

## Factors affecting the early and mid-term success of needling for early failure of filtering bleb

Gülizar Demirok, Ahmet Kaderli, Sema T Kaderli, Güner Üney, Mehmet Yakin, Ümit Ekşioğlu

**Purpose:** The purpose of this study is to evaluate the factors affecting the success of needling surgery for early filtering bleb failure after trabeculectomy. **Methods:** Patients who underwent a single needling surgery within 3 months after trabeculectomy were retrospectively evaluated. Glaucoma type, intraocular pressure (IOP), and medical treatments before trabeculectomy; the presence of hypotony after trabeculectomy; bleb type; IOP before needling; lens status; complications; IOP after 1, 6, and 12 months; and medical treatments after needling were recorded. Risk factors were evaluated for complete success at 1, 6, and 12 months after needling. **Results:** Thirty-three eyes of 33 patients were analyzed. The mean IOP after needling at 1, 6, and 12 months was  $16.09 \pm 3.70$ ,  $15.64 \pm 2.68$ , and  $15.79 \pm 2.61$  mmHg, respectively. The mean age of the patients was 53.97 (25–79) years. The mean IOP after needling at 1, 6, and 12 months was  $16.09 \pm 3.70$ ,  $15.64 \pm 2.68$ , and  $15.79 \pm 2.61$  mmHg, respectively. The pre-needling IOP and IOP decrease on the first day affected the complete and qualified success at 1, 6, and 12 months, but the glaucoma type, presence of hypotony after trabeculectomy, lens status, interval between trabeculectomy and needling, and bleb type were not found to affect success. In the receiver operating curve analysis, the pre-needling IOP value was found to be significant in determining complete success. Complete success at 1 month was more likely when the pre-needling IOP cutoff value was  $<24.5$  mmHg. **Conclusion:** According to the results of single needling surgery performed within 3 months after trabeculectomy, the pre-needling IOP and IOP decrease with needling were found to be factors affecting success. Regardless of the time between the primary trabeculectomy and needling, effective needling will be successful before the IOP rises to high levels. Keeping the IOP at low values with medical treatment until the needling process is performed will have a positive effect on success.

**Key words:** Early bleb failure, needling, trabeculectomy

Trabeculectomy is the gold standard surgery for medically uncontrolled glaucoma. The success of surgery depends on the continuity of the fistula formed between the anterior chamber and sub-Tenon's space. The most common cause of failure is episcleral fibrosis, especially over the long term.<sup>[1,2]</sup> In the case of trabeculectomy failure, transconjunctival bleb needling is a less invasive technique than secondary trabeculectomy or drainage tube implantation to restore the output of aqueous flow from the current sclerotomy.<sup>[3-5]</sup> The use of antimetabolites during needling to prevent fibroblast proliferation has become a routine procedure. Failed blebs often require multiple needling procedures; however, needling may be unsuccessful.<sup>[6]</sup> In this study, the aim was to evaluate the factors that may affect the early and late success of needling performed within 3 months after trabeculectomy.

### Methods

The eyes of patients who underwent bleb needling due to early trabeculectomy failure were retrospectively reviewed from the patient records. Only patients who underwent one needling within 3 months after trabeculectomy were included

Department of Ophthalmology, Mugla Sitki Kocman University, Kotekli, Mugla, Turkey

**Correspondence to:** Dr. Ahmet Kaderli, Department of Ophthalmology, Mugla Sitki Kocman University Hospital, Kotekli, Mugla, Turkey. E-mail: akaderli@hotmail.com

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in the study. All of the patients were diagnosed with primary trabeculectomy and had not had previous glaucoma surgery. All of the pseudophakic patients had undergone uncomplicated phacoemulsification and intraocular lens implantation surgery prior to trabeculectomy. Ethical approval was obtained from the Republic of Turkey Ministry of Health, University of Health Sciences, Ankara Training and Research Hospital Ethical Committee (24.08.2016/0653). All of the patients underwent a complete preoperative ophthalmic examination, including applanation tonometry, ophthalmoscopy, and gonioscopy. Glaucoma type, intraocular pressure (IOP), medical treatments prior to trabeculectomy, antimetabolite used in trabeculectomy, presence of hypotony after trabeculectomy, bleb appearance, IOP just before needling, interval between trabeculectomy and needling, lens status, complications, and IOP at 1, 6, and 12 months after needling were recorded. In the case of bleb failure, ocular massage was routinely performed. Cases with suture lysis were excluded from the study. All of

