

Objective documentation of anterior chamber depth following trabeculectomy and its correlation with intraocular pressure and bleb functionality

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Abstract

The purpose of this study was to objectively evaluate the anterior chamber depth (ACD) after trabeculectomy and to correlate its variations with the intraocular pressure (IOP) and bleb functionality.

Fifty eyes (46 patients) were included in this prospective study. ACD was documented with the use of a non-contact optical device (IOL Master-Carl Zeiss Meditec) and IOP was measured with the Goldmann applanation tonometer.

Ophthalmological examination, IOP, and ACD measurements were performed before surgery, the day after and weekly thereafter.

Linear regression Analysis between the 2 variables was performed and correlation coefficients were estimated. A 2-tailed *t* test was used and a *P* value < .05 was considered as statistically significant.

Correlation coefficients between ACD and IOP, during the follow-up period, resulted in a moderate to strong positive relationship ($r=0.2-0.7$), which since the 1st week resulted statistically significant at 5%.

Twenty seven eyes (54%) needed at least 1 needling procedure. Considering each group separately, until the 3rd post-op week, the correlation coefficients in the needling group resulted higher than those in the non-needling group. Furthermore, in the needling group, the relationship between ACD and IOP, for the 1st, 2nd, 3rd, and 4th week was statistically significant at 5%.

The objective documentation of the ACD in the early post-trabeculectomy period presents a moderate to strong positive correlation with the IOP.

Furthermore, the brisk deepening of the ACD during the first 2 to 4 post-operative weeks is strongly correlated with the increase of the IOP and early signs of bleb encapsulation.

Abbreviations: Δ ACD = Difference in Anterior Chamber Depth, Δ IOP = Difference in Intraocular Pressure, ACD = Anterior Chamber Depth, IOP = Intraocular Pressure, POAG = Primary Open Angle Glaucoma, PXG = Pseudoexfoliative Glaucoma.

Keywords: anterior chamber depth, correlation, intraocular pressure, trabeculectomy

1. Introduction

The reduction of intraocular pressure (IOP) is currently considered the evidence-based and most accepted therapeutical approach of glaucoma patients.^[1,2] If the maximal tolerated medical treatment is not capable to prevent further progression of the glaucomatous damage, then the trabeculectomy is considered

the main anti-glaucoma operation.^[3,4] This filtering operation creates a guarded fistula between the anterior chamber and the subconjunctival area, which represents the space where the aqueous humor is accumulated and thereafter adsorbed by the vascular and lymphatic bed. However, one of the most common reasons of failure is represented by filtering bleb encapsulation, which occurs due to the intensive fibroblastic proliferative reaction and activation of the inflammatory cascade.^[5,6] This wound healing response, which initiates immediately after the initial surgical trauma,^[7] can lead to gradual obstruction of the area around the scleral flap, ending up in blockage of the aqueous outflow. Encapsulation of the filtering bleb with consecutive outflow disturbance and a gradual increase of the IOP represent the most common early post-operative complication, occurring from 4% to 30% of cases.^[8-10]

It is well documented that the depth of the anterior chamber following a filtering procedure is subjected to variations of the axial length, usually is shallower in the 1st days to weeks and gradually deepens during the advancement of the post-operative period.^[11]

Our clinical impression is that during the early post-trabeculectomy period, the variations of the anterior chamber depth (ACD) could be related to variations of the IOP and that eventual changes of the former could also be related to modifications of bleb functionality.

To our knowledge, there are no published studies dealing with non-contact, objective, documentation of the ACD, following

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trabeculectomy, and correlation of its variations with intraocular pressure (IOP) fluctuations and bleb functionality.

2. Methods

This, prospective, interventional study adheres to the tenets of the Declaration of Helsinki and was performed after the permission of the institutional ethics committee of "G.Gennimatas" General Hospital. Patients were informed about the study procedure and provided written, informed consent.

In the study were included 50 phakic eyes of 46 patients that underwent 5-Fluorouracil (5-FU) augmented trabeculectomy. All patients were Caucasians, 26 were male and 20 female. The period of patient selection was extending between January of 2014 and June of 2015, during which more than 150 filtering procedures were carried out in our clinic.

Among the 50 eyes that were included in the study, the great majority belonged at the 2 main glaucoma types most common in our area: 26 cases with primary open angle glaucoma (POAG) and 20 cases with pseudoexfoliative glaucoma (PXG). The rest were represented by chronic angle closure (3 eyes) and pigmentary glaucoma (1 eye).

Inclusion criteria for the participation in the study were: phakic patients with medically uncontrolled glaucoma due to unacceptable target IOP (visual field or optic disc structural damage progression), age >25 years old, patients capable to be presented in every follow-up appointment (7 post-operative appointments). Exclusion criteria included: the so called "refractory" glaucomas, like neovascular, inflammatory, post-traumatic glaucoma, patients with corneal haze, causing inability to measure the ACD, and patients with previous anti-glaucoma surgical procedures.

For each patient, specific pre-operative data were collected: gender, age, best corrected visual acuity, type of glaucoma, IOP (as measured the day before surgery with Goldmann applanation tonometer and taking into consideration the average of 3 measurements checked every 5 minutes), and last, number and type of anti-glaucoma medications used.

