• Clinical Research •

Functional evaluation of the filtering bleb by ultrasound biomicroscopy after trabeculectomy with mitomycin C

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Abstract

• AIM: To study the role of ultrasound biomicroscopy (UBM) in the assessment of the bleb function after trabeculectomy with mitomycin C (MMC).

• METHODS: This was a cross-sectional study including all cases had undergone trabeculectomy with MMC 0.2 mg/mL for 3min. Participants were recruited from the follow-up cases at Department of Ophthalmology, Tanta University in the period from August 2015 to August 2016. Full history taking and ophthalmological examination were performed. Intraocular pressure (IOP) was measured using Goldmann applanation tonometry and the history of prescribed postoperative antiglaucoma medications was recorded. Accordingly, the trabeculectomy blebs were divided clinically into successful blebs when the IOP post-operative was ≤18 mm Hg without medications. Scanning examination of the filtering bleb using UBM examination was performed at the period from 2 to 36mo after trabeculectomy (13.6±9.7mo).

• RESULTS: This study included 33 trabeculectomy filtering blebs of 25 patients (9 males and 16 females). The mean age of patients was 53.2±14.2y (range 25-71y). We had 20 eyes with complete success, 9 eyes with qualified success, and 4 eyes with failure after trabeculectomy with MMC. The blebs were classified into successful blebs (IOP ≤18 mm Hg without antiglaucoma medications), others were classified into qualified successful and failed blebs. There was a significant correlation between certain UBM findings (intra-bleb reflectivity, draining sub-scleral tract, bleb height, and intrableb fluid cysts) and cases with different grades of clinical functional success (*P*<0.01).

• CONCLUSION: UBM is an objective tool in the functional assessment of the post-trabeculectomy filtering bleb through a significant correlation between certain UBM parameters and the different grades of clinical functional success.

• KEYWORDS: filtering bleb; bleb reflectivity; sub-scleral tract; ultrasound biomicroscopy; sclerotomy site

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INTRODUCTION

Filtering glaucoma surgery, particularly trabeculectomy, is the most effective strategy to reduce intraocular pressure (IOP) in glaucoma patients[1]. In trabeculectomy, the IOP is lowered as aqueous humor exits through the bleb by multiple pathways including transconjunctival filtration and absorption through the episcleral veins[2]. The main determinant of long-term surgical success is related to the healing response[3-5]. Excessive postoperative wound healing with subsequent fibrosis may lead to obstruction of the created channel, that in turn results in filtration failure with consequent visual field loss[6]. The key to a successful trabeculectomy long term outcome is to modulate the wound healing cascade that leads to closure of the newly created aqueous outflow pathway[7]. Mitomycin C (MMC) has been used to modulate the wound healing process and increase surgical success[8-9]. The bleb is the visible component of trabeculectomy and the major contributor to success, failure, and complications[10]. Clinically, bleb outcomes can be described by using one of many grading systems such as Wuerzburg bleb classification score (WBCS)[11], the Indiana Bleb Appearance Grading Scale (IBAGS)[12], and the Moorfields Bleb Grading System (MBGS)[13]. However, the slit lamp evaluation lacks the depth of description required for following up the bleb morphological changes over time, and there is a wide range of possible variations in each of these descriptions[14]. Ultrasound biomicroscopy (UBM) as a high frequency ultrasound non-invasive tool is superior to slit lamp as allowing an objective demonstration of internal structures and architectures of the bleb[15]. It can also visualize the fluid spaces of the bleb, sclerectomy site, the patent iridectomy and the ciliary body[16].

SUBJECTS AND METHODS

This observational cross-sectional study included all cases of open angle glaucoma had undergone to primary trabeculectomy with MMC (0.2 mg/mL for 3min). Participants were recruited from the follow-up cases seen at Department of Ophthalmology, Tanta University in the period from August 2015 to August 2016. IOP measurements were performed using Goldmann applanation tonometry just before UBM examination of the filtering blebs. History of postoperative prescribed antiglaucoma medications was documented in this study. The study complied with the principles of the Declaration of Helsinki, and was approved by the Institutional Ethics Committee. A written informed consent was obtained from each participant.

