

Massive Subretinal Hemorrhages Treated with Subretinal Alteplase Injection: A Series of Clinical Cases Over a Decade

Alteplase Subretiniana para o Tratamento de Hemorragias Maculares Maciças: Uma Série de Casos Clínicos ao Longo de uma Década

 Renato Correia Barbosa ¹, Rui Carvalho ¹, Ana Rita Viana ¹, Alexandre Silva ¹, Catarina Francisco ¹, Paula Tenedório ¹

¹ Ophthalmology Department, Hospital Pedro Hispano – ULSM, Matosinhos, Portugal

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ABSTRACT

INTRODUCTION: Massive macular subretinal hemorrhages are accumulations of a large amount of blood between the neurosensory retina and the retinal pigment epithelium, occupying the macular area. The purpose of this study is to describe a series of patients who underwent surgical treatment for this complication and to report their functional outcomes.

METHODS: A case-series report of consecutive eyes, including 6 eyes diagnosed with large macular subretinal hemorrhages, which underwent pars plana vitrectomy with subretinal injection of alteplase, followed by SF₆ tamponade. All surgeries were performed in Hospital Pedro Hispano – ULSM, by the same surgeon.

RESULTS: Cases 1 and 4 report macular subretinal hemorrhages in patients with previously diagnosed neovascular age-related macular degeneration. Cases 2 and 3 consist of hemorrhages in the context of retinal macroaneurysms. Case 5 depicts a large post-traumatic macular hemorrhage.

CONCLUSION: Neovascular age-related macular degeneration is the most common cause of catastrophic subretinal macular hemorrhages, but this complication may be associated with a broader spectrum of retinal diseases. Untreated cases have a very poor visual prognosis, and one of the existing therapeutic options consists of pars plana vitrectomy with subretinal injection of a fibrinolytic agent, followed by an expansible gas tamponade. The final visual outcome may depend on several factors, including the timing of surgery, the patient's age, prior retinal diseases, and original visual acuity. In selected cases, a quick and appropriate intervention may exponentially improve the final visual outcomes.

KEYWORDS: Fibrinolytic Agents; Retinal Hemorrhage; Vitrectomy.

RESUMO

INTRODUÇÃO: As hemorragias maculares subretinianas maciças consistem na acumulação de uma grande quantidade de sangue entre a retina neurosensorial e o epitélio pigmentar da retina, que ocupa a região da mácula. O objectivo deste trabalho é descrever uma série de casos de doentes

com hemorragia macular submetidos a tratamento cirúrgico e os resultados funcionais obtidos.

MÉTODOS: Relato de uma série de casos de olhos consecutivos, incluindo 6 olhos diagnosticados com hemorragias subretinianas maculares maciças, submetidos a tratamento cirúrgico com a realização de vitrectomia via *pars plana* e injeção subretiniana de alteplase, seguida de tamponamento com SF₆. Todas as cirurgias foram realizadas no Hospital Pedro Hispano – ULSM, pelo mesmo cirurgião.

RESULTADOS: Os casos 1 e 4 descrevem hemorragias maculares no contexto de degenerescência macular da idade neovascular previamente diagnosticada. Os casos 2 e 3 consistem em hemorragias no contexto de macroaneurismas da retina. O caso 5 relata uma hemorragia macular de grandes dimensões em contexto pós-traumático.

CONCLUSÃO: A degenerescência macular da idade neovascular é a causa mais comum de hemorragias subretinianas catastróficas, mas esta complicação pode estar associada a um espectro mais vasto de doenças da retina. Os casos não tratados têm um prognóstico visual sombrio, e uma das alternativas terapêuticas consiste na realização de uma vitrectomia via *pars plana* com injeção subretiniana de um agente fibrinolítico, seguida do tamponamento com gás expansível. O outcome final pode depender de vários factores, incluindo o momento da cirurgia, a idade do doente, patologias da retina prévias e a acuidade visual inicial. Em casos seleccionados, uma intervenção rápida e adequada permite melhorar exponencialmente os resultados visuais finais.