During the post-operative period, measurements of the ACD and the IOP in the prefixed appointments (1st post-operative day – 1st, 2nd, 3rd, 4th, 6th, and 8th week) were performed by 2 ophthalmologists (masked to the study and to the patients data), following a specific temporal sequence, with the documentation of the ACD preceding of 30' the IOP measurement.

The objective documentation of the axial ACD, both pre- and postoperatively, was done with the IOL Master biometric device (slit-beam photographic technique), in particular with the specific software "IOLMaster Advanced Technology Software Version 5" under dark room circumstances in order to minimize possible external reflections that could represent source of artifacts.

The IOL Master (Carl Zeiss Meditec, Jena, Germany) is a non-contact device that measures axial length, ACD, and corneal curvature with high precision (5 μm) and good resolution (12 μm).^[12–14] Each time, 5 measurements of the ACD and their average are offered by the device.

In order to check the morphologic features of the blebs, the operated eyes were evaluated with a combination of slit-lamp examination and color photographs of the anterior ocular segment, according to the instructions of the Moorfields Bleb Grading System.

2.1. Surgical technique—trabeculectomy

All 5-FU augmented trabeculectomies in the trial were performed by the same surgeon (A.D.) with standardized technique.

Following peribulbar anesthesia with 5 to 6 mL of a mix of lidocaine 1% and ropivacaine 2 mg/mL, the eyes were prepared and draped. A 7-0 silk traction suture was placed in the upper cornea adjacent to the limbus and a fornix-based conjunctival flap centered at 12 o' clock was prepared, by blunt posterior dissection of conjunctiva and Tenon's in each side of the superior rectus. A one-half thickness trapezoidal scleral flap of approximately 3 × 4 mm was dissected extending 1 mm from the limbus, followed by the application of 3 sponges soaked in 50 mg/mL 5-FU for 3 minutes. After copious irrigation with 20 mL of balanced salt solution, 2 10-0 nylon sutures were preplaced in the 2 corners of the flap and a paracentesis in the anterior chamber was carried out. The sclerostomy (1 × 2 mm) was created using Vannas scissors and a basic iridectomy was performed. The 2 pre-placed sutures were stitched (3-1-1) and control of the flow was verified by anterior chamber irrigation. Conjunctiva was sealed with 2 or 3 10-0 nylon sutures. A mix of dexamethasone and lanomycin was injected subconjunctivally in the inferior fornix. Postoperatively, a topical fixed combination of chloramphenicol and dexamethasone 1 mg/mL was administered 6 times daily for 4 weeks and then gradually tapered over 6 to 8 weeks.

2.2. Surgical technique—bleb needling

During the follow-up period, a separation of the sample in 2 groups occurred according to the need of at least 1 needling procedure or not.

All needling procedures were performed by the same surgeon (A.D.) at the slit lamp. The criterion to proceed to the above intervention was the presence of relatively high IOP values in combination with conjunctival signs of intensified healing response, such as a pronounced vascular plexus (corkscrew vessels) around and over the bleb area and/or the initiation of the formation of the "ring of steel". Furthermore, there was a gonioscopic verification of a patent corneo-scleral ostium.

Following the topical instillation of lidocaine 1% gel and diluted povidone iodine 5% solution, a speculum was placed and the subconjunctival area over the bleb was entered using a TB syringe with a 27g needle. Multiple punctures with sideways movements in the bleb margins, to the area of early fibrosis, were followed by injection in an adjacent area of a mix of 0.2 mL of dexamethasone and 0.1 mL of 5-FU (5 mg). The needling procedure didn't include advancement under the scleral flap and consequent anterior chamber entrance.

Following the withdrawal of the needle, a cotton-tip was placed over the puncture point for a minute and thereafter a drop of tobramycin was instilled. The ACD and IOP were both documented within 30 minutes after the procedure.

The patients continued with their initial treatment following the trabeculectomy and were reviewed as scheduled, a week after.

2.3. Statistical analysis

For the purpose of the study we performed descriptive and exploratory data analysis. Means ± standard deviation (SD) for continuous variables is estimated or percentage distributions are presented. We examined the normality and the homogeneity of the 2 variables under investigation (ACD, IOP) employing the Smirnov–Kolmogorov test, the normal probability plots, and the Leven's test. To evaluate the changes (differences) in the mean values of the variables under consideration before and after the glaucoma filtration surgery, we employed a Paired Sample *t* test. Furthermore, the correlation coefficients between the 2 variables

in consideration are presented. We estimated correlation coefficients between ACD and IOP at successive points of time, as well as their weekly difference (Δ IOP and Δ ACD).

The correlation analysis was performed for the total sample, as well as, for each subgroup that occurred during the follow-up (needling and no-needling group). The difference in the correlation coefficients between these 2 groups was evaluated on the basis of the z-score test at the 5% level of significance. Statistical analysis was performed using SPSS for Windows (version 22, IBM).

3. Results

Mean age of the patients was 66.62 (SD \pm 9.98) ranging from 34 to 84 years old. The average pre-operative IOP, under maximum tolerated topical anti-glaucoma medication and occasionally in addition with systemic acetazolamide, was 26.14 mmHg (SD \pm 6.51) and the mean value of the ACD was 3.05 mm (SD \pm 0.35).

