic and clinical features as independent variables. For statistical analysis, visual acuity was converted into a logarithm of minimum angular resolution (logMAR). For eyes that could not be examined by automated visual field (AVF) perimetry using HFA 30-2 or SITA G program because of poor visual function, the vision level of these eyes was assigned an MD value of 30.0 dB. Eyes categorized as "no light perception," were assigned an MD value of 40.0 dB. A p value < 0.10 was considered to be statistically significant.

The study was approved by the research ethics board of the hospital and adhered to the tenets of the Declaration of Helsinki.

Results

Eighty-two glaucoma patients were interviewed for this study. Fifty percent of the participants were diagnosed with PACG, 32% with POAG, and 18% with SG. The sociodemographic profiles of the participants are shown in Table 1. The mean age of the participants was 61.6 years ± 13.3 standard deviation, with an age range of 19 to 90 years. A total of 26 males and 56 females participated in the study.

Table 1. Sociodemographic and clinical characteristics of participants

Category	N (82)	Percentage (100)	Mean	Standard deviation	Range
Age, years			61.6	13.9	19-90
18-39	6	7			
40-60	27	33			
> 60	49	60			
Gender					
Male	26	32			
Female	56	68			
Education					
No formal education	2	2			
Elementary	27	33			
High school	34	42			
College and above	19	23			
Living status					
Alone	1	1			
Living with a partner	7	9			
Living with family	74	90			
Marital status					
Married	71	87			
Unmarried	11	13			
Duration of glaucoma (years)			5.82	5.83	0.08-29
Type of glaucoma					
POAG	26	32			
PACG	41	50			
SG	15	18			
Number of medications			2	1.03	0-5 bottles

Category	N (82)	Percentage (100)	Mean	Standard deviation	Range
Laser treatment					
No	46	56			
Yes	36	44			
Surgical treatment					
No	19	23			
Yes	63	77			
LogMAR BCVA					
Better eye			0.12	0.16	0-0.88
Worse eye			1.54	1.61	0-4
IOP, mmHg					
Eye with lower IOP			12	4.44	4-24 mmHg
Eye with higher IOP			22	13.99	7-80 mmHg
AVF MD (dB)					
Better eye			8.75	7.16	0.1-25.2
Worse eye			20.47	11.04	0.2-40
HADS-P total score			10	5.68	1.0-27
HADS-A subscore			6	3.56	0-16
HADS-D subscore			4	2.92	0-11

IOP: intraocular pressure

The mean duration of glaucoma was 5.82 years ± 5.83 standard deviation, with a range of 0.8 to 29 years. The mean total HADS-P score was 10 ± 5.68, ranging from 1.0 to 27. The mean subscores of HADS-A and HADS-D among the participants were 6 ± 3.56 (range from 0 to 16) and 4 ± 2.92 (range from 0 to 11), respectively.

The prevalence of anxiety and depression among the participants is shown in Figures 1 and 2, respectively. HADS-A score ≥ 11 was seen in 15% of cases, indicating anxiety in glaucoma patients. Borderline cases of anxiety were observed in 20% (HADS-A score of 8-10), and 65% were normal, with a HADS-A

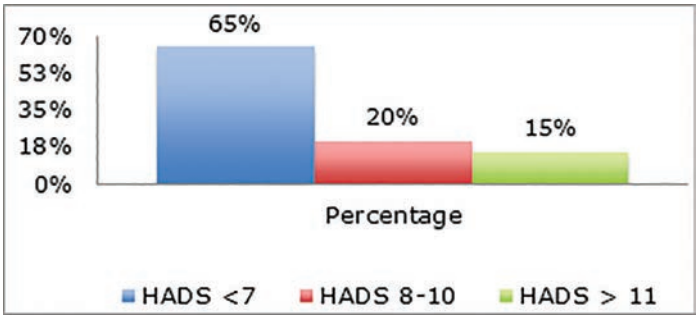

Fig. 1. HADS-P score for anxiety.

score ≤7 (Fig. 1). Similarly, clinically diagnosed (HADS-D score of ≥11) cases of depression were 1%, borderline cases (HADS-D 8-10) were 12%, and patients with normal HADS-D score were 87% (Fig. 2).