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the patients had a patent internal trabeculectomy ostium on gonioscopy. The patients who underwent another surgery during the 12-month follow-up were excluded from the study. Clinical signs of scarring, such as increased IOP and bleb vascularization, were the main indicators for needling, which was performed using 5-fluorouracil (5-FU) in all of the patients. Risk factors were evaluated for complete and qualified success at 1, 6, and 12 months after needling. An IOP >5 mmHg and ≤18 mmHg, without the use of any antiglaucoma medication, was defined as complete success, and that with the use of antiglaucoma medications was defined as qualified success. Ankara Research and Training Hospital Ethics committee approved the study. Date: 24.08.2016, Number:0653.

### Needling procedure

Although this procedure can be managed safely in an outpatient department, all of the needlings herein were performed in an operating room. After sub-Tenon or subconjunctival anesthesia, a 25-g bent needle was passed approximately 6–7 mm from the edge of the failed bleb, underneath the conjunctiva, and the fibrotic tissue was broken up using a sweeping motion [Fig. 1]. If a bleb did not form, the needle was entered under the scleral flap and occasionally the anterior chamber. When the bleb elevated, the needle was retracted. Finally, 0.1 mL of 5-FU was injected superior to the bleb. After checking for leakage, the procedure was completed. Postoperative topical antibiotics were used for 3 weeks and topical corticosteroids were administered for 8 weeks, gradually decreasing.

### Statistical analysis

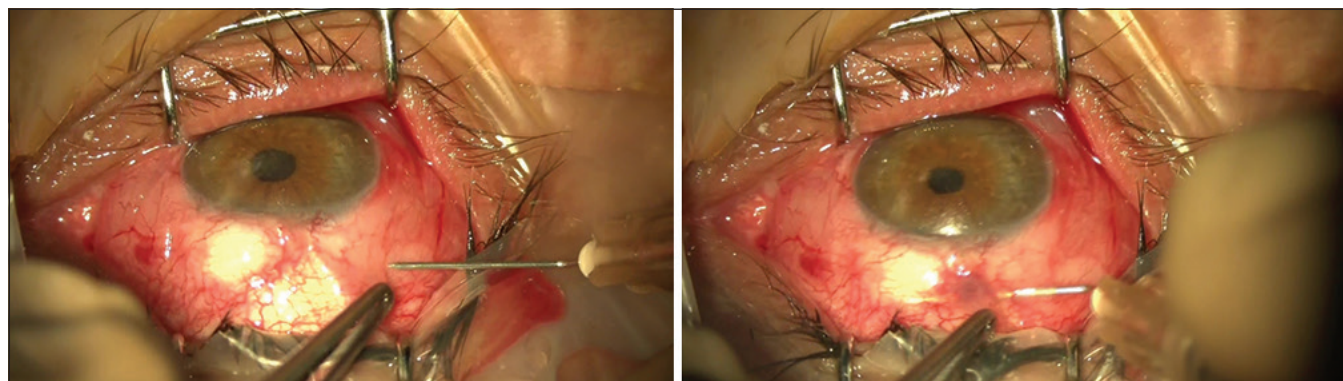
Data analyses were performed using IBM SPSS Statistics 23.0 (Armonk, NY, USA). Whether the distribution of continuous variables was normal or not was determined using the Kolmogorov–Smirnov test. The Levene test was used for the evaluation of the homogeneity of the variances. Unless specified otherwise, continuous data were described as the mean ± SD for normal distributions, and median (range) for skewed distributions. Categorical data were described as the number of cases (%). Differences in the normally distributed variables among more than two independent groups were analyzed using one-way ANOVA; otherwise, the Kruskal–Wallis test was applied for comparisons of the not normally distributed data. When the *P* value from the one-way ANOVA or Kruskal–Wallis test statistics was statistically significant, post-hoc LSD or the Conover nonparametric multiple comparison test was used to identify which groups differed from which others. Nominal data were analyzed using Pearson's Chi-square. First,