Table 1 summarizes the demographic as well as the pre- and post-operative values of the variables (both for the total sample and for the 2 groups that resulted during the follow-up period) and highlights the eventual statistical significance.

A statistically significant difference ($t = -1.889, P = .044$) was found between the pre-operative IOP of the eyes that during the follow-up period underwent at least 1 needling procedure (IOP = 27.70 mmHg) and the IOP of the eyes that an intervention wasn't necessary (IOP = 24.30 mmHg).

Furthermore, different at a statistically significant level ($P = .026$) resulted the age of the patients between the 2 groups (no needling group = 70 years old, needling group = 63.74 years old).

Overall the IOP was significantly reduced ($P < .001$) at all post-operative visits: 6.85 ± 2.68 mmHg on the 1st day, 8.61 ± 4.01 on the 1st week, 13.00 ± 6.31 mmHg on the 2nd week, 15.80 ± 5.96 mmHg on the 3rd week, 14.00 ± 6.84 mmHg on the 4th week, 15.09 ± 6.28 mmHg on the 6th week, and 13.72 ± 4.59 mmHg on the 8th week of follow-up (Fig. 1).

The average percentage of change (reduction) from baseline during each follow-up visit resulted accordingly: -73.8% (1st day), -67.07 (1st week), -50.27 (2nd week), -39.56 (3rd week), -46.45 (4th week), -42.28 (6th week), and -47.52 (8th week).

Accordingly, ACD resulted in statistically significant changes (reductions) at all follow-up visits ($P < .002$), except the last one ($P = .478$):

2.72 mm \pm 0.44, 2.70 mm \pm 0.45, 2.79 mm \pm 0.40, 2.93 mm \pm 0.39, 2.80 mm \pm 0.47, 2.82 mm \pm 0.40, and 2.95 mm \pm 0.41 on the last visit during the 8th post-operative week.

The average percentage of change (reduction) from baseline during each follow-up visit resulted in the following outcomes:

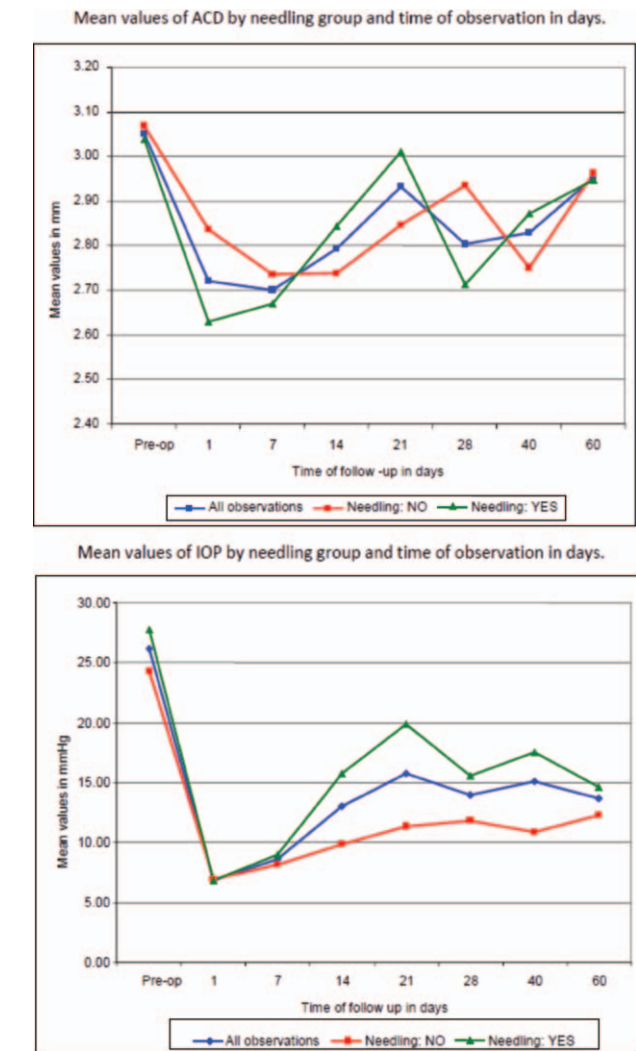


Figure 1. Mean values of ACD and IOP by needling group and time of observation in days. ACD=anterior chamber depth, IOP=intraocular pressure.

-10.82% (1st day), -11.48% (1st week), -8.53% (2nd week), -3.94% (3rd week), -8.2% (4th week), -7.55% (6th week), and -3.28% (8th week).

Table 2 presents the average pre- and post-operative values for the 2 variables (IOP/ACD) of the 2 groups that occurred during the follow-up period.

Table 1
Descriptive statistics core variables by gender and needling category.