PALAVRAS-CHAVE: Fibrinolíticos; Hemorragia Retiniana; Vitrectomia.

INTRODUCTION

Massive subretinal macular hemorrhages are accumulations of a large amount of blood between the neurosensory retina and the retinal pigment epithelium (RPE) occupying the macular area. It is a dramatic complication of diseases such as age-related macular degeneration (AMD), retinal macroaneurysms, high myopia, trauma, or inflammatory diseases¹ and results in irreversible anatomical and functional damage to the photoreceptors.² Submacular blood impairs retinal function through several mechanisms, including the blockage of metabolic exchange between the RPE and outer retinal layers, direct neurotoxicity from iron resulting from the blood lysis and mechanical stress due to fibrin retraction.¹⁻⁴ They are associated with a very poor visual prognosis, and untreated cases generally result in irreversible visual loss, so prompt treatment is essential to preserve macular function⁵ and prevent fibrotic tissue proliferation, with atrophic scarring.

Alteplase is a glycoprotein produced by recombinant deoxyribonucleic acid (DNA) synthesis in cell culture. Its inactive form becomes active after coupling to fibrin and promotes the conversion of plasminogen into plasmin, being classified as a tissue plasmin activator (tPA). Its action results in a potent thrombolytic effect, and it is commonly used for intravenous administration in conditions such as acute ischemic stroke, pulmonary embolism, and acute myocardial infarction.⁵

The first attempts to treat massive submacular hemorrhages consisted of intravitreal injections (IVI) of expandable gas with or without tPA and face-down positioning of the patient, in an attempt to displace the submacular blood.⁶ However, subretinal penetration of tPA is poor,⁷

which has led to the development of other surgical techniques involving vitrectomy and subretinal tPA injection. Although there is no clear consensus on the exact indications, surgical technique, or dose of rTPA, several reports have shown the potential to improve the otherwise very poor visual prognosis in these patients.^{1,3,5}

This study aimed to describe our center's cases of vitrectomy with subretinal alteplase injection for the treatment of massive subretinal hemorrhages and to describe the etiology, clinical evolution, and functional outcome of each case.

METHODS

A case-series report of consecutive eyes, including 6 eyes of 5 patients diagnosed with massive submacular hemorrhages of different etiologies, which underwent surgical treatment in Hospital Pedro Hispano – ULSM.

All cases of massive submacular hemorrhage treated with surgery in Hospital Pedro Hispano were included, which corresponded to the period from 2014 and 2023. Information regarding clinical data, multi-modal imaging, and surgical procedures was gathered. All surgeries were performed by the same surgeon.

The adopted surgical technique in all cases consisted of a pars plana vitrectomy, followed by a macular subretinal injection of alteplase (100 µg in 0.1 mL), using a 41G needle. Then, a fluid-air exchange was made, with subsequent injection of SF₆ at a concentration of 20%. Finally, the sclerotomies were sutured, and subconjunctival injection of depomedrol and cefuroxime was made. The patients were then kept in prolonged sitting positioning during the postoperative period, in order to displace the liquefied blood to

the lower periphery of the retina, away from the macula, through the action of gravity. None of the patients was administered intravitreal anti-vascular endothelial growth factor agents during the surgery.

RESULTS

Each case was reported individually below. The etiology, initial visual acuity, and final visual outcomes for each case are presented in Table 1.

CASE 1

A 78-year-old female patient presented to the emergency department with complaints of decreased visual acuity (VA) in her right eye (OD) for 1 month. Relevant ophthalmological history included bilateral cataract surgery 1 year prior, and dry AMD (dAMD). Her daily medication included acetylsalicylic acid. On presentation, the best-corrected visual acuities (BCVAs) were OD: 20/60 and left eye (OS): 20/20. Fundoscopy revealed the presence of neovascular AMD in the right eye, with a large subretinal macular hem-

orrhage temporal and superior to the fovea but sparing it. Fluorescein angiography (FA) confirmed neovascular AMD as the cause of the subretinal hemorrhage, so monthly IVIs of ranibizumab were started.