single-variable binominal logistic regression was used for all of the data, with risk factors that were thought to be related with complete success. Risk factors with *P* < 0.25 using the logistic regression were included for use on the multivariable logistic regression model. Whether all of the independent variables were significant on the model was analyzed using Wald statistic. How much of the independent variable explained the dependent variable was evaluated with Nagelkerke *R*<sup>2</sup>. Moreover, the adaptation of the estimates of the model was evaluated using the Hosmer and Lemeshow model adaptation

**Table 1: Preoperative data for patients undergoing needling**

	Subjects (n=33)
Age (years)	
Mean (range)	53.97 (25-79)
Gender (n, %)	
Male	19 (58%)
Female	14 (42%)
Diagnosis (n, %)	
POAG	12 (36%)
PACG	2 (6%)
UG	8 (24%)
PEG	9 (27%)
PG	2 (6%)
Bleb types (n, %)	
Cystic	6 (18%)
Diffuse	4 (12%)
Encapsulated	7 (21%)
Flat	16 (48%)
Mean pre-trabeculectomy IOP (mmHg)	32.48±4.53
Antimetabolite used in trabeculectomy (n, %)	
5-FU	9 (27%)
MMC	24 (73%)
Mean post-trabeculectomy IOP on day 1 (mmHg)	10.85±4.88
Mean post-trabeculectomy IOP after 1 week (mmHg)	18.97±3.63
Mean IOP before needling (mmHg)	24.09±3.94
Number of medications used before needling	1.42±0.97
Interval between trabeculectomy and needling (days)	46.82±16.75 (14-75)

POAG=Primary open angle glaucoma; PACG=Primary angle closure glaucoma; UG=Uveitic glaucoma; PEG=Pseudoexfoliative glaucoma; PG=Pseudophakic glaucoma; IOP=Intraocular pressure; 5-FU=5-fluorouracil; MMC=Mitomycin-C



**Figure 1: Needling procedure**

test. Receiver operating curve (ROC) analysis was used to determine the cutoff points.  $P < 0.05$  was accepted as significant and  $0.05 < P < 0.10$  was accepted as borderline for all of the statistical analyses.

### Results

The study included the 33 eyes of 33 patients who had completed a 12-month follow-up and had not undergone any eye surgeries other than the one needling during that period. Table 1 presents the preoperative patient data. Medical treatment prior to needling comprised between 0 and 3 topical molecules and none of the patients received oral antiglaucoma treatment.

The mean IOP after the needling procedure was  $16.09 \pm 3.70$  mmHg at 1 month,  $15.64 \pm 2.68$  mmHg at 6 months, and  $15.79 \pm 2.61$  mmHg at 12 months. The mean number of medications used was  $0.88 \pm 0.96$ ,  $1.45 \pm 0.97$ , and  $1.97 \pm 1.19$  at 1, 6, and 12 months, respectively.

No complications were observed in 28 patients after needling. Subconjunctival hemorrhage occurred in three patients, hypotony in one patient, and hyphema in one patient.

Table 2 summarizes the factors that significantly affected the qualified and complete successes after the needling procedure at 1, 6, and 12 months.

Considering the follow-ups of 33 patients after 12 months, while 24 patients were followed up with or without medication, 6 patients did not continue to follow up, 2 patients had tubes inserted, and 1 patient underwent trabeculectomy again. Needling had been attempted on one of the tube patients previously, however had been unsuccessful.