	Sample	Age		IOP (pre-op)		ACD (pre-op)	
		Median	Standard deviation	Median	Standard deviation	Median	Standard deviation
Sample	50	66.62	9.98	26.14	6.51	3.05	0.35
Men	28	64.93	11.50	25.79	6.76	3.09	0.32
Women	22	68.77	7.34	26.59	6.29	3.00	0.39
Test			0.179 t-test		0.669 t-test		0.387 t test
No-Needling	23	70.00	8.03	24.30	5.99	3.07	0.36
Needling	27	63.74	10.70	27.70	6.63	3.04	0.35
Test			0.026 t test		0.044 t test		0.769 t test

ACD=anterior chamber depth, IOP=intraocular pressure.

Table 2**Average pre- and post-operative values of IOP and ACD for the 2 groups.**

Time	No needling group		Needling group	
	IOP (mmHg) \pm SD	ACD (mm) \pm SD	IOP (mmHg) \pm SD	ACD (mm) \pm SD
Pre-op	24.21 \pm 6.0	3.04 \pm 0.39	27.67 \pm 6.65	3.0 \pm 0.32
Day 1	6.53 \pm 1.84	2.89 \pm 0.41	6.76 \pm 3.09	2.67 \pm 0.5
Week 1	7.62 \pm 2.30	2.75 \pm 0.51	8.86 \pm 5.43	2.71 \pm 0.47
Week 2	9.13 \pm 3.90	2.71 \pm 0.41	15.94 \pm 8.1	2.76 \pm 0.40
Week 3	10.64 \pm 2.67	2.88 \pm 0.41	20.13 \pm 5.0	3.01 \pm 0.39
Week 4	11.78 \pm 2.28	3.04 \pm 0.44	16.00 \pm 8.9	2.68 \pm 0.51
Week 6	10.72 \pm 2.41	2.79 \pm 0.31	17.45 \pm 6.72	2.85 \pm 0.42
Week 8	12.00 \pm 2.57	2.91 \pm 0.47	13.81 \pm 4.87	2.88 \pm 0.33

ACD=anterior chamber depth, IOP=intraocular pressure.

Our next step was to evaluate, during the follow-up period, the level of correlation between the average values of the 2 variables (ACD, IOP), considering both the entire sample and each group (needling/no needling) separately (Table 3).

Regarding the total sample, correlation between the 2 variables was positive, during all the post-operative visits and gradually increasing. During the 1st, 2nd, and 3rd follow-up week, the correlation coefficients were statistically significant ($P < .05$) (Figs. 2 and 3).

For the "no needling group" correlation coefficients between the average post-operative values of IOP and ACD were positive and of moderate strength. In particular, on the 2nd and 4th follow-up week, the 2 variables appeared strongly correlated ($r = .435$ and $r = .716$) and statistically significant ($P < .05$).

For the "needling group" IOP and ACD resulted positively correlated and of moderate strength. On the 1st and 2nd post-operative week, correlation coefficients were statistically significant at the 0.05 level.

The application of the Z-statistic test resulted in no statistically significant differences between the correlation coefficients of the 2 groups under investigation.

4. Discussion

Trabeculectomy remains the most common^[15,16] surgical glaucoma procedure when medical or laser therapy have failed to control the IOP and there is a need to reset the target-IOP at lower values.

Trabeculectomy's risk profile is relatively high, with a wide range of complications. The most commonly occurring is represented by bleb encapsulation^[17,18] which is not sight

threatening, but if not timely recognized can lead to total bleb fibrosis and surgical failure.

Since 1968, when this filtering procedure was first introduced, the techniques have evolved and anti-metabolites, like 5-FU and Mitomycin C, are used routinely as wound healing modulators, improving the long term outcomes.^[19]

The clinical impression that led us to this study was that during the early post-trabeculectomy follow-up period, variations in ACD were correlated with variations in IOP and in particular, brisk deepening during the 1st week was followed by high IOP values and early signs of bleb encapsulation.

Wound healing process in the interface between episclera, Tenon's, and conjunctiva is well documented. It starts immediately following the operation^[20] and after 2 to 3 weeks, there is a massive increase in fibroblasts proliferation and recruitment, leading to outflow resistance around the area of the scleral flap. Consequently, this results in accumulation of aqueous humor in the anterior chamber with increase of its depth and secondary increase of the measured IOP.

The most critical period for the presence of a cystic bleb is between the 2nd and 4th to 5th post-operative week.^[21,22]

Taking that into consideration, we decided to assess closely both variables and their relationship during that time.

Although there have been a few studies^[23] that have reported variations of the ACD in the early post-trabeculectomy period, the authors did not correlate these variations with the IOP and the functionality of the bleb.

Furthermore, most of the studies evaluated the ACD changes with a contact method, which could represent a source of low reliability results. Studies where the ACD was evaluated either

Table 3**Correlation coefficients between ACD and IOP by time of observation in days.**

Time (day)	All observations		No needling group		Needling group		Z statistic *
	N	Correlation	N	Correlation	N	Correlation	
PRE	50	-0.149	23	-0.164	27	-0.127	0.12
1	48	0.173	21	0.012	27	0.274	1.04
7	46	0.344	21	0.295	25	0.409	0.41
14	45	0.430	21	0.435	24	0.466	0.12
21	44	0.379	21	0.304	23	0.373	0.24
28	34	0.336	14	0.716	20	0.427	1.15
40	33	0.343	12	0.374	21	0.328	0.13
60	28	0.252	11	0.538	17	0.193	0.92

* The Z statistics evaluate the difference in the correlation coefficients between the needling and no-needling groups.

