European Journal of Ophthalmology / Vol. 14 no. 1, 2004 / pp. 40-47

Comparative study of vitrectomy with and without vein decompression for branch retinal vein occlusion: a pilot study

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PURPOSE. *To report the clinical outcomes in patients undergoing pars plana vitrectomy with and without vein decompression for treatment of branch retinal vein occlusion (BRVO).*
METHODS. *Thirty-five eyes with macular edema and visual acuity worse than 20/100 secondary to BRVO were prospectively evaluated. Vitrectomy with posterior hyaloid removal and vein decompression at the arteriovenous crossing was performed on 15 eyes (Group 1); consecutively, the same technique without vein decompression was performed on 20 eyes (Group 2). Primary outcome was visual acuity and secondary outcomes were resolution of macular edema and development of neovascularization.*
RESULTS. *No differences were found between groups in either patient age (p=0.566) or preoperative visual acuity (p=0.505). No differences were found in visual acuity at 3 (p=0.651), 6 (p=0.697), 9 (p=0.763), 12 (p=0.881), or 18 (p=0.748) months. Mean time for macular edema resolution and visual acuity improvement was 9 months in both groups, with a mean improvement of 3.5 ± 2.35 lines in Group 1 and 3.2 ± 2.97 lines in Group 2. No eyes in either group developed new vessels.*
CONCLUSIONS. *Results suggest that vitrectomy with posterior hyaloid removal without vein decompression can resolve macular edema, improve vision, and prevent development of new vessels in BRVO. (Eur J Ophthalmol 2004; 14: 40-7)*

KEY WORDS. *BRVO, Sheathotomy, Vein decompression, Vitrectomy*

Accepted: November 23, 2003

INTRODUCTION

Branch retinal vein occlusion (BRVO) is the second most common retinal vascular disease, affecting 1.6% of the population above the age of 40 (1). Several studies have shown that the anterior location of the artery is one of the risk factors for BRVO (2-4). Arteriosclerotic changes in the artery and the artery's anterior location to the vein cause an abrupt alteration of vein direction and a reduction of vein lumen. With increased compression, venous blood flow velocity at the crossing site gradually increases until local shear stress causes endothelial cell loss, thrombus formation, and vein occlusion (5-7).

Several medical and surgical strategies have been employed to treat BRVO. The only therapy of documented value for BRVO is retinal argon laser photocoagulation. Laser photocoagulation has been shown to improve the visual prognosis in patients with secondary complications of BRVO, including persistent macular edema and retinal neovascularization. In the BRVO study, a comparison of the natural history of macular edema was performed, showing that laser treatment increases the probability of visual improvement,

1120-6721/040-08$15.00/0

Presented in part at the XXIII meeting of the Club Jules Gonin; Montreaux, Switzerland; September 2002

but the mean improvement in treated eyes was only 1.33 lines (8, 9). Consequently, other surgical techniques are presently under investigation in an attempt to achieve better visual results. Among these are laser chorioretinal anastomosis, surgical vein decompression at the arteriovenous (AV) crossing, vitrectomy with posterior hyaloid removal, and vitrectomy with internal