To show the relationship between the independent variables and anxiety (HADS-A subscore), Pearson correlation and linear regression were conducted. The results showed that there was a statistically significant correlation between HADS-A and age ($r = -0.273$, $p = 0.0119$; Table 2), logMAR BCVA of the worse eye ($r = 0.191$, $p = 0.085$; Table 2), and MD of the worse eye ($r = 0.247$, $p = 0.025$; Table 2). The linear regression analysis was conducted to confirm the Pearson correlation results and revealed statistically significant relationships between: HADS-A subscore and age ($B = -0.07$, $p = 0.0129$; Table 3, Fig. 3); logMAR BCVA of the worse eye and HADS-A subscore ($B = 0.424$, $p = 0.086$; Table 3); and MD of the worse eye and HADS-A subscore ($B = 0.078$, $p = 0.025$; Table 3).

Pearson correlation and linear regression were conducted to determine the relationship between the independent variables and depression (HADS-D

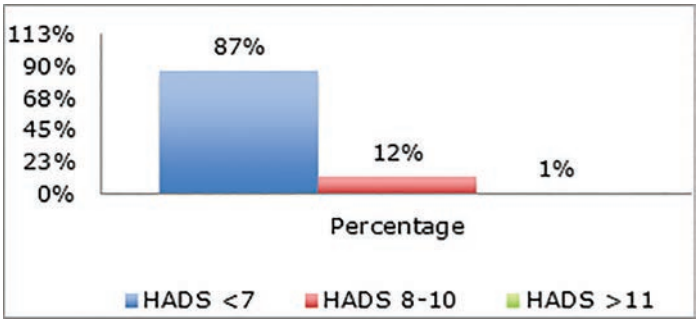

Fig. 2. HADS-P score for depression.

Table 2. Pearson correlation for anxiety (HADS-A)

Category	Correlation with HADS-A	p Value
Age, years	−0.273393685	0.0119[a]
LogMAR BCVA		
Better eye	−0.017163989	0.879
Worse eye	0.191386096	0.085[a]
AVF MD (dB)		
Better eye	0.114971832	0.297
Worse eye	0.247043223	0.0252[a]

[a]p < 0.1 considered significant

Table 3. Linear regression analysis for anxiety (HADS-A)

Category	DFn, DFd	F	R^2	Constant	B	p Value
Age, years	1, 80	6.463	0.07474	10.7	−0.07011	0.0129[a]
LogMAR BCVA						
Better eye	1, 80	0.02679	0.0003347	6.47	−0.4080	0.8704
Worse eye	1, 80	3.032	0.03652	5.729	0.4240	0.0855[a]
AVF MD (dB)						
Better eye	1, 80	1.072	0.01322	5.878	0.05711	0.3037
Worse eye	1, 80	5.200	0.06103	4.747	0.07965	0.0253[a]

DFn: the degree of freedom for the numerator of the F ratio; DFd: denominator [a]p < 0.1 considered significant

subscore). The results showed that there was a statistically significant correlation between age (r = −0.275, p = 0.0115; Table 4), logMAR BCVA of the worse eye (r = 0.299, p = 0.006; Table 4), and MD of the worse eye (r = 0.266, p = 0.016; Table 4) and better eye (r = 0.238, p = 0.032; Table 4). The linear regression analysis revealed the following statistically significant relationships: HADS-D subscore and age (B = −0.06, p = 0.0125; Table 5, Fig. 4); logMAR BCVA of the worse eye and HADS-D subscore (B = 0.541, p = 0.006; Table 5); MD of the worse eye and HADS-D subscore (B = 0.070, p = 0.016; Table 5); and MD of the better eye and HADS-D subscore (B = 0.097, p = 0.032; Table 5).

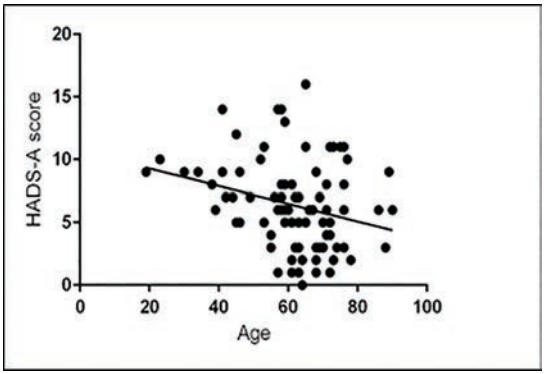

Fig. 3. Linear regression plot between age and HADS-A score.