At a follow-up consultation, 2 months after the initial observation, OD BCVAs had decreased to counting fingers, and fundoscopy revealed a reduction in the area of the hemorrhage, but also a progression of blood to the foveal area. Vitrectomy with subretinal alteplase injection was therefore proposed, and the patient underwent surgery 2 days later, which was uneventful. In the immediate postoperative period, she presented with an OD intraocular pressure (IOP) of 48 mmHg and mild hyphema, so acetazolamide and triple topical hypotensive medication were started.

One month after the surgery, after the gas had disappeared from the vitreous cavity, OD BCVA was counting fingers, and fundoscopy revealed extramacular subretinal hemorrhage, with macular fibrosis. At this point, she was proposed to 3 monthly injections of bevacizumab. At subsequent follow-up appointments, the peripheral subretinal blood disappeared, but the macula and perimacula had developed massive fibrosis. The final OD BCVA was hand motion.

Table 1. Etiology and visual outcomes of patients submitted to surgery.

	Age	Etiology	VA at presentation	Time from symptom onset until surgery (days)	Postoperative complications	Final VA
Case 1	78	Neovascular AMD	CF	40	Immediate: · Ocular hypertension (48 mmHg) · Mild hyphema Long-term: · Severe macular fibrosis	HM
Case 2	75	Macroaneurysm	CF	6	Immediate: · Ocular hypertension (36 mmHg) · Severe hyphema · Inferior exsudative retinal detachment Reintervention with silicone oil tamponade and 360° retinopexy Long-term: · Moderate macular atrophy after the removal of silicone oil	20/40
		Macroaneurysm	CF	11	Immediate: · Mild hyphema Long-term: · Mild macular atrophy	20/100 (left optotypes)
Case 3	81	Macroaneurysm	CF	14	Immediate: None Long-term: · Mild macular atrophy with distruption of the central ellipsoid layer	20/60
Case 4	69	Neovascular AMD	20/400	8	Immediate: · Ocular hypertension (34 mmHg) Long-term: · Macular atrophy with distruption of the ellipsoid layer	20/100
Case 5	19	Trauma	20/400	1	Immediate: None Long-term: · Choroidal rupture scar temporal to the fovea	20/22

CF – counting fingers, HM – hand motion.

CASE 2

A 75-year-old female patient presented to the emergency department with a sudden decrease in OS VA. She had undergone bilateral cataract surgery three years before. Her daily medication included acetylsalicylic acid. BCVAs were OD: 20/20 and OS: counting fingers, and fundoscopy revealed OS massive subretinal macular hemorrhage, with intra- and pre-retinal components (Fig. 1). She underwent spectral domain optical coherence tomography (SD-OCT) and FA, which revealed the presence of a retinal macroaneurysm as the cause of hemorrhage. She was proposed to vitrectomy with a subretinal injection of alteplase, which she did after 5 days.

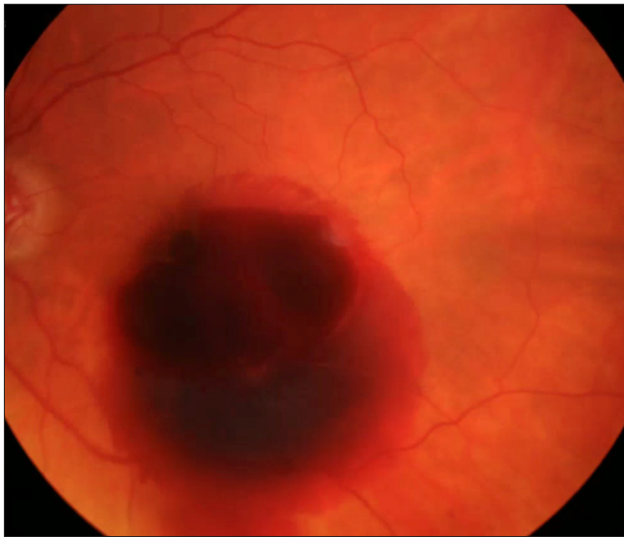


Figure 1. Case 2 – Color fundus photography showing a subretinal hemorrhage occupying the central and inferior macula.