The target of success was IOP reduction after glaucoma surgery ≥20% reduction. According to the IOP and the postoperative prescribed antiglaucoma medications; the clinical success grades of the included eyes were divided into three groups:

Complete success: cases with IOP ≤18 mm Hg without any antiglaucoma medications;

Qualified success: cases with IOP ≤18 mm Hg with antiglaucoma medications;

Failure: cases with IOP >18 mm Hg and <20% reduction of IOP despite all lines of antiglaucoma medications.

UBM examination was performed with VuMAX 50 MHz transducer (Sonomed Escalon, USA). Scanning examination of the filtering bleb with radial and transverse scans using an over-sized optic cup (24 mm) diameter. The quantitative and qualitative data of the UBM were collected and analyzed. Six UBM parameters were evaluated:

Intrableb reflectivity: it was described by Yamamoto *et al*[17]. High reflectivity: it was related to its similarity to the scleral reflectivity of the same image; Low reflectivity: it was related to its similarity (isoechoic) to a standard UBM bleb image of a functionally successful filtering bleb (Figure 1); Moderate reflectivity: when it was found to lie between the reflectivity of the standard image and the sclera.

Bleb height: it was described by Yamamoto *et al*[17], it is the length of the perpendicular line from the highest point on the bleb to the longest line from the outer surface of the sclera to that of the corneal surface. It was classified into low bleb height if length <1 mm, moderate bleb height if length 1-2 mm, and high bleb if length ≥2 mm.

The presence of intra bleb cysts (fluid spaces): it was graded as present or absent.

Drainage tract under scleral flap: it may be visible along the entire tract of scleral flap or partially visible (could not be seen along the entire scleral flap), and invisible if the tract could not be seen at all.

Sclerectomy site: patent or occluded.

Peripheral iridectomy: complete or incomplete.

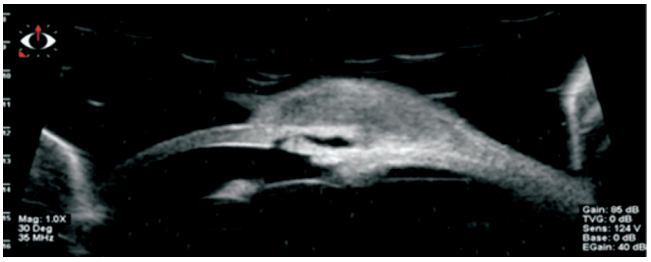

Figure 1 UBM image of hypo-reflective bleb in successful study case (study case with normal IOP of 12 mm Hg without antiglaucoma medications, standard image).

The UBM findings of the examined filtering blebs were recorded and correlated with cases of different grades of functional success.

Statistical Analysis It was performed with IBM SPSS software version 24. Cramer's V measures based on Pearson Chi-square tests were used to investigate the association between different variables. Data were expressed as mean± standard deviation for metric values and as a frequency (percentage) for categorical variables. *P* values less than 0.01 were considered statistically significant.