Bold/underlined: Statistically significant at .05.

ACD=anterior chamber depth, IOP=intraocular pressure.

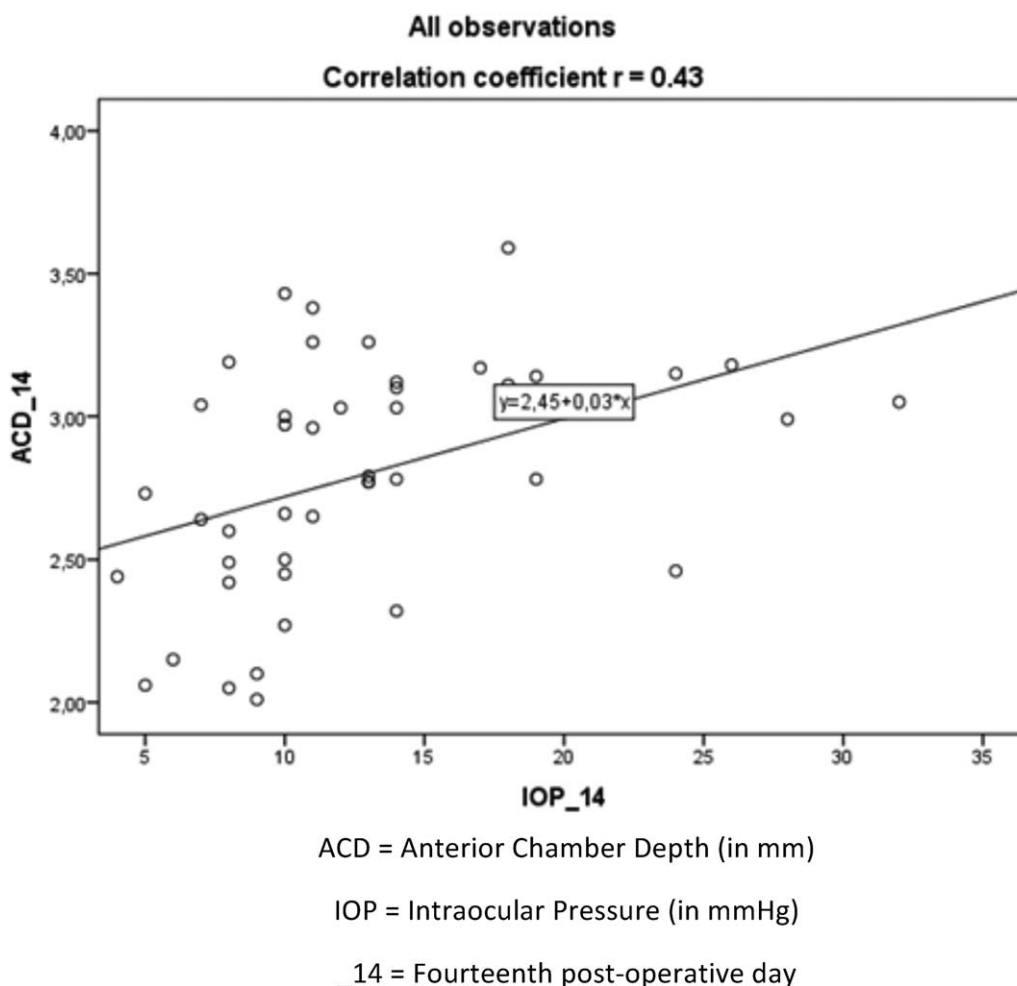


Figure 2. Scatter plots between ACD and IOP for the total sample & the 2 groups: 2nd week. ACD=anterior chamber depth, IOP=intraocular pressure.

with A-scan^[24,25] or with ultrasound biomicroscopy^[26,27] reported constantly, most probably falsely due to corneal immersion, greater amount of ACD reduction during the post-operative period.

As expected, the IOP values for the total sample at each post-operative visit, until the 8th post-operative week, were statistically significantly ($P < .001$) reduced from the baseline IOP, which correlates well with clinical experience and, furthermore, is in accordance with the bibliography. ACD during the follow-up period resulted statistically significantly reduced ($P < .002$), except the 8th week measurements which were reduced but not at a statistically significant level ($P = .478$).

Our results, particularly for the first 4 weeks, are in accordance with the published literature^[26,28], where the major reduction in the ACD is observed during the 1st 2 weeks with a gradual increase later, but differently from these studies, our results reached a statistical significance. A study^[26] where ACD was assessed on the 1st, 3rd, and 8th post-operative week documented a shallower anterior chamber which reached a statistical significance only for the 1st week ($P < .001$). A more recent work,^[28] which evaluated the ACD with the IOL-Master, as we did, documented that ACD was reduced during the follow-up visits (2nd day, 1st week, 1–3rd month), but not at a statistically significant level.

To the best of our knowledge, this is the first study where a detailed, objective and non-contact documentation of the ACD variations, during the early post-trabeculectomy period, were correlated, firstly, with eventual variations of the IOP and secondly, with blebs morphologic characteristics.

We were able to document both a quantitative and a qualitative association between the ACD variations, the IOP levels, and the blebs clinical features.