The surgery was uneventful, but she had diffuse hyphema and an IOP spike during the immediate post-operative period, with nausea and vomits. She was prescribed topical hypotensives and underwent an anterior chamber wash-out in the operating room, 1 week after the initial surgery. The hyphema slowly improved over the following weeks, but as the vitreous gas subsided, an inferior flat exudative retinal detachment (RD) was objectified, so she underwent another vitrectomy with silicone oil tamponade and 360° LASER retinopexy. During the post-operative weeks, she had a VA 20/100 with the silicone oil in the posterior segment. After 6 months, the silicone oil was removed, and her retina remained attached, with moderate macular atrophy, and a BCVA of 20/200. She maintained those BCVAs over the following follow-up consultations.

However, 3 years later, she returned to the emergency department, this time with complaints of an acute decrease in OD VA, which was now counting fingers. Fundoscopy of the OD now also revealed a massive macular subretinal hemorrhage, which was then found to be also related to a macroaneurysm. She was now proposed for a vitrec-

tomy with subretinal alteplase injection of the OD, which was uneventful. During the postoperative period, she had a mild hyphema, but the IOP was normal. One month after the surgery, the submacular hemorrhage had totally subsided and only a few extramacular intraretinal hemorrhages were left. She then had 3 monthly doses of bevacizumab.

Final BCVAs were OD: 20/40 and OS 20/100 (only the rightmost optotypes), and the final appearance of the fundus showed diffuse macular and extramacular atrophy, predominantly in the inferior retina.

CASE 3

An 81-year-old female patient, with a history of bilateral cataract surgery, presented in the emergency department due to a sudden decrease in OS VA for 8 days. Her daily medication included acetylsalicylic acid and apixaban. BCVAs were OD: 20/25 OS: counting fingers, and fundoscopy revealed an OS massive subretinal macular hemorrhage (Fig. 2). SD-OCT and FA imaging showed the presence of an inferior retinal macroaneurysm. She was proposed for vitrectomy with subretinal alteplase injection, which took place 4 days later. The surgery was uneventful, and the immediate postoperative IOPs were 10 mmHg, without hyphema. After one month, AD BCVA was 20/100, and the submacular hemorrhage had completely reabsorbed, with residual peripheral blood. SD-OCT of the macula showed a disruption of the central ellipsoid layer.

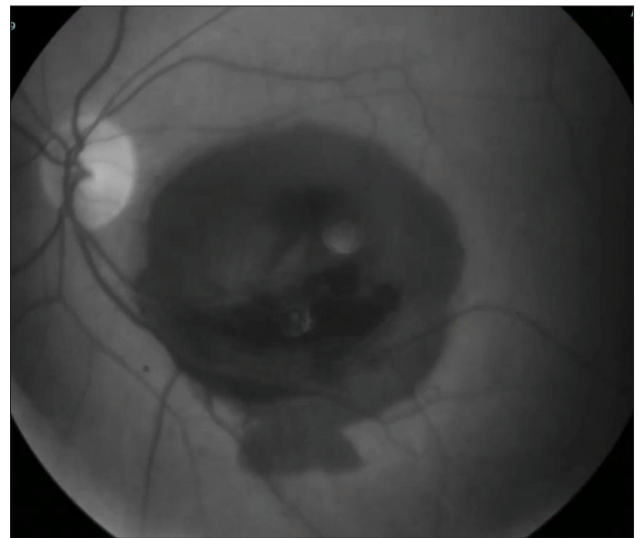


Figure 2. Case 3 – Red-free fundus photograph showing a subretinal hemorrhage occupying most of the macula and the inferior perimacula.

During the long-term follow-up period, the macroaneurysm appeared to have thrombosed, and the final OS BCVA was 20/60, with mild macular atrophy.