In the multivariate logistic regression analysis, the only significant factor predicting success at 1 month was found to be the IOP drop after needling ( $P < 0.05$ ). The probability

of complete success increased by 2.6% when the IOP drop after needling increased by 1 mmHg (OR 2.623). Lens status was found to be a partially significant factor affecting success at 6 months ( $P < 0.10$ ). The complete success rate was 12.5% higher in phakic patients when compared with that of the pseudophakic patients at 6 months (OR 12.50). No significant variable was found in the multiple analyses for first year success ( $P > 0.10$ ). The time between trabeculectomy and the needling was not found to be a significant variable affecting success in any of the analyses ( $P = 0.985/0.559/0.696$ , at 1, 6, and 12 months, respectively).

In the sensitivity and specificity given for success in the first month, the qualified success rate was higher when the IOP before needling was  $< 25.5$  mmHg, and the complete success rate was higher when it was  $< 24.5$  mmHg [Table 3]. Fig. 2 presents the mean pre-needling IOP, which was the most significant factor affecting the success at 1 month. Figs. 3 and

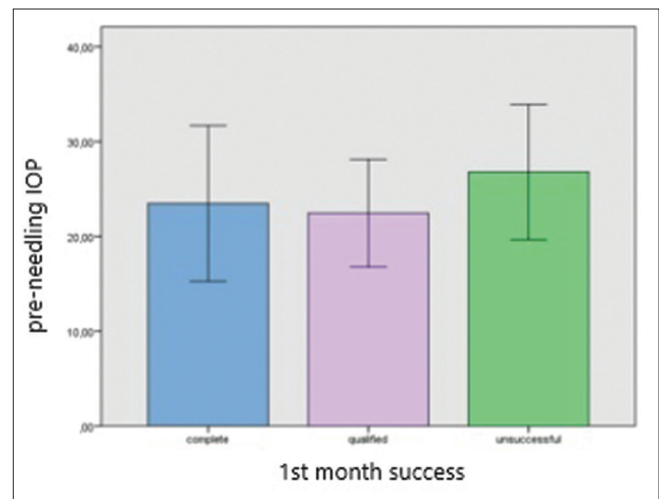


Figure 2: Pre-needling IOP values for 1 month success

Table 2: Factors affecting the complete and qualified success of needling at 1, 6, and 12 months

	Complete success (n)	Qualified success (n)	Unsuccessful (n)	P
<b>Month 1</b>				
(mmHg)	15	9	9	
Pre-needling IOP	23.47±4.10	22.44±2.83	26.78±3.56	<b>0.041<sup>b,c</sup></b>
IOP drop (pre-needling to month 1)	10.33±5.37	5.89±4.59	3.44±1.67	<b>0.003<sup>a,b</sup></b>
IOP 1 day after needling	13.13±4.24	17.78±3.56	23.33±3.35	<b>&lt;0.001<sup>a-c</sup></b>
<b>Month 6</b>				
(mmHg)	7	20	6	
Pre-needling IOP	23.71±2.93	23.25±3.89	27.33±3.98	0.077
IOP drop (pre-needling to month 6)	10.0±9.0	6.0±21.0	2.5±2.0	<b>0.006<sup>b,c</sup></b>
IOP 1 day after needling	13.86±3.13	16.15±5.14	24.50±3.21	<b>&lt;0.001<sup>b,c</sup></b>
<b>Month 12</b>				
(mmHg)	5	24	4	
Pre-needling IOP	23.20±3.35	23.71±4.01	27.50±3.11	0.178
IOP drop (pre-needling to month 12)	10.0±9.0	5.0±21.0	3.0±7.0	<b>0.006<sup>a-c</sup></b>
IOP 1 day after needling	13.40±3.05	16.96±5.50	23.25±5.12	<b>0.028<sup>b,c</sup></b>