RESULTS

Thirty-three trabeculectomy filtering blebs of 25 patients (9 males and 16 females) were included. The patients' age ranged from 25 to 71y with 53.2±14.2y. Different types of glaucoma were included in this study as: primary open angle glaucoma (*n*=23), Plateau iris syndrome (*n*=1), traumatic glaucoma (*n*=1), juvenile glaucoma (*n*=1), Vogt koyanagi harada syndrome (*n*=2), iridocorneal endothelial syndrome (*n*=1), primary angle-closure glaucoma (*n*=1), secondary angle-closure glaucoma (*n*=1), corticosteroid induced glaucoma (*n*=1), pseudophakic glaucoma (*n*=1). UBM examination was performed 2 to 36mo after trabeculectomy with 13.6±9.7mo. The different grades of functional success were divided according to the IOP post-operative with significant difference (*P*=0.001). We had 20 eyes (60.6%) of functionally complete successful blebs with IOP (12.8±2.28 mm Hg), 9 eyes (27.3%) of qualified success blebs with IOP (15.7±4.9 mm Hg), and 4 eyes (12.1%) of functionally failed blebs with IOP (23.5±1.9 mm Hg). Cases with qualified success were using one line of antiglaucoma medications in 6 eyes, 2 lines in 2 eyes and 3 lines in one case, however, failed cases were using 3 lines of treatment (Table 1).

The different UBM findings and parameters of the different grades of functional successful blebs were documented as follow: there was a highly significant correlation between certain UBM findings, (intrableb low reflectivity and visible sub-scleral tract) with clinical cases of complete success (*P*<0.001). Also, the low bleb height was significantly correlated with failed cases (*P*=0.003). The presence of fluid cysts inside the bleb was correlated significantly to cases with

Table 1 The baseline characteristics of participants

Parameters	Complete success	Qualified success	Failure	*P*
No. of eyes	20	9	4	0.286
Mean age±SD (y)	49.27±15.04	54.25±13.13	62±4.12	
Male/Female	5/10	2/4	2/2	
Mean duration between trabeculectomy and UBM examination±SD (mo)	13.2±10.11	16.11±9.29	10.5±4.97	0.282
Mean IOP±SD (mm Hg)	12.8±2.28	15.7±4.9	23.5±1.9	0.001[b]

[b]Statistically significant <0.01.

Table 2 UBM findings and parameters of the studied eyes

UBM parameters	The grade of success				Cramer's V measure[1]	*P*
	Complete success (*n*=20)	Qualified success (*n*=9)	Failure (*n*=4)	Total (*n*=33)		
Intrableb reflectivity						0.000[b]
Low	19	0	0	19		
Moderate	1	7	1	9	0.751	
High	0	2	3	5		
Bleb height						0.003[a]
High	3	0	0	3		
Moderate	17	5	1	23	0.493	
Low	0	4	3	7		
Cysts inside bleb						0.006[a]
Present	20	8	2	30	0.554	
Absent	0	1	2	3		
Tract under scleral flap						0.000[b]
Visible	20	7	0	27		
Partially visible	0	2	2	4	0.634	
Invisible	0	0	2	2		
Sclerectomy site						0.024
Present	20	9	3	32	0.476	
Absent	0	0	1	1		
Iridectomy						0.024
Complete	20	9	3	32	0.476	
Incomplete	0	0	1	1		

[1]Chi-square tests; [a]Statistically significant; [b]Statistically highly significant.

complete success (*P*=0.006). The sclerectomy site was present in all cases and occluded in one case by the iris tissue. The presence of the sclerectomy or the patency of iridectomy were not significantly correlated to the different grades of functional success (*P*=0.024) (Table 2; Figure 2).

In this study, we developed a point scoring system "UBM Bleb Image Score (UBIS)" using the four significant UBM parameters (intrableb reflectivity, bleb height, cysts inside the bleb, sub-scleral tract).

According to the summation of these points, we could predict of the degree of bleb functionality objectively and classify it into: good, fair and poor functioning blebs.

UBIS summation of 5 equals to "good functioning bleb", 3 or 4 equals to "fair functioning bleb" and 2 or less equals to "poor functioning bleb" (Table 3; Figure 3).

There was a highly significant correlation between the UBIS pointing system and the different grades of clinical functional success. The good UBIS was significantly correlated with cases of complete success, fair UBIS was significantly correlated with cases of qualified success. The poor UBIS was correlated significantly with cases of functional failure (*P*=0.000; Table 4).