CASE 4

A 69-year-old male patient, with a history of bilateral cataract surgery and mild amblyopia in the left eye was

under bilateral IVI treatment with aflibercept due to bilateral neovascular AMD, when he presented in the emergency department complaining of a sudden decrease in OS VA. OS BCVA was 20/400 (previous record of 20/100) and fundoscopy revealed extensive macular subretinal hemorrhage, occupying almost the entire area of the macula. He was proposed to vitrectomy with subretinal injection of alteplase, which he underwent after 2 days. During the immediate postoperative period, he had a short period of ocular hypertension with PIOs of 34 mmHg and started acetazolamide and triple topical hypotensive therapy. One month after surgery, after the reabsorption of the gas, OS BCVA was 20/200 and the submacular hemorrhage had been reabsorbed, with residual peripheral hemorrhage. SD-OCT showed central atrophy of the outer retinal layers, with mild subretinal fluid. The patient kept doing IVI of aflibercept every 2 months until the present, with final OS BCVAs of 20/100 and absence of subretinal fluid.

CASE 5

A 19-year-old male patient presented to the emergency department after being physically assaulted and suffering direct OS periocular trauma with a glass bottle. The eyeball was

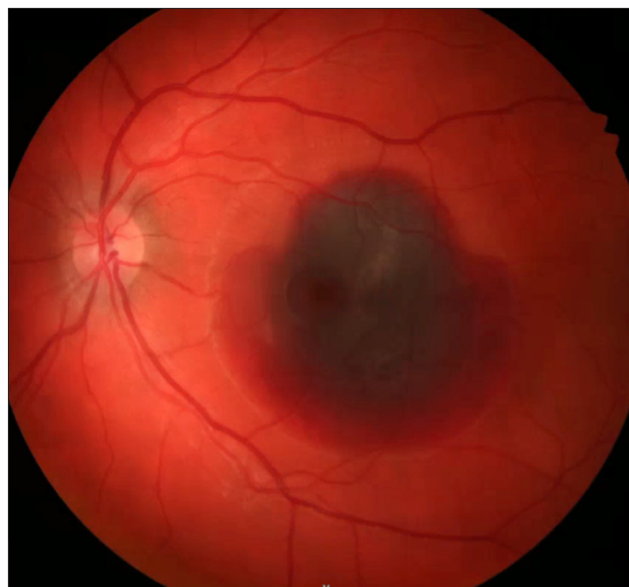


Figure 3. Case 5 – Color fundus photograph at presentation, showing a post-traumatic subretinal hemorrhage occupying the central macula.

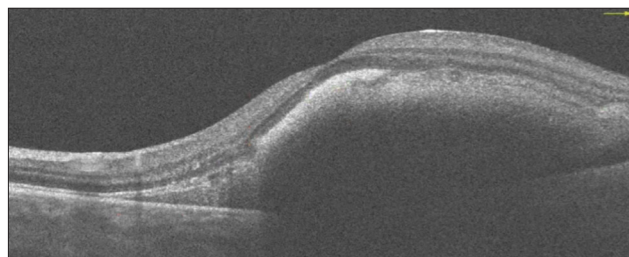


Figure 4. Case 5 – SD-OCT at presentation, showing a massive post-traumatic macular subretinal hemorrhage.

intact, with periorbital edema and hematoma, and subconjunctival hemorrhage, with no anterior chamber reaction. OS BCVA was 20/400 and fundoscopy revealed Berlin's edema of the peripheral retina, mainly temporal, and the presence of a massive subretinal hemorrhage, with complete involvement of the fovea (Figs. 3 and 4). Given the traumatic cause and the patient's age, he underwent surgery the following day, with vitrectomy and subretinal alteplase injection. The surgery was uneventful, and 2 weeks later, the BCVA was 20/25, and he had a residual subretinal hemorrhage in the lower periphery and a choroidal rupture scar temporal to the fovea. During the rest of the follow-up, the BCVA improved to 20/22 and the macula remained free of blood or subretinal fluid (Figs. 5 and 6). To date, he maintained a good VA, without recurrence.