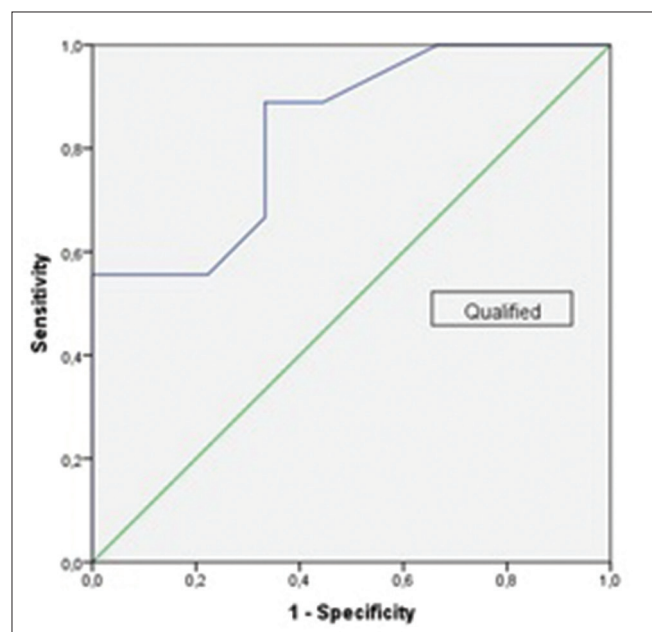
Continuous variables were compared with a one-way ANOVA or the Kruskal–Wallis test. LSD or the Conover–Iman test was performed for the binary comparisons among the groups, and the  $P < 0.05$  was accepted as statistically significant. Significant differences were found among (a) complete versus qualified; (b) complete versus unsuccessful; and (c) qualified versus unsuccessful. IOP=Intraocular pressure. Bold values were evaluated as statistically significant



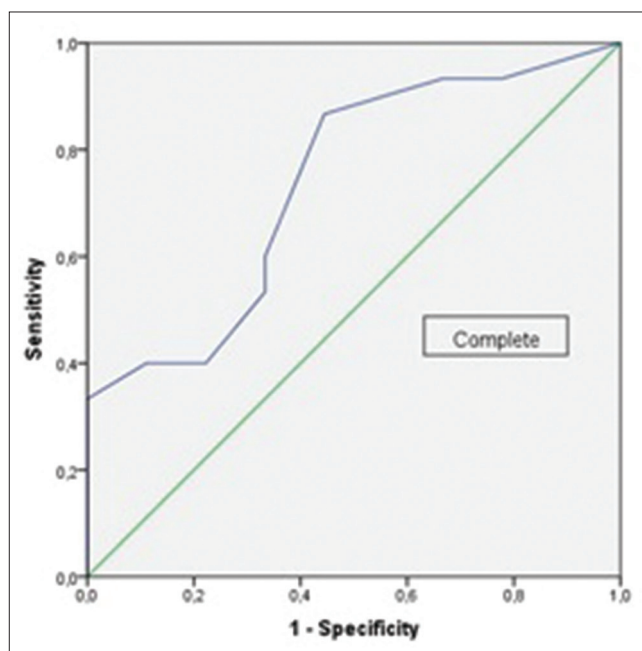
**Table 3: ROC curve for qualified and complete success (1 month)**

Variable: IOP before needling	AUC	Std. error	P	95% Confidence interval		Cutoff	Sensitivity (%)	Specificity (%)
				Lower bound	Upper bound			
Qualified success	0.833	0.096	0.017	0.645	1.000	21.5	55.6	100.0
						<b>25.5</b>	88.9	66.7
Complete success	0.737	0.106	0.056	0.529	0.945	23.5	4.0	77.8
						<b>24.5</b>	53.3	66.7

Bold values are provided as significant



**Figure 3:** Predictive value of IOP before needling for the qualified success group at 1 month



**Figure 4:** Predictive value of IOP before needling for the complete success group at 1 month

4 present the predictive values of the qualified and complete success at 1 month.

## Discussion

Trabeculectomy is the most common surgical procedure performed to increase aqueous outflow and control IOP in glaucoma patients. The success of surgery and regulation of IOP is dependent on subconjunctival fibrosis, which varies from person to person. Because the drainage of the aqueous humor from the anterior chamber is through the bleb, the bleb morphology should be well known for interventions in case of failure. If an adequate IOP decrease cannot be achieved by medical treatment following bleb failure, invasive surgical methods, such as repeat trabeculectomy or drainage tube implantation, may be attempted or revision of the existing trabeculectomy may be considered.