DISCUSSION

The bleb morphology after trabeculectomy is an important clinical parameter of success; a careful evaluation of bleb morphology may reveal certain features that can predict the functional outcome[18]. Several scoring systems offer a framework for structured patient examination and facilitate the interpretation of clinical findings[10,13,18]. The WBCS aims at standardized assessment of the developing filtering bleb after

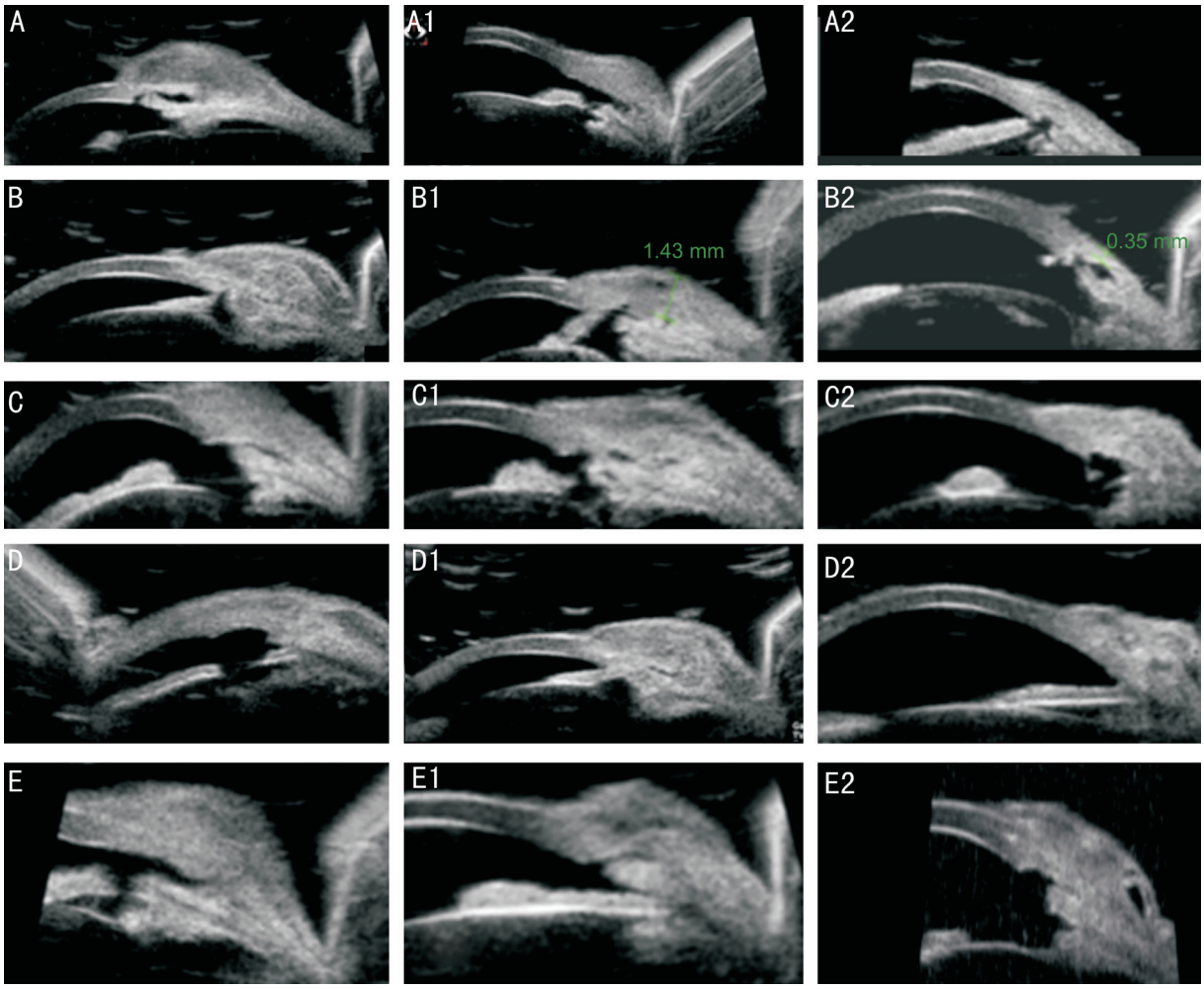

Figure 2 Different UBM findings A: Low reflectivity; A1: Moderate reflectivity; A2: High reflectivity; B: High bleb height; B1: Moderate bleb height; B2: Low bleb height; C: Visible sub-scleral tract; C1: Partially visible sub-scleral tract; C2: Absent sub-scleral tract; D: Present sclerectomy; D1: Present sclerectomy but occluded by iris; D2: Absent sclerectomy; E, E1, E2: Presence of intrableb cystic changes in different sizes (microcysts and fluid cavities) .

Table 3 UBIS pointing system of the four imaging parameters

UBM parameter	Grade	Points
Intrableb reflectivity	Low to moderate	1
	High	0
Subscleral tract	Visible	2
	Partially visible	1
	Invisible	0
Bleb height	High to moderate	1
	Low	0
Intrableb cysts	Present	1
	Absent	0
Sum of points (bleb score)		0-5