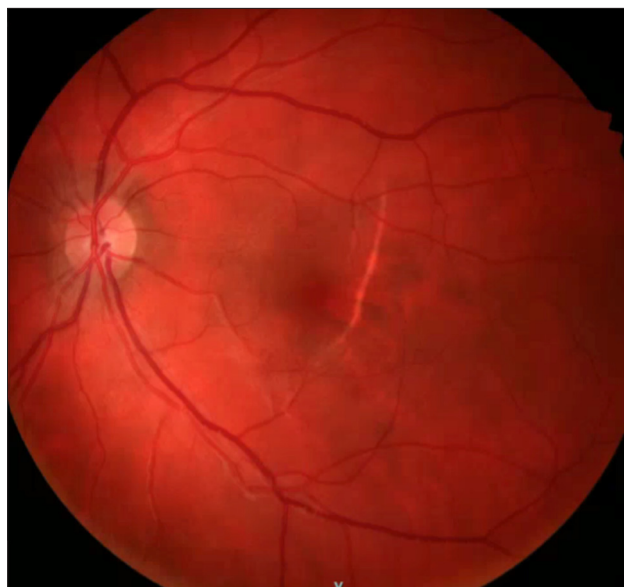


Figure 5. Case 5 – Color fundus photograph 1 month after surgery, showing the absence of subretinal hemorrhage, and a choroidal rupture scar temporal to the fovea.

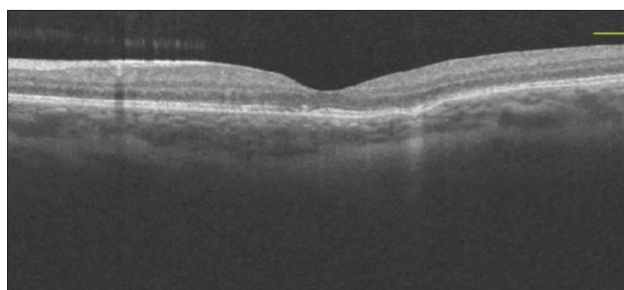


Figure 6. Case 5 – SD-OCT 1 month after surgery, showing the absence of subretinal blood, atrophy of the ellipsoid layer and a choroidal rupture scar.

DISCUSSION

Over the last few decades, various therapeutic strategies have been developed for the treatment of extensive

macular subretinal hemorrhages. Initially, mechanical removal of the blood was tried, without any therapeutic adjuvant, which resulted in low rates of therapeutic success, with final visual outcomes similar to the natural history of the disease, since the procedure was highly traumatic for the retina, and resulted in high rates of post-operative retinal detachment.¹ Subsequently, the use of fibrinolytic drugs was introduced to liquefy the clot formed after blood deposition and facilitate its displacement from the foveal area. Initially, intravitreal injection of fibrinolytic agents was tried to dissolve and displace the blood clot, however, this approach was hampered by the fact that the molecular weight of the therapeutic agent was too large to cross the neuroretina into the subretinal space, so any residual therapeutic effect could only be explained by the existence of retinal microlesions that allowed for a partial diffusion space.⁷ At present, one of the therapeutic alternatives for treating this condition, proposed by Heriot, consists of injecting subretinal alteplase after performing a pars plana vitrectomy, with subsequent tamponade with expandable gas and sitting positioning.⁸⁻¹² This positioning along with the gas bubble and the action of gravity will allow the liquefied blood to flow down from the macular region, displacing it from its original posterior position.

Regarding the timing of the surgery, it seems clear that a fast intervention results in a better visual prognosis. This has been demonstrated in animal studies, which showed a degree of photoreceptor damage proportional to the time that has passed since the hemorrhagic event,^{1,3} meaning that the surgical intervention should be executed as soon as possible after the diagnosis.