In early bleb failure, ocular massage, scleral flap suture lysis, or releasable suture removal may be useful to restore the bleb.<sup>[7]</sup> Transconjunctival bleb needling is required rather than the abovementioned methods when there are fibrous bands and loculations that restrict flow in the bleb.<sup>[8]</sup> Needling is a minimally invasive technique that can be applied to both early and late bleb failure. Subconjunctival injection of antimetabolites, such as 5-FU or mitomycin-C, improves the

success rate of the procedure.<sup>[9-12]</sup> Needling success rates have ranged from 54% to 84% in some series, depending on how success was defined.<sup>[13-16]</sup>

The current study was a retrospective analysis, and the number of patients was small because patients who underwent multiple needlings and those who had suture lysis were excluded.

Although the IOPs were above the normal limits (min: 10 mmHg, max: 22 mmHg) in some patients at the 12-month follow-up, they were followed up in this way if retinal nerve fiber damage did not develop.

Some studies have shown that needling may be successful, even if years have passed between the initial trabeculectomy and the needling.<sup>[17,18]</sup> Lee *et al.* found greater success rates in needling performed more than 4 months after the original filtration surgery.<sup>[19]</sup> In contrast, Gutierrez-Ortiz *et al.* reported that needling performed more than 4 months after trabeculectomy was associated with failure.<sup>[5]</sup> Fibrotic reaction caused by the ongoing inflammatory effect of previous filtration surgery can be considered as the reason for failure in early needling. In patients with secondary glaucoma receiving long-term drug therapy, there is a risk of fibrosis in every surgical intervention, because the conjunctiva is already inflamed. In the present study, because the needling

was performed within 3 months after trabeculectomy, the time factor could be ruled out. However, the time between trabeculectomy and needling was not statistically significant for success. For the relationship between bleb morphology and needling success, flatter and smaller central area blebs have been associated with failure after needling.<sup>[19]</sup> Similarly, Rotchford and King found less needling success in flat blebs.<sup>[20]</sup> In the current study, although bleb morphology did not directly affect the needling success statistically, failure was more common in flat blebs. Various risk factors for needling failure, such as fornix-based trabeculectomy,<sup>[21]</sup> pre-needling IOP >30 mmHg,<sup>[22]</sup> IOP >10 mmHg immediately after needling,<sup>[15]</sup> and history of diabetes mellitus,<sup>[19]</sup> have been identified. Herein, it was found that pre-needling IOP was the most important factor in short- and long-term success after needling. The ROC analysis for 1 month success revealed that the probability of complete success was higher when the pre-needling IOP was <24.5 mmHg.

In the multivariate analysis, it was found that the probability of complete success at 1 month increased by 2.6% for every 1 mmHg IOP drop after needling. Broadway *et al.* found that a low immediate post-needling IOP (<11 mmHg) was associated with a higher success rate with a 0.5 hazard ratio.<sup>[15]</sup>

Shetty *et al.* found that bleb needling was more successful in pseudophakic patients than in phakic patients.<sup>[23]</sup> In a more recent study, a greater proportion of aphakic and pseudophakic patients achieved success when compared with phakic patients (72.2% vs. 22.2%).<sup>[24]</sup> In contrast to the literature, in the study herein, the needling success in phakic eyes was found to be higher only for month 6.

In the current study, not receiving patients that had surgery in the 12 months after needling could have been a selective bias that would have led to successful results. An analysis study, in which patients underwent sequential glaucoma surgery, is also ongoing. Another limitation of the current study was that an objective grading system was not used for bleb typing.

## Conclusion

In conclusion, the factors affecting success were not the amount of time after trabeculectomy, but the level of IOP before needling, the change in IOP depending on the effectiveness of the needling, and the IOP level on the first day after needling. Considering that the IOP decreased sufficiently on postoperative day 1, this showed that all of the fibrotic bands were separated and effective clearance was achieved, and it was rational that this was the factor affecting success. Effectiveness of needling and lowering of IOP with medical treatment until the needling process were found to be factors that increased success.

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## Conflicts of interest

There are no conflicts of interest.

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