We found a moderate to strong positive correlation (coefficient of correlation ranging from 0.173 to 0.716) between the 2 quantitative variables (ACD and IOP), which, furthermore, appeared statistically significant ($P < .05$) during some post-operative visits (Table 3).

Considering the appearance of the blebs and documenting their clinical features, according to the Moorfields Bleb Grading System (vascularity of the bleb, bleb area and height), we observed that those appeared with more pronounced vascularity (especially the presence of corkscrew vessels) presented the brisk deepening of the ACD, between the 2nd and the 4th post-operative week, followed by increasing levels of IOP. Those were the cases that constituted the "needing group."

It should be mentioned that the relatively high rate^[29] (54%) of eyes that presented early signs of cystic blebs and proceeded to

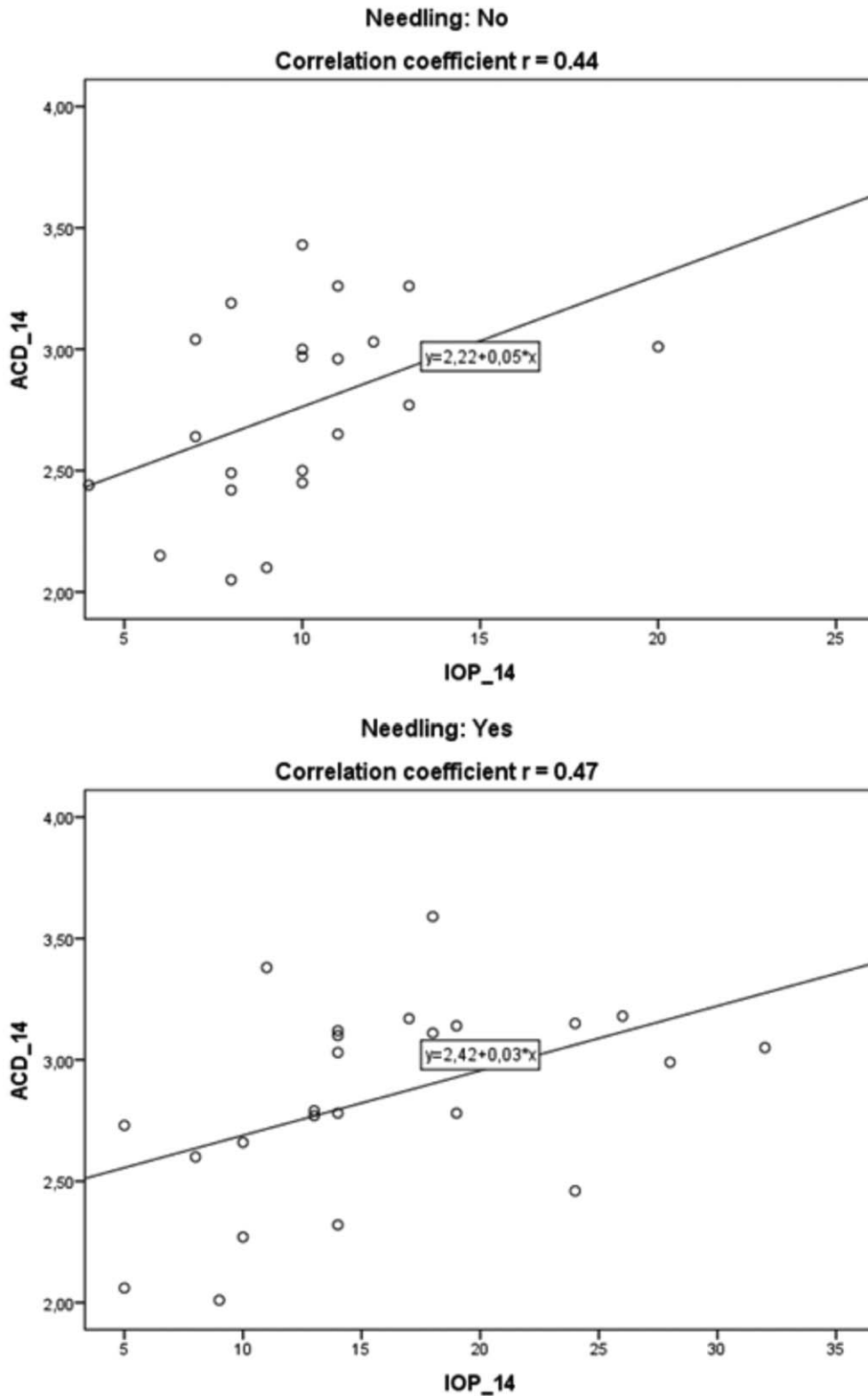
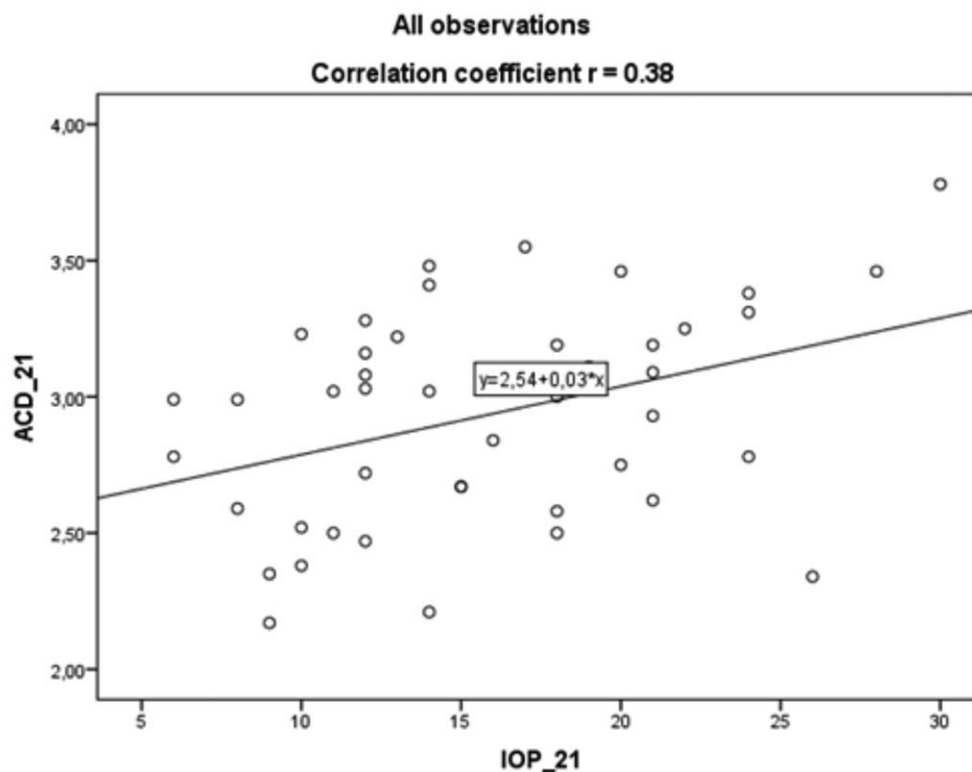