Table 4. Pearson correlation for depression (HADS-D)

Category	Correlation with HADS-D	p Value
Age, years	−0.274682999	0.0115[a]
LogMAR BCVA		
Better eye	0.026691152	0.8124
Worse eye	0.298974388	0.006[a]
AVF MD (dB)		
Better eye	0.237480083	0.032[a]
Worse eye	0.265541095	0.016[a]

[a]$p < 0.1$ considered significant

Tables 6 and 7 show the average BCVA of both the better and worse eye in logMAR to each HADS subclass; it is noted that patients with poorer BCVA in the worse eye would also correspond to a higher HADS score.

The average and range of VF MD in decibels are also presented in Tables 8 and 9 to show the corresponding VF defect and equivalent HADS score of the patients who participated in the study.

The patients were also categorized based on the type of glaucoma they had and the equivalent scores for each HADS subclass, as shown in Tables 10 and 11. The patients were grouped into PACG, POAG, and SG.

Table 5. Linear regression analysis for HADS-D

Category	DFn, DFd	F	R^2	Constant	B	p Value
Age, years	1, 80	6.529	0.07545	7.546	−0.0578	0.0125[a]
LogMAR BCVA						
Better eye	1, 80	0.05845	0.0007301	3.928	0.4943	0.8096
Worse eye	1, 80	7.850	0.08936	3.156	0.5414	0.0064[a]
AVF MD (dB)						
Better eye	1, 80	4.781	0.0564	3.141	0.09675	0.0317[a]
Worse eye	1, 80	6.069	0.07051	2.55	0.07022	0.0159[a]

DFn: the degree of freedom for the numerator of the F ratio; DFd: denominator [a]p < 0.1 considered significant

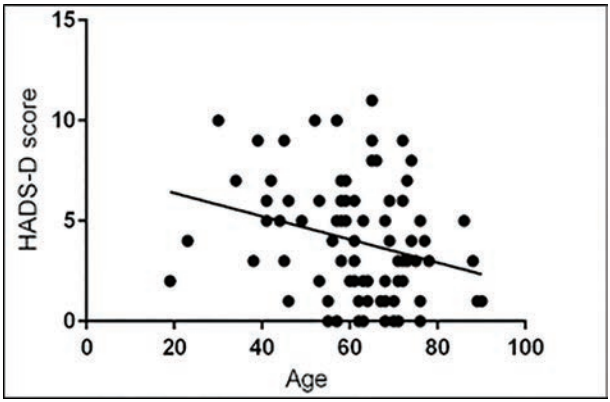

Fig. 4. Linear regression plot between age and HADS-D score.

Table 6. Mean and range of BCVA for each HADS-A category

HADS-A	Mean BCVA of the better eye (logMAR value)	Range of BCVA of the better eye (logMAR value)	Mean BCVA of the worse eye (logMAR value)	Range of BCVA of the worse eye (logMAR value)
HADS ≤ 7	0.13	0-0.88	1.34	0-4.0
HADS 8-10	0.07	0-0.48	1.97	0-4.0
HADS ≥ 11	0.15	0-0.40	1.83	0.18-4.0

Table 7. Mean and range of BCVA for each HADS-D category

HADS-D	Mean BCVA of the better eye (logMAR value)	Range of BCVA of the better eye (logMAR value)	Mean BCVA of the worse eye (logMAR value)	Range of BCVA of the worse eye (logMAR value)
HADS ≤ 7	0.11	0-0.88	1.44	0-4.0
HADS 8-10	0.14	0-0.30	2.15	0-4.0
HADS ≥ 11	0.40	0.40	2.00	2.0

Table 8. Mean and range of AVF (MD) for each HADS-A category

HADS-A	Mean AVF of the better eye (MD in dB)	Range of AVF of the better eye (MD in dB)	Mean AVF of the worse eye (MD in dB)	Range of AVF of the worse eye (MD in dB)
HADS ≤ 7	8.05	0.1-25.2	18.77	0.2-40
HADS 8-10	10.71	0.4-23.1	23.28	7.1-40
HADS ≥ 11	9.32	0.2-22.41	24.4	2.92-40

Table 9. Mean and range of AVF (MD) for each HADS-D category

HADS-D	Mean AVF of the better eye (MD in dB)	Range of AVF of the better eye (MD in dB)	Mean AVF of the worse eye (MD in dB)	Range of AVF of the worse eye (MD in dB)
HADS ≤ 7	8.14	0.1-25.2	19.91	1.4-40
HADS 8-10	12.44	0-25.2	23.50	0.2-40
HADS ≥ 11	15.5	15.5	30	30

Table 10. Percentage of patients in each HADS subclass for each glaucoma category.