The most common cause for the development of a large submacular hemorrhage is neovascular AMD, followed by other causes of choroidal neovascularization such as presumed ocular histoplasmosis syndrome, pathological myopia, angioid streaks, or inflammatory diseases. Other associated conditions include retinal macroaneurysms, sickle cell anemia, neoplasms, or severe coagulopathies.^{1,3,5,13,14} Two of the patients described consisted of known cases of neovascular AMD, where catastrophic central hemorrhage occurred. On the other hand, three cases were attributed to the bleeding of retinal macroaneurysms, which is atypical, given that proportionally, it is a much less common cause. The fact that the patient of case 3 had two separate and independent episodes, due to bilateral retinal macroaneurysms is also surprising, given the rarity and severeness of this disease. Finally, case 5 was caused by a direct eyeball trauma. It should be noted that in this patient's case, the anterior segment appeared innocent upon initial examination, without the presence of an anterior chamber inflammatory reaction. This highlights the importance of a thorough ocular examination following a traumatic injury involving the periocular region, which should always include a funduscopy.

The VA upon presentation after the catastrophic event was unanimously low, as in all cases described in the literature, due to the separation between the RPE and neurosensory retina, mimicking the mechanism of a traditional retinal detachment. None of the eyes initially had visions

higher than counting fingers. Long-term outcomes after the surgical intervention were highly variable, which can be explained by several factors. Firstly, and as already mentioned, the timing of the surgery, from the moment of the event to the surgical intervention, seems to be paramount regarding the long-term visual prognosis.^{1,5} The time that passed from the onset of symptoms to the surgical intervention was variable (1 to 40 days), mainly due to the patient's delay in recurring to the emergency services. The case in which the final visions were most favorable was case 5, where the patient underwent surgery on the day after the trauma occurred. In this case, the final VA was very close to 20/20, despite the presence of a parafoveal scar corresponding to the point where the Bruch's membrane ruptured after the trauma. The maximum duration for which surgery remains worthwhile is not clear in the literature, but since the natural history of the disease has a very negative outcome, it is believed that surgery is justified in most cases.^{1,2}

The presence of prior retinal diseases and the original VAs, before the event took place, were also an important determinant for long-term visual prognosis. Final VAs will naturally be lower in eyes with previous retinal disease, such as those with a history of neovascular AMD, reflecting the lower visual potential of a previously unhealthy retina.^{3,4} Age may also be a determining factor in visual prognosis since a younger patient's retina tends to respond better to treatment due to having a higher functional reserve.

The main limitations of our study were its retrospective nature and the relatively small sample size, which is explained by the rarity of this complication. The absence of a control group, not subjected to any intervention, also prevented a direct comparison between the results of this technique and the natural history of the disease.

Massive macular subretinal hemorrhages are a severe complication of neovascular AMD but may affect a wider spectrum of patients of different ages, due to the various types of diseases that can cause it. They are a very serious condition, with a poor visual prognosis. In certain cases, a quick and appropriate intervention can exponentially improve the final visual result. We believe that pars plana vitrectomy with subretinal alteplase injection followed by expandable gas tamponade is currently the best approach for the treatment of this condition.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

This article was written by RCB.

All other authors contributed equally to data collection, analysis and discussion of the results. All authors approved the final version to be published.

Este artigo foi escrito por RCB.

Todos os outros autores contribuíram igualmente para a recolha de dados, análise e discussão dos resultados. Todos os autores aprovaram a versão final a ser publicada.

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REFERENCES

1. Ali Said Y, Dewilde E, Stalmans P. Visual Outcome after Vitrectomy with Subretinal tPA Injection to Treat Submacular Hemorrhage Secondary to Age-Related Macular Degeneration or Macroaneurysm. *J Ophthalmol*. 2021;2021:3160963. doi: 10.1155/2021/3160963.
2. Novelli FJ, Preti RC, Monteiro ML, Nóbrega MJ, Takahashi WY. A New Method of Subretinal Injection of Tissue Plasminogen Activator and Air in Patients With Submacular Hemorrhage. *Retina*. 2017;37:1607-11. doi: 10.1097/IAE.0000000000001491.
3. Childs AL, Bressler NM, Bass EB, Hawkins BS, Mangione CM, Marsh MJ, et al. Surgery for hemorrhagic choroidal neovascular lesions of age-related macular degeneration: quality-of-life findings: SST report no. 14. *Ophthalmology*. 2004;111:2007-14. doi: 10.1016/j.optha.2004.07.024.
4. Jackson TL, Bunce C, Desai R, Hillenkamp J, Lee CN, Lois N, et al. Vitrectomy, subretinal Tissue plasminogen activator and Intravitreal Gas for submacular haemorrhage secondary to Exudative Age-Related macular degeneration (TIGER):