Figure 2. (Continued)

needling, can be attributed, apart from the pre- and post-operative clinical characteristics, to our lower tolerance in delaying any intervention, which is justified by the literature,^[30] highlighting the better outcomes of early bleb needling. Furthermore, as anti-scarring agent was used the less potent 5-

FU, instead of Mitomycin C, due to the fact that resulted more easily accessible during the study period.

A fact that was observed during the study which confirmed our initial clinical suspicion and represented the motivation for the research was that between the 2 groups that occurred (no



ACD = Anterior Chamber Depth (in mm)

IOP = Intraocular Pressure (in mmHg)

_21 = Twenty-first post-operative day

Figure 3. Scatter plots between ACD and IOP for the total sample & the 2 groups: 3rd week. ACD=anterior chamber depth, IOP=intraocular pressure.

needling/needling) there was a different pattern of increase for both variables (IOP and ACD). In the group of eyes that a needling procedure wasn't necessary the deepening of the ACD and the increase of the IOP, between each follow-up visit, were more linear with a gradual profile. On the other hand, eyes that were submitted to at least 1 needling procedure, before that, presented a more brisk pattern of ACD deepening and of IOP increase.

In particular, the differences (Δ IOP/ Δ ACD) between the 2 groups from the 3rd to the 2nd post-operative week and from the 2nd to the 1st week were: for the "no-needling" group Δ IOP= 1.51 mmHg for both time intervals and Δ ACD=0.17 mm (3rd to 2nd week), -0.04 (2nd to 1st week). Contrary, for the "needling group," the corresponding weekly differences were significantly more pronounced with Δ IOP=4.19 mmHg (3rd to 2nd week) and 7.08 mmHg (2nd to 1st week), whilst Δ ACD=0.25 mm (3rd to 2nd week) and 0.05 mm (2nd to 1st week).

Bringing the results of this study in the everyday clinical practice, following a trabeculectomy, it is not the ACD as a solitary magnitude that should be assessed (shallow or deep), but the brisk variations of it. Especially, in relation to eventual variations of the IOP, it should represent an alarming sign of aqueous humor flow obstruction, due to gradual fibrotic reaction leading to a cystic bleb (encapsulation).

Another observation that resulted from our study was that in respect of the 2 groups that occurred during the follow-up, the

"needling group" had statistically significantly higher pre-operative IOP [27.67 mmHg vs 24.21 mmHg ($P = .044$)].

There is not clear evidence in the literature about higher values of pre-operative IOP leading to higher rates of bleb encapsulation, although a recently published work^[31] documented that higher IOP during the first post-operative week led to significantly higher risk for bleb needling failure.

We can't be conclusive if the higher pre-operative IOP, as a potential risk factor for the formation of a cystic bleb, is a result of the aqueous humor dynamics carrying inflammatory factors from the anterior chamber to the intrableb area or is an indirect reflection of chronic, maximal topical treatment.

In this study, there are several advantages and some limitations. It is a prospective, interventional study where all the surgical manipulations, both in the operating room (trabeculectomy) and in the slit lamp (needling), were performed by the same surgeon, ensuring high levels of consistency. Another positive feature, in contrast to most of the published studies, is that all the measurements of the ACD were performed by a non-contact method, eliminating the indentation factor which could affect the reliability of the depth calculations.