HADS-A	PACG (n = 41) (%)	POAG (n = 26) (%)	SG (n = 15) (%)
HADS ≤ 7	66	58	80
HADS 8-10	10	35	20
HADS ≥ 11	24	8	0

Table 11. Percentage of patients in each HADS subclass for each glaucoma category.

HADS-D	PACG (n = 41) (%)	POAG (n = 26) (%)	SG (n = 15) (%)
HADS ≤ 7	85	85	87
HADS 8-10	12	15	7
HADS ≥ 11	2	0	0

Discussion

The chronic nature of glaucoma and associated long-term treatment, risk of blindness, cost of medicines, and surgical procedures may all be factors in the development of anxiety and depression. The prevalence of clinical anxiety (15%) and borderline anxiety (20%) is higher than that of clinical depression (1%) and borderline depression (12%), perhaps due to the stress of frequent clinic visits, economic burden of treatment, and the absence of a guaranteed cure. Patients with glaucoma might be anxious about the risk of blindness and the consequent inability to earn a living or perform normal activities of daily life. The higher prevalence of anxiety over depression is reflected in other studies. In a study by Fasih *et al.*,[18] it was noted that anxiety (33%) is more prevalent than depression (22%) among patients diagnosed with POAG. Similarly, a study by Mabuchi showed that patients with glaucoma are more likely to have anxiety (13%) than depression (10%).[8]

The tendency toward psychological disturbances among glaucoma patients could be due to worrying and feelings of panic as a result of the poor prognosis associated with the disease. The initial anxiety may arise from coming to terms with the condition and their hopes to find a cure that will avoid blindness.

Risk factors of glaucoma patients that make anxiety more likely include age, logMAR BCVA of the worse eye, and MD (AVF) of the worse eye. There is a negative correlation between age and the HADS-A subscore, which showed that younger patients with the condition tend to be more anxious. This is similar to the study of Mabuchi, and also Zhou, which revealed that younger patients were more likely to be anxious once they had been diagnosed with glaucoma.[8,9] Younger patients also showed anxious behaviors when diagnosed with other chronic diseases, such as cancer and cardiovascular disease.[12,19] As glaucoma can potentially result in bilateral blindness, younger glaucoma patients may have been more anxious about maintaining their visual function in light of their longer remaining life span. Patients with poor visual acuity and severe generalized depression, as depicted in the MD, showed a statistically significant positive correlation with the HADS-A subscore. Having poor visual acuity causes the patient to be anxious, probably due to the fear of losing their vision and their reduced future productivity.

However, there were no significant relationships between anxiety and the type of glaucoma, duration of glaucoma, number of eye drops, or gender in this study.

Although only 1% of the participants had clinical depression and 12% had borderline depression based on the HADS-D subscore, it was still noted that younger age, logMAR BCVA of the worse eye, and MD (AVF) in both the worse and better eyes had significant correlation. This differs from the study of Mabuchi, which showed that older patients were more prone to depression.[8] The fact that only a small proportion of the population is thought to suffer from depression probably accounts for the disparity between this study and Mabuchi's in the correlation between age and HADS-D subscore. Different races and ethnicities may have different coping mechanisms and psychological reactions toward the disease. In a Filipino study by de Guzman,[20] the validation of the translated HADS questionnaire showed that both anxiety and depression were higher among patients in the younger age group (18-35 years), which is similar to the negative correlation shown in this study. This psychopathological finding is probably due to the combination of stresses caused by coping with a chronic, potentially blinding condition during a person's most productive years. Similar to the study of Mabuchi *et al.*,[8] depression had a positive correlation with poor visual acuity and increased severity in the MD of the AVFs. This can probably be attributed to worsening visual prognosis, which may have contributed to depression in the patient. In this study, the likelihood of patients suffering from anxiety or depression was not impacted by whether they had POAG, PACG, or SG. Factors such as marital status, educational status, or whether subjects lived with others or alone made no statistical difference. This may be because the majority of participants are likely to be in a low-income bracket, as this study was conducted in a single-center, government tertiary hospital.