trabeculectomy[11]. They found that the presence of a higher quantity of microcysts, lower quantity of conjunctival vessels and cork screw vessels, lower prevalence of encapsulation and low bleb height, all were correlated with a favorable outcome. As the clinicians are aware that the presence of microcysts in the bleb wall is an important indicator of aqueous flow through the bleb, so, ideally any bleb grading system should include an index to reflect microcystic changes. The microcystic changes of the conjunctiva were not as easily amenable to slit lamp photography. In the study performed by Avitabile *et al*[19], they found that the blebs with lower reflectivity and visible tract under the scleral flap were having a better bleb function. It was reported that the clinical classifications were unable to distinguish between low, diffuse and completely flat blebs on the stereo or mono photographs. Also, the aqueous drainage under the scleral flap was imperceptible on visual examination and needs an objective imaging tool[20]. In such respects, imaging tools as UBM and anterior segment optical coherence tomography (AS-OCT) may contribute to more valuable data in bleb characterization, and the shown different bleb imaging modalities are able to provide an objective evaluation of the microcystic change, bleb height, and bleb wall thickening by OCT. In this study, we used the UBM as a high-frequency imaging tool to develop a point scoring system for the bleb morphology. The use of UBM permits a detailed non-invasive observation of the inner architecture of the bleb after trabeculectomy[21]. The study under question was depending