One limitation is that due to the nature of the study (longitudinal measurements on operated eyes) some data, especially ACD measurements, are missing because of the varying post-operative conditions of the eyes. Furthermore, the study included only phakic patients, which from one side promises more reliable results on the

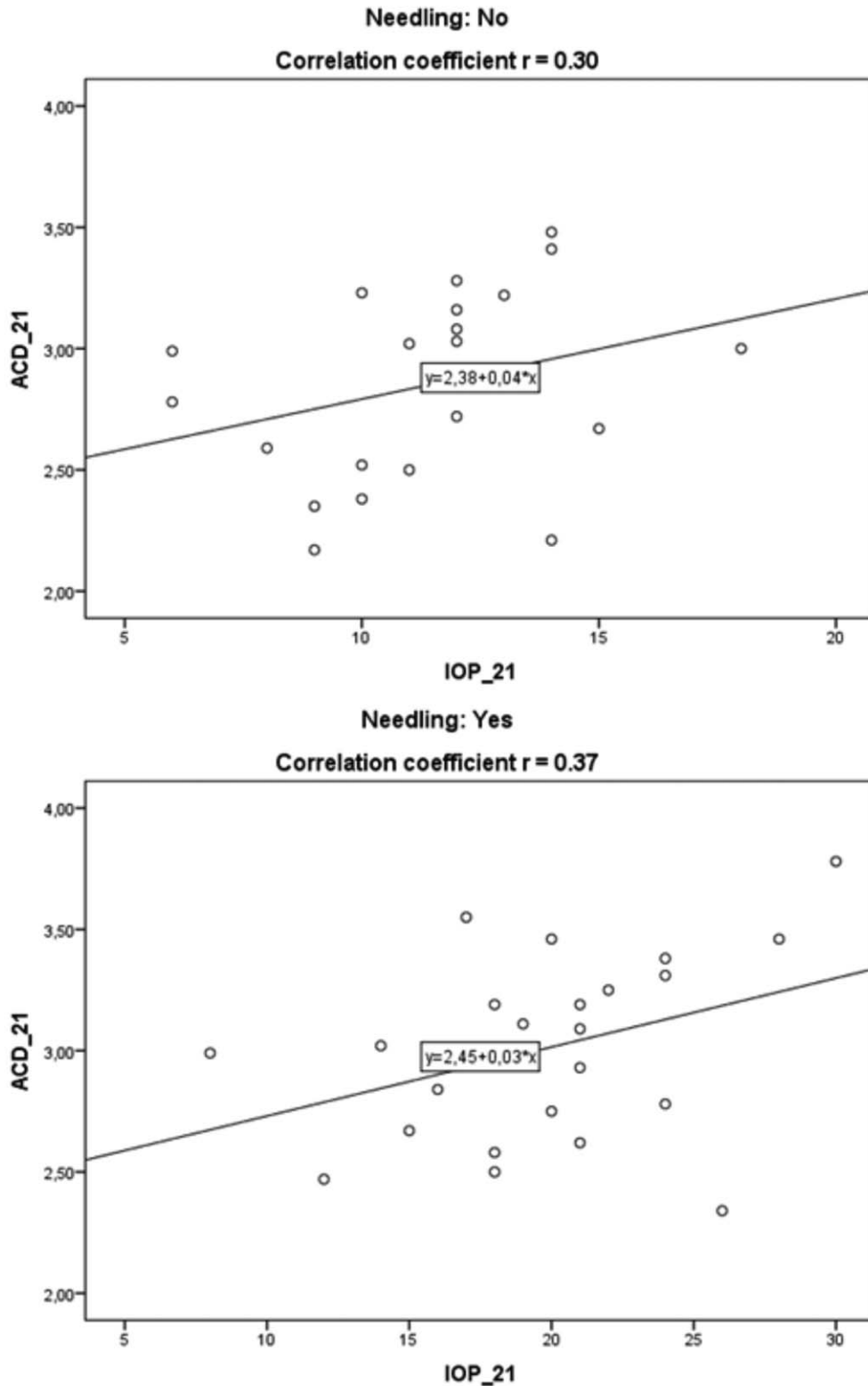


Figure 3. (Continued)

documentation of the ACD,^[32] but from the other side, it wasn't possible to generalize the conclusions.

Considering the results of this study it seems that following trabeculectomy, there is a dynamic relationship

between change of the IOP and the state of the ACD. In particular, brisk deepening of the anterior chamber, followed by increase in the IOP, could indicate early bleb encapsulation.

5. Conclusions

It is well known that the long-term outcomes of trabeculectomy are closely related with the proper post-operative management, especially during the first weeks.

ACD assessment, with an objective non-contact method like the IOL-Master, could be part of the routine examination in the context of close surveillance for the earliest signs of cystic bleb formation.

Author contributions

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Methodology: Athanasios Vergados.

Supervision: Chryssanthi Koutsandrea.

Writing – original draft: Andreas Diagourtas.

Writing – review & editing: Dimitrios Papaconstantinou, Konstantinos Andreanos, Chryssanthi Koutsandrea.

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