Integrated therapies for neovascular age-related macular degeneration related submacular hemorrhages: vitrectomy, tPA, and bevacizumab synergy

Serhat Ermis[1], *Ece Ozal*[1], *Murat Karapapak*[1], *Emre Avci*[1], *Hakan Baybora*[1], *Yusuf Cem Yilmaz*[1], *Serife Ciloglu Hayat*[1], *Sadik Altan Ozal*[1]

ABSTRACT

Purpose: To evaluate the functional and structural outcomes of a combination of vitrectomy, gas tamponade, subretinal tissue plasminogen activator (tPA) and intravitreal anti-vascular endothelial growth factor (anti-VEGF) injection in patients with submacular hemorrhage (SMH) secondary to neovascular age-related macular degeneration (nAMD) and to investigate preoperative prognostic factors.

Materials and Methods: This retrospective study involved 24 eyes from 24 patients (15 males, 9 females). We assessed preoperative SMH duration, thickness, and area, along with the hemorrhage displacement ratio total or subtotal subretinal hemorrhage within 1500 µm centered on the fovea post-vitrectomy. At the 12-month visit BCVA, lens status, preoperative intravitreal anti-VEGF injection count, and concurrent medical conditions were also documented.

Results: The patients had a mean age of 73.3 ± 8.2 years. The average BCVA significantly improved from a baseline logMAR of 2.0 ± 0.4 to logMAR 1.3 ± 0.6 at 12-month visit ($p<0.001$). Throughout follow-up, both SMH area and thickness showed statistically significant decreases ($p<0.001$). In the total displacement group, baseline BCVA was better, and values were maintained or even improved during follow-up. Correlation analysis revealed a strong positive relationship between BCVA at the 12-month visit, baseline BCVA, and SMH duration. ($p=0.009$, $p=0.008$)

Conclusıon: Vitrectomy, submacular tPA, anti-VEGF injection, and SF6 tamponade are safe and effective procedures in patients with nAMD secondary to SMH. The timing of surgery and the initial level of BCVA are the most critical factors determining the 12-month visit BCVA outcome.

Keywords: Submacular hemorrhage, tissue plasminogen activator, age-related macular degeneration, anti-VEGF.

INTRODUCTION

Submacular hemorrhage (SMH) refers to the accumulation of blood between the neurosensory retina and the retinal pigment epithelium, resulting from pathologies in retinal or choroidal circulation. It may originate from choroidal neovascular membranes (CNVM) and pass through breaks in Bruch's membrane. Hemorrhages stemming from retinal circulation are mainly associated with retinal macroaneurysms, while the most common causes originating from the choroid are age-related macular degeneration (AMD), polypoidal choroidal vasculopathy, trauma, and myopia.[1,2]

Photoreceptor cells and retinal pigment epithelium (RPE) cells are susceptible to oxidative damage from unstable radicals released during the degradation of red blood cells. Iron toxicity is another factor contributing to damage in photoreceptor cells and RPE. Taking immediate action is crucial for visual prognosis to minimize the impact of oxidative and toxic damage.[2,3] Therefore, it is essential to promptly address subretinal hemorrhages. Various treatment

1- Department of Ophthalmology, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye

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Correspondence author:
Serhat Ermis
Email: serhatermis88@hotmail.com

modalities have been applied for submacular hemorrhage removal, including direct removal of the hemorrhage,[4,5] macular relocation,[6] pneumatic displacement with or without pars plana vitrectomy (PPV),[7-9] fibrinolysis with subretinal tissue Plasminogen Activator (tPA) injection,[9-11] and intravitreal anti-vascular endothelial growth factor (VEGF) injections for AMD and PCV causing underlying choroidal neovascularization.[12-14]

The main objective of this study is to assess prognostic factors influencing the 12-month visit visual outcomes in SMH related to nAMD. Secondary outcomes include evaluating SMH displacement (total/subtotal) and visual prognosis results during the 12-month visit. Additionally, the third outcome involves assessing lens status and the impact of anti-VEGF injections on visual prognosis.

MATERIALS AND METHODS

Study Design

Patients diagnosed with SMH secondary to neovascular age-related macular degeneration (nAMD) between January 2020 and January 2022 were included in this retrospective study. Ethical approval for this study was obtained from the local committee to collect and analyze clinical data, and the study was conducted in accordance with the principles of the Declaration of Helsinki. Each patient included in the study was informed about the risks and benefits, and written informed consent was obtained.

Participants

The study enrolled patients aged 50 and above who had a diagnosis of nAMD with SMH and an area ratio of SMH to the optic disc (AHD) greater than one. Patients with other ocular conditions (severe myopia, a history of uveitis, glaucoma), those who had undergone vitreoretinal surgery for any reason previously, and individuals with SMH secondary to other causes were excluded from the study.

Preoperative Assessment

In the initial assessment, a comprehensive ophthalmic evaluation was conducted, encompassing the best-corrected visual acuity (BCVA), biomicroscopic anterior and posterior segment examinations, intraocular pressure (IOP) measurement via applanation tonometry, swept-source optical coherence tomography (SS-OCT) using (Triton Topcon Corporation, Tokyo, Japan), color fundus photographs and fundus fluorescein angiography (FFA) (Topcon Medical Systems, Inc., NJ., USA).

Demographic information, including age, gender, laterality, additional diseases, intraocular pressure (IOP), lens status, history of treatment with intravitreal anti-VEGF, SMH duration, preoperative BCVA, axial length (AL), and preoperative SMH thickness, was collected among the gathered data. The caliper feature of SS-OCT was used to measure the thickness of SMH, and the thickest scan was included. Color fundus photographs were obtained through dilated pupils using the Topcon TRC-NW8F digital imaging device (Topcon Medical Systems, Inc., NJ, USA), and the area of SMH was calculated using the manual caliper function of the ImageNet software as described by Shin et al.[15] For statistical analysis, BCVA was converted to the logarithm of the minimal resolution angle (LogMAR) scale. To ensure consistency, all measurements were performed by the same individual (SE).

Surgical Technique

Surgical procedures were carried out by a single experienced vitreoretinal surgeon (SAO). Patients underwent either isolated PPV or a combination of PPV surgeries with cataract extraction. In cases where the procedures were combined, standard cataract surgery with intraocular lens implantation was performed prior to PPV.

A standard 3-port vitrectomy was performed for all patients using a 25-gauge vitrectomy system (Alcon Surgical, Fort Worth, Texas, USA) and a non-contact viewing system (EIBOS 2, Carl Zeiss Meditec, Jena, Germany. If the posterior hyaloid did not detach spontaneously, it was detached after core vitrectomy. Injection of tPA (Actilyse, 10 mg/mL, Boehringer-Ingelheim, Germany) (10 µg/0.1 mL, range: 0.3-0.4 mL) was introduced inferotemporally into the retina approximately 3-4 disc diameters from the fovea using a 41-gauge needle. Additionally, subretinal tPA injection was applied in at least two separate areas in all patients. Following a complete fluid-air exchange, an anti-VEGF injection (bevacizumab 1.25 mg/0.05 mL) was administered intravitreally. Subsequently, air-SF6 (20%) exchange was performed, and the sclerotomies were closed with Vicryl 8-0. At the conclusion of the surgery, intracameral 1 mg/mL cefuroxime sodium (Aprokam, Laboratoires THEA S.A.S., Clermont-Ferrand, France) or subconjunctival gentamicin was injected following combined or isolated PPV procedures. After spending 1 hour in the supine position, patients were advised to maintain a reading position with the head at a 45-degree angle to the ground for 5 days.

Postoperative Assessment

Patients were scheduled for follow-up visits at months 1, 3, 6, and 12 postoperatively. Alongside routine eye examinations, BCVA, SMH area, SMH thickness and

IOP values were documented. If an active CNVM was identified by FFA, additional anti-VEGF injections were administered as needed. At the 12-month visit, the displacement of SMH was categorized as total or subtotal. Subtotal displacement was defined as the presence of hemorrhage debris within the 1,500 µm area centered on the fovea despite the absence of hemorrhage in the foveola, while total displacement was defined as the clearance of all SMH.[16]

Statistical Analysis

In the study, continuous variables were presented as mean ± standard deviation and median (interquartile range [IQR]) values, while categorical variables were expressed as numbers and percentages. The normal distribution of numerical data was assessed using the Shapiro-Wilk test. The Friedman test was employed for more than two repeated measurements. For pairwise comparisons before and after the procedure, the Wilcoxon test was utilized, and Bonferroni correction was applied based on the distribution structure. To examine differences between groups, either the t-test or Mann-Whitney U test was employed for independent groups, depending on the distribution structure. Relationships between variables were explored using Pearson correlation coefficient and Spearman correlation coefficient. Statistical analyses were conducted using the IBM SPSS Statistics program (Version 28). The significance level was set at 95%, and results were considered statistically significant for a p-value less than 0.05.

RESULTS

In this study, we examined 24 eyes of 24 patients who were under our clinic's observation due to SMH associated with nAMD. The average age of the patients (± standard deviation [SD]) was 73.3 ± 8.2, and the female-to-male ratio was 9/15. The mean duration of SMH was 8.55 ± 6.75 days (range: 1-24). Demographic and clinical information is summarized in Table 1.

The mean BCVA demonstrated a progressive improvement from preoperative logMAR 2.0 ± 0.4 to logMAR 1.5 ± 0.6, logMAR 1.2 ± 0.5, logMAR 1.0 ± 0.5, and logMAR 1.3 ± 0.6 at postoperative 1, 3, 6, and 12-months visits respectively. The enhancement in BCVA(logMAR), SMH area and SMH thickness was statistically significant compared to the baseline during all follow-up visits ($p < 0.001$, Figure 1-3).

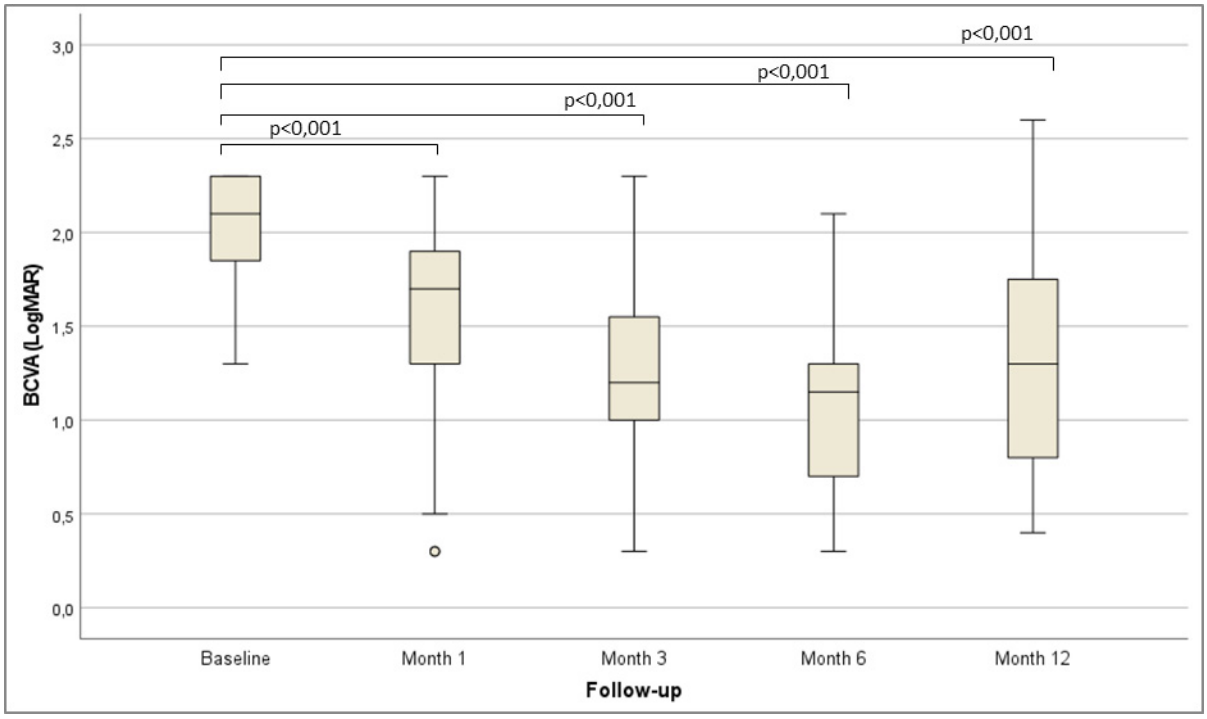
The postoperative 1-month visit BCVA (logMAR) averages in the phakic lens group were found to be statistically significantly decrease when compared to the pseudophakic group ($p < 0.05$). However, there was no significant difference in terms of other parameters based on lens status ($p > 0.05$, Table 2).

In all patients, the 12-month visit visual outcomes indicated total displacement (n = 17, 70.8%) or subtotal

Table 1: *Demographic and clinical characteristics for submacular hemorrhage patients with neovascular age related macular degeneration*

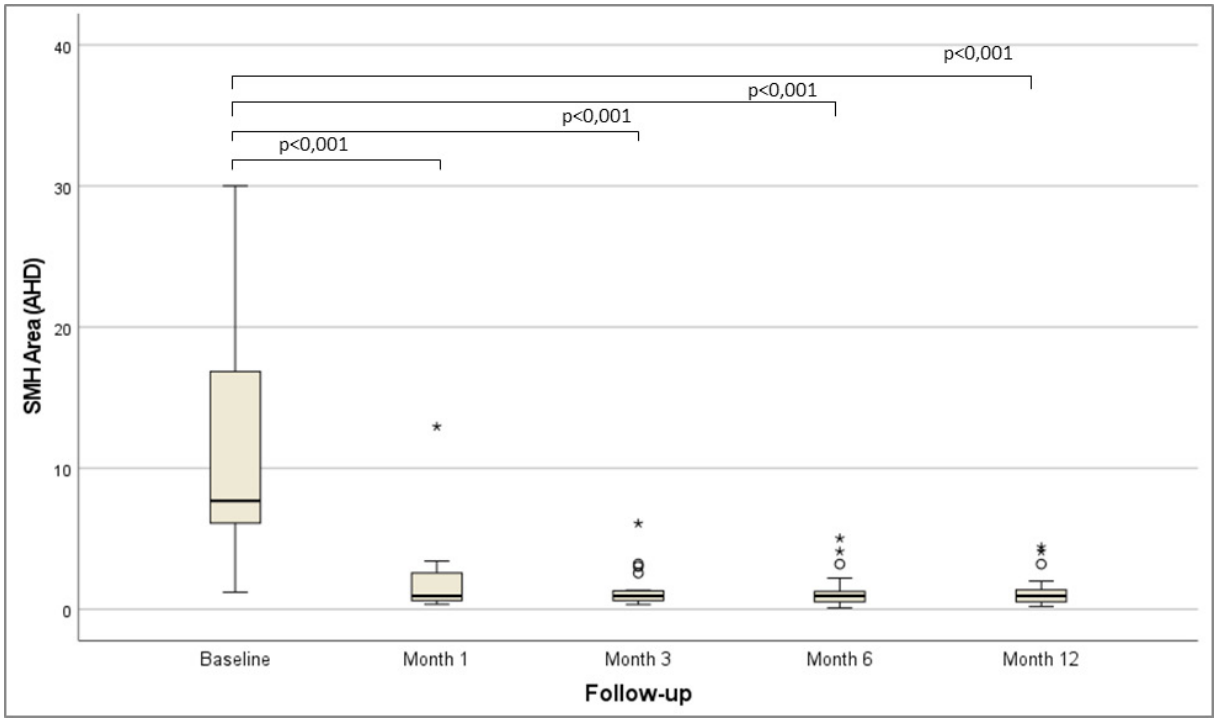
Age (years)		73,3±8,2
Gender	Male	15 (62,5)
	Female	9 (37,5)
Lens status	Phakic	13 (54,2)
	Pseudophakic	11 (45,8)
SMH duration (days)		8,55±6,75
SMH thickness (µm)		618,1±181,1
SMH area (AHD)		10,9±8,1
Eyes naive to treatment		16 (66,7)
Mean preceeding anti-VEGF injections (n=8)		5,6±2,5
Comorbidity	Diabetes mellitus	6 (25)
	Hypertension	15 (62,5)
Baseline BCVA (LogMAR)		2,0±0,4
IOP (mmHg)		13,8±2,9

Continuous variables are presented as the mean ± standard deviation or median (interquartile range [IQR]). Categorical variables are presented as number (%). VEGF, vascular endothelial growth factor; LogMAR, logarithm of the minimum angle of resolution; BCVA, best-corrected visual acuity; SMH, submacular hemorrage; AHD; area ratio of the SMH to the optic disc; IOP, intraocular pressure.



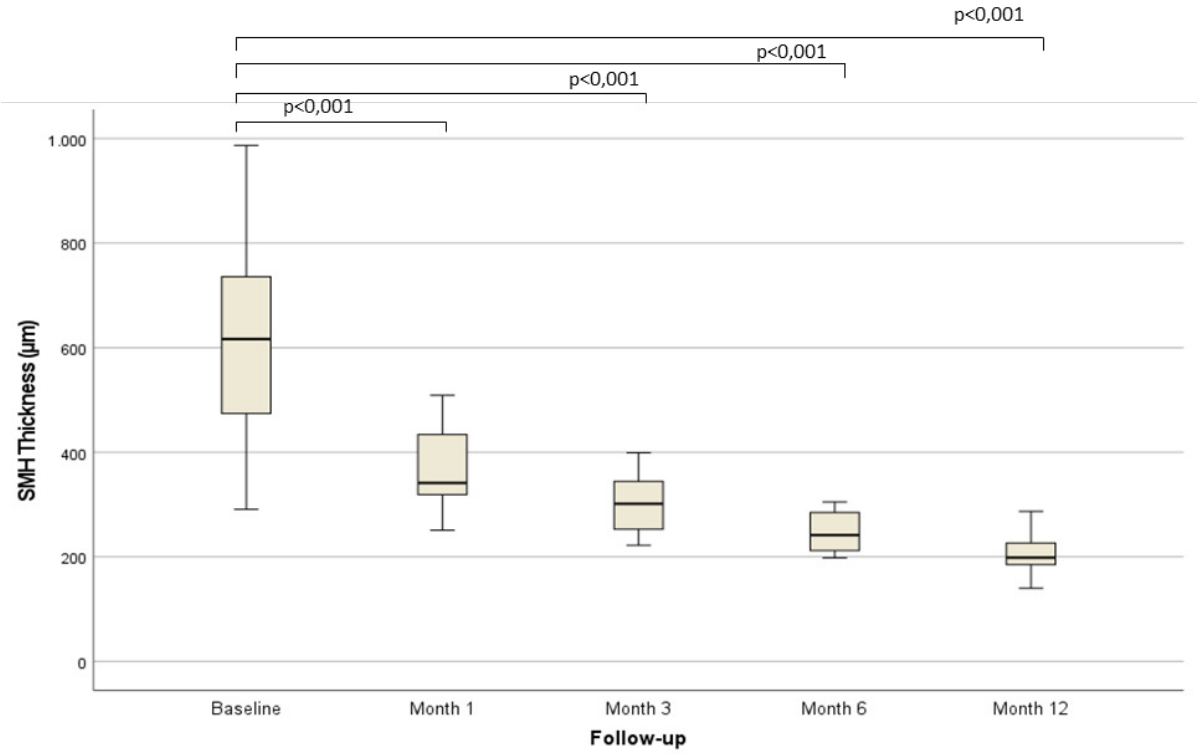
LogMAR, logarithm of the minimum angle of resolution; BCVA, best-corrected visual acuity.

Figure 1: *Boxplot representing the BCVA variation from baseline at each time point. Bold lines within boxes represent the median (50th percentile), upper and lower limits of the box represent the first (25th percentile) and the third quartiles (75th percentile), respectively, and bars represent the extreme values (maximum and minimum observations). Asterix and round signs represent contradictory values.*



SMH, submacular hemorrage; AHD, area ratio of the SMH to the optic disc; LogMAR, logarithm of the minimum angle of resolution; BCVA, best-corrected visual acuity.

Figure 2: *Boxplot representing the submacular hemorrhage (SMH) area variation from baseline at each time point. Bold lines within boxes represent the median (50th percentile), upper and lower limits of the box represent the first (25th percentile) and the third quartiles (75th percentile), respectively, and bars represent the extreme values (maximum and minimum observations). Asterix and round signs represent contradictory values.*



SMH, submacular hemorrage.

Figure 3: *Boxplot representing the submacular hemorrhage (SMH) thickness from baseline at each time point. Bold lines within boxes represent the median (50th percentile), upper and lower limits of the box represent the first (25th percentile) and the third quartiles (75th percentile), respectively, and bars represent the extreme values (maximum and minimum observations). Asterix and round signs represent contradictory values.*

displacement (n = 7, 29.2%) of SMH. When assessing the displacement of SMH, baseline, postoperative 1, and 12-month BCVA (logMAR) averages were significantly higher in the subtotal displacement group compared to the total displacement group ($p < 0.05$, Table 3). When the baseline SMH area was examined, it was determined to be 13.5±8.2 AHD in the subtotal displacement group, whereas in the total displacement group, it was 4.8±2.5 AHD, and this difference was statistically significant (p=0,005) In follow-ups, no differences were observed between the two groups in terms of SMH area. Regarding SMH thickness in both total and subtotal displacement groups, no significant differences were detected in all follow-up visits.

While the percentage of patients who received anti-VEGF treatment before the operation was 33.3% (8 patients), 66.7% (16 patients) had not received any treatment. Among those who received treatment before the development of SMH, two patients (8.3%) had 3, two patients (8.3%) had 4, one patient (4.2%) had 6, one patient (4.2%) had 7, and two patients (8.3%) had 9 intravitreal ranibizumab (0.5 mg Lucentis; Genentech, Inc./ Novartis) injections. In the group that received treatment before SMH development, the average number of injections was 5.6 ± 2.5. There were no significant differences between the two groups in terms of BCVA, SMH area, SMH thickness, and SMH duration values.

There was no significant correlation between the BCVA measured at the 12-month visit and age, gender, SMH thickness, and SMH area ($p > 0.05$). However, a positive correlation was observed between the BCVA(logMAR) at the 12-month visit and SMH durations, and a positive correlation was observed between the BCVA(logMAR) at the 12-month visit and the BCVA at baseline, 1, 3, and 6-month visits (Table 4). The presence of additional diseases such as hypertension and/or diabetes mellitus did not result in any statistical differences in parameters such as BCVA, SMH area, and SMH thickness during the follow-up. No perioperative complications were observed in any patient.

DISCUSSION

In this study, we investigated prognostic factors influencing visual, anatomical, and functional outcomes

Table 2: *General characteristics of two groups based on the preoperative status of the lens*

		Lens Status				p
		Phakic (n=13)		Pseudophakic (n=11)		
		Mean±SD	Median (IQR)	Mean±SD	Median (IQR)	
BCVA (LogMAR)	Baseline	2±0,4	2,1(1,8-2,3)	2±0,4	2,1(1,9-2,3)	0,691†
	1 month	1,2±0,7	1,3(0,5-1,9)	1,8±0,4	1,9(1,5-1,9)	0,034††,*
	3 month	1,1±0,5	1,3(1-1,3)	1,3±0,5	1,1(1-1,6)	0,308††
	6 month	1±0,5	1,3(0,7-1,3)	1±0,5	0,8(0,7-1,3)	0,997††
	12 month	1,2±0,6	1,3(0,6-1,7)	1,3±0,7	1(0,8-1,8)	0,876††
SMH area (AHD)	Baseline	9±6,4	8,4(2,9-15,2)	12,6±9,2	7,1(6,6-18,6)	0,331†
	1 month	1,2±1,1	0,9(0,4-1,2)	2,4±3,3	1,7(0,6-2,6)	0,459†
	3 month	1±0,8	0,9(0,4-1,2)	1,5±1,6	1,1(0,6-1,3)	0,531†
	6 month	1,1±1,1	0,9(0,4-1,2)	1,4±1,4	1,1(0,5-1,3)	0,531†
	12 month	1,1±1,1	0,9(0,4-1,2)	1,4±1,2	1,1(0,5-1,5)	0,569†
SMH Thickness (µm)	Baseline	552,5±161	552(466-680)	673,6±184,2	672(540-804)	0,104††
	1 month	357,5±85,1	318(299-436)	382,2±68,3	350(327-405)	0,207†
	2 month	294,4±47	303(245-318)	310,1±60,7	300(257-348)	0,492††
	6 month	249,4±36,9	243(213-291)	247,6±38,9	239(208-280)	0,912††
	12 month	214,4±43,4	199(183-246)	198,6±26,7	198(189-216)	0,288††
SMH durations (days)		9,3±7,5	7,7±6,5	6(2-14)	9,3±7,5	7(4-11)

†Mann Whitney U test, ††Independent Samples t test, *p<0,05. SD: Standart Deviation, IQR: Interquartile Range
LogMAR, logarithm of the minimum angle of resolution; BCVA, best-corrected visual acuity; SMH, submacular hemorrage; AHD; area ratio of the SMH to the optic disc.

during a 12-month follow-up period after applying PPV, subretinal tPA injection, and SF6 tamponade for SMH secondary to nAMD. Our observations revealed that SMHs were subtotally or totally displaced in all treated patients, and this surgical approach was deemed safe and effective. Throughout all follow-up visits, a statistically significant reduction was noted in the mean BCVA (logMAR), SMH area, and SMH thickness. SMH duration and baseline BCVA values emerged as the most significant prognostic factors influencing 12-month visual acuity. Visual outcomes in our patients were comparable to those reported in previous studies on SMH secondary to nAMD.[17-19] However, anatomically, an improvement in SMH area was observed at a higher rate compared to some studies in the literature.[20,21] In our study, an enhancement in BCVA was observed in 17 eyes (70.8%). Moreover, in the group showing BCVA improvement, the increase remained stable throughout the 12-month follow-up period. The most significant response, in terms of mean BCVA improvement, was observed at the postoperative 3-month visit. Similarly, in another study applying the same surgical method for SMH secondary to nAMD, at least a one-line improvement was reported in 82% of eyes, and an improvement of three lines or more was observed in 19.6%. However, unlike our study, this research did not find a significant relationship between SMH duration and 12-month BCVA.[20]

When reviewing studies related to the duration of SMH, it becomes evident that early surgical intervention is among the most effective parameters for determining the final visual prognosis.[9,22-25] In a study conducted by Avcı et al. where PPV, subretinal tPA and bevacizumab were combined, the group undergoing early surgery with an average SMH duration of less than 10 days demonstrated a significant improvement in final BCVA compared to patients with a duration of more than 10 days.[9] In a study by Arias et al. early surgery (within the first 5 days) was performed in 8 eyes with SMH secondary to nAMD, resulting in both an increase in BCVA and complete resolution of hemorrhage in all eyes.[25] While studies suggest that clinical outcomes may be unfavorable for eyes with SMH lasting more than two weeks, in our study, we refrained from establishing a specific threshold for surgical timing, believing that even a slight improvement in visual

Table 3: *General characteristics of two groups in which total or subtotal displacement of the submacular hemorrhage was achieved*

		12 month hemorrage displacement				p
		Subtotal (n=7)		Total (n=17)		
		Mean±SD	Median (IQR)	Mean±SD	Median (IQR)	
BCVA (LogMAR)	Baseline	2,2±0,2	2,3(2,1-2,3)	1,6±0,3	1,3(1,3-1,8)	<0,001*
	1 month	1,7±0,6	1,9(1,3-1,9)	1,1±0,5	1,3(0,5-1,5)	0,024*
	3 month	1,2±0,5	1,1(1-1,6)	1,2±0,4	1,3(0,7-1,5)	0,740
	6 month	1±0,5	0,8(0,7-1,3)	1,1±0,3	1,3(0,6-1,3)	0,951
	12 month	1,8±0,5	1,4(1,4-2,3)	1,1±0,5	0,8(0,6-1,3)	0,005*
SMH area (AHD)	Baseline	13,5±8,2	14,7(7-17,7)	4,8±2,5	5,8(1,2-6,6)	0,005*
	1 month	2,1±3	0,9(0,6-2,6)	1,2±0,9	0,8(0,4-1,7)	0,455
	3 month	1,4±1,4	0,9(0,6-1,3)	1±0,8	0,8(0,4-1,1)	0,418
	6 month	1,4±1,4	0,9(0,5-1,3)	0,9±0,6	0,8(0,4-1,1)	0,534
	12 month	1,4±1,3	0,9(0,5-1,5)	0,9±0,6	0,8(0,4-1,1)	0,494
SMH Thickness (µm)	Baseline	660,4±155,7	661(552-765)	515,6±209,1	466(343-707)	0,074
	1 month	382,8±69,5	365(324-436)	341,9±87,9	327(265-390)	0,237
	2 month	307,6±51,5	305(266-341)	291,4±63,3	290(240-348)	0,520
	6 month	252,2±33,9	249(231-280)	239,3±45,7	221(202-301)	0,452
	12 month	202,6±30,5	198(183-216)	213,6±47,3	199(189-246)	0,505
SMH durations (days)		9,6±7,8	7(3-15)	6±3,7	5(2-9)	0,133

†Mann Whitney U test, ††Independent Samples t test, *p<0,05. SD: Standart Deviation, IQR: Interquartile Range
LogMAR, logarithm of the minimum angle of resolution; BCVA, best-corrected visual acuity; SMH, submacular hemorrage; AHD; area ratio of the SMH to the optic disc.

Table 4: *Correlations between 12-month BCVA and other variables.*

	12 month BCVA (logMAR)	
	r	p
Baseline BCVA (logMAR)	0,559†	0,009*
Baseline SMH area (AHD)	-0,129†	0,549
Baseline SMH thickness (µm)	-0,258††	0,224
SMH duration (days)	0,830†	0,008*
1 month BCVA (logMAR)	0,578†	0,009*
3 month BCVA (logMAR)	0,574††	0,003*
6 month BCVA (logMAR)	0,684††	<0,001*

†Spearman rank correlation coefficient, †† Pearson correlation coefficient, *p<0,05.
LogMAR, logarithm of the minimum angle of resolution; BCVA, best-corrected visual acuity; SMH, submacular hemorrage; AHD; area ratio of the SMH to the optic disc.

prognosis could lead to significant enhancements in the quality of life for patients.[23, 24] In our study, the average SMH duration was 8.55±6.75 days. It was observed as 9.6±7.8 days in the subtotal displacement group, while in the total displacement group, it was 6±3.7 days. Although the time until surgery was longer in the total displacement group, which may seem contradictory, we believe this is due to the need for numerous subretinal injections to move

the hemorrhage away from the fovea and the formation of a larger detachment area. Additionally, in our study, we identified a positive and strong correlation between SMH duration and 12-month BCVA.

The preoperative SMH area, with an average of 10.9±8.1 AHD, decreased to 1.8±2.6 AHD at postoperative 1-month and further decreased to 1.2±1.1 AHD at postoperative 12-month. The reduction in SMH area was statistically significant in all follow-up examinations. Despite the observed decrease in SMH area during the follow-ups in our study, there was no correlation between the preoperative SMH area and the 12-month BCVA, possibly due to factors such as the duration until surgery, the toxicity of iron to photoreceptors, and the presence of pre-existing CNVM.

In studies related to SMH thickness, a consistent linear correlation between hemorrhage thickness and final BCVA has not been observed.[26,27] However, some authors have reported that an SMH thickness exceeding 400 microns is associated with poor visual outcomes.[28] In our study, the SMH thickness measured by OCT was initially 618.1±181.1 μm and decreased to 205.8±35.4 μm at the 12-month follow-up. The reduction in SMH thickness was statistically significant in all follow-up examinations. Despite the success in both SMH displacement and the successful treatment of many patients with anti-VEGF agents during the follow-up period, no correlation was observed between preoperative SMH thickness and 12-month visit BCVA, possibly due to the underlying CNVM and destructive effects of subretinal hemorrhage.

Our study included 13 phakic patients (%54.2) and 11 pseudophakic patients. In all phakic patients participating in the study, cataract extraction was combined with PPV surgery. The primary reason for opting for combined surgery in the entire phakic patient group was the presence of advanced cataracts in all patients, posing a risk of suboptimal clinical assessment due to cataract progression after vitrectomy during follow-ups. Postoperative 1, 3, 6, and 12-month BCVA (logMAR) averages in the pseudophakic lens group were higher than those in the phakic group, but statistically significant differences were observed only at the 1-month follow-up. This observed difference at the postoperative 1-month is attributed to the additional cataract surgery contributing to the visual prognosis. This difference continued to progress similarly to the initially pseudophakic group in subsequent follow-up visits. The reason for this may be interpreted as stemming from the progression of underlying CNVM. When examining based on preoperative lens status, no differences were observed between the groups in terms of SMH area, thickness, and duration at the 12-month follow-up.

At the 12-month follow-up, when assessing hemorrhage displacement, it was observed that the baseline BCVA was better in the total displacement group, and BCVA values were maintained and increased during follow-ups. In our study, SMH thickness did not play a significant role in hemorrhage displacement. Our findings, in addition to being consistent with studies suggesting that delays in surgery and the presence of larger hemorrhages can lead to tighter organization of the hemorrhage and inadequate displacement, also showed that high baseline BCVA and early surgical intervention contribute positively to displacement and have a strong prognostic impact on 12-month BCVA.[23,24]

One of the most debated topics is the recurrence of SMH, with reported rates reaching up to %30 in various series. According to recent studies, the combination of anti-VEGF injection with PPV has been reported to reduce the recurrence rate.[23,24,29-31] In our study, no cases of SMH recurrence were observed at the 12-month follow-up. While we attribute this outcome to the intraoperative administration of anti-VEGF to all patients, the absence of a control group without injections prevents making a definitive conclusion regarding this matter.

Limitations

The study has limitations, including its retrospective design, a relatively small number of patients, and the delegation of postoperative anti-VEGF injection procedures based on clinician discretion guided by imaging characteristics. However, all patients were subjected to a single treatment protocol administered by the same experienced surgeon, enabling the examination of prognostic effects of the variables under investigation in the study.

CONCLUSION

According to the results of this study, SMH shows significant benefits in improving visual acuity through PPV with subretinal tPA and pneumatic displacement. However, long-term visual acuity varies based on the underlying prognosis of CNV. The time elapsed until surgery and the initial BCVA are crucial prognostic factors influencing 12-month visit visual acuity. Patients with a good initial BCVA and a small SMH area are more likely to experience total hemorrhage displacement. Further studies are needed to analyze prognostic factors impacting both functional and anatomical outcomes.

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