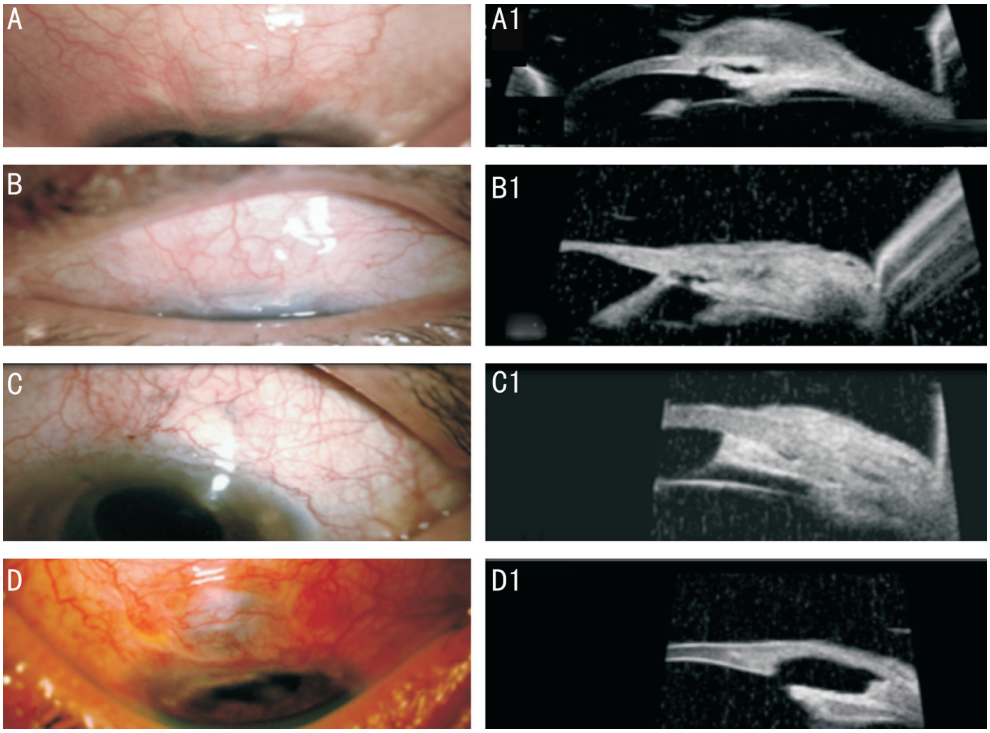

Figure 3 Slit lamp and UBM photos of filtering blebs of different point scoring A, A1: Score pointing of good functionally bleb (low reflectivity, visible sub-scleral tract, present microcysts inside the bleb, moderate bleb height); B, B1: Score pointing of fair functionally bleb (moderate reflectivity, partial visible sub-scleral tract, small cysts inside the bleb, moderate bleb height); C, C1: Score pointing of poor functionally bleb (high reflectivity, invisible sub-scleral tract, absent cysts inside the bleb, low bleb height, occluded sclerectomy site with iris tissue); D, D1: Score pointing of poor functionally bleb (torn scleral flap, high reflectivity, no cysts inside the bleb, low bleb height).

Table 4 The correlation between the UBIS pointing system and the clinical functional success

The clinical functional grades of success	UBIS						Total
	Poor (*n*=3)			Fair (*n*=8)		Good (*n*=22)	
	0	1	2	3	4	5	
Complete success	0	0	0	0	0	20	20
Qualified success	0	0	0	2	5	2	9
Failure	1	1	1	1	0	0	4
Total	1	1	1	3	5	22	33

UBIS: UBM Bleb Image Score. Cramer's V 0.856, *P*=0.000, Chi-square test.

on using four UBM parameters as intrableb reflectivity, bleb height, cysts inside the bleb and tract under the scleral flap. According to the sum of these points and calculated score, we could expect the functionality of the blebs objectively and classify it into good, fair and poor success. The bleb assessment with UBM can also influence the clinical decision-making regarding laser suture lysis or needling procedures following trabeculectomy. Leung *et al*[22] reported that the deep structures of the anterior ocular segment have been observed non-invasively since the advent of AS-OCT for clinical use in 2005, however, the AS-OCT could delineate scleral flaps of diffuse filtering blebs in only half percentage of cases. Hamanaka *et al*[23] reported that the border of the bulging part of the blebs was very difficult to determine, with AS-OCT. A recent study reported that the intrableb structures could be visualized more clearly but by using the three dimensional cornea and anterior segment optical coherence tomography (3-D CAS OCT), although, the study was in need to identify the correlation between bleb-related parameters and IOP as achieved by the current study[24]. The limitations of the current work were the inability to the evaluate the correlation of early bleb morphology with later functional outcome in relation to the postoperative period, this may enable us to intervene in the intrableb scarring process in an appropriate time with appropriate manner.

In conclusion, UBM had an important and objective role in the functional assessment of the post trabeculectomy filtering bleb through a pointing system entitled UBIS. This system was depending on the significant correlation between certain UBM parameters as (intrableb reflectivity, bleb height, cysts

inside the bleb and sub-scleral tract) and the different grades of clinical functional success.

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