The limitations of this study are as follows: the majority of participants had moderate or advanced generalized VF defects, which probably resulted in a statistically significant positive correlation for the HADS score. Most of the patients seen in this institution were referrals from other hospitals, meaning the disease could either be advanced or already end-stage, which could have affected the HADS scores. The majority of patients also belonged to a lower socioeconomic background and had a lower educational status, which could have affected their HADS scores. Although the HADS is simple and lends itself to studies such as this, a questionnaire is not comparable with a formal psychiatric diagnosis of depression or anxiety. A follow-up study can be conducted where patients with high HADS scores will be formally referred to a specialist for further evaluation. A multicenter study is recommended to broaden the mix of patients' socioeconomic status and severity of glaucoma. A larger sample size is also recommended in order to strengthen the statistical relationships between the variables presented.

Conclusion

Our study shows that the prevalence of anxiety is higher than that of depression in patients with glaucoma. It is therefore suggested that in addition to evaluation and treatment of glaucoma patients, ophthalmologists should be aware of the possible psychological disturbances this condition brings to a patient, and prompt referral for further evaluation of this conditions should be conducted.

It can also be concluded that young age was found to be a risk factor for both anxiety and depression. The patient's visual acuity in the worse eye and VF severity are also risk factors for both anxiety and depression. It is therefore essential for physicians to be aware of the risk factors for anxiety and depression in patients with glaucoma and to provide glaucoma patients with appropriate psychological care, in addition to ophthalmological care, to reduce or eliminate the likelihood of developing anxiety and depression.

Acknowledgment

The authors have no financial, proprietary, or commercial interest in any of the materials used in this study.

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Appendix A. HADS-P questionnaire

Hospital Anxiety and Depression Scale-Pilipino Translation (HADS-P)

Direksyon: Maari pong pakisagutan ang mga sumusunod na tanong sa pamamagitan ng paglagay ng ☑ sa kahon na mahahayag ng inyong palagay. Wala pong tama o maling kasagutan sa bawat tanong.

1. Naliligalig at punong-puno na ako. Mas madalas kaysa hindi Madalas Paminsan-minsan Hinding-hindi	2. Pakiramdam ko parang pinapabagal ako. Halos lagi-lagi Napakadalas Minsan Hinding-hindi
3. Ikinasasaya ko pa rin ang mga bagay na dati ko nang ikinasasaya. Katulad din ng dati Hindi na kasingdalas Konti lang Halos hindi na	4. Para akong natatakot na may nararamdamang sobrang nerbiyos. Hinding-hindi Paminsan-minsan Medyo madalas Madalas na madalas
5. Para akong nakakaramdam na may mangyayaring masama. Lagi-lagi at medyo malala Palagi pero di-gaanong malala Konti pero di ako nag-aalala Hinding-hindi	6. Nawalan na ako ng interes sa aking hitsura. Talaga Hindi ako nangangalaga ng dapat Pwedeng hindi ako magalaga ng nararapat Pinangangalagaan ko pa rin ito tulad ng dati
7. Kaya ko pang tumawa at mapansin ang nakakatuwang bahagi sa mga bagay-bagay. Lagi-lagi tulad ng dati Mas madalang na ng kaunti jaysa dati Hindi na katulad ng dati Hinding-hindi	8. Hindi ako mapakali na parang gusto kong may pinakakaabalahan. Talagang madalas Medyo madalas Di naman gaano Hinding-hindi
9. Pag-aalala ang nasa isip ko. Madalas na madalas Madalas Di gaanong madalas Konting-konti	10. Masaya akong umaasa sa bagay-bagay Kasingdalas ng nakagawian ko Di-kasingdalas ng nakagawian ko Mas madalang kaysa nakagawian ko Halos hindi na
11. Masaya and aking pakiramdam. Hindi kailanman Madalang Paminsan-minsan Kadalasan	12. Bigla akong nakakaramdam ng pagkasindak. Madalas na madalas Medyo madalas Di gaanong madalas Hinding-hindi
13. Kaya kong umupo ng kumportable at mag-relax. Palagi Madalas Madalang Hinding-hindi	14. Kaya akong maaliw sa isang magandang libro o programa sa radio o TV. Madalas Paminsan-minsan Madalang Hinding-hindi

Appendix B. HADS questionnaire (English)

Hospital Anxiety and Depression Scale (HADS)

Tick the box beside the reply that is closest to how you have been feeling in the past week.
Don't take too long over you replies: your immediate is best.

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Please check you have answered all the questions

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