study protocol for a phase 3, pan-European, two-group, non-commercial, active-control, observer-masked, superiority, randomised controlled surgical trial. *Trials*. 2022;23:99. doi: 10.1186/s13063-021-05966-3.

5. Ochinciu R, Balta F, Branisteanu DC, Burcea M, Zemba M, Ochinciu U, Barac R. Subretinal alteplase injections in massive subretinal hemorrhage due to age-related macular degeneration: A case report series. *Exp Ther Med*. 2020;20:208. doi: 10.3892/etm.2020.9338.
6. Ohji M, Saito Y, Hayashi A, Lewis JM, Tano Y. Pneumatic displacement of subretinal hemorrhage without tissue plasminogen activator. *Arch Ophthalmol*. 1998;116:1326-32. doi: 10.1001/archophth.116.10.1326.
7. Kamei M, Misono K, Lewis H. A study of the ability of tissue plasminogen activator to diffuse into the subretinal space after intravitreal injection in rabbits. *Am J Ophthalmol*. 1999;128:739-46. doi: 10.1016/s0002-9394(99)00239-1.
8. Handwerker BA, Blodi BA, Chandra SR, Olsen TW, Stevens TS. Treatment of submacular hemorrhage with low-dose intravitreal tissue plasminogen activator injection and pneumatic displacement. *Arch Ophthalmol*. 2001;119:28-32.
9. Lincoff H, Kreissig I. Intravitreal injection of tissue plasminogen activator and gas in subretinal hemorrhage caused by age-related macular degeneration. *Retina*. 2001;21:191. doi: 10.1097/00006982-200104000-00021.
10. Hesse L, Schmidt J, Kroll P. Management of acute submacular hemorrhage using recombinant tissue plasminogen activator and gas. *Graefes Arch Clin Exp Ophthalmol*. 1999;237:273-7. doi: 10.1007/s004170050232.
11. Hassan AS, Johnson MW, Schneiderman TE, Regillo CD, Tornambe PE, Poliner LS, Blodi BA, Elner SG. Management of submacular hemorrhage with intravitreal tissue plasminogen activator injection and pneumatic displacement. *Ophthalmology*. 1999;106:1900-6; discussion 1906-7. doi: 10.1016/S0161-6420(99)90399-8.
12. Ron Y, Ehrlich R, Axer-Siegel R, Rosenblatt I, Weinberger D. Pneumatic displacement of submacular hemorrhage due to age-related macular degeneration. *Ophthalmologica*. 2007;221:57-61. doi: 10.1159/000096524.
13. Singh RP, Patel C, Sears JE. Management of subretinal macular haemorrhage by direct administration of tissue plasminogen activator. *Br J Ophthalmol*. 2006;90:429-31. doi: 10.1136/bjo.2005.085001.
14. Hauptert CL, McCuen BW 2nd, Jaffe GJ, Steuer ER, Cox TA, Toth CA, et al. Pars plana vitrectomy, subretinal injection of tissue plasminogen activator, and fluid-gas exchange for displacement of thick submacular hemorrhage in age-related macular degeneration. *Am J Ophthalmol*. 2001;131:208-15. doi: 10.1016/s0002-9394(00)00734-0.



**Corresponding Author/
Autor Correspondente:**

Renato Correia Barbosa
Department of Ophthalmology,
Hospital Pedro Hispano,
R. de Dr. Eduardo Torres,
4464-513 Sra. da Hora, Portugal
E-mail: renato-barbosa@sapo.pt



ORCID: 0000-0002-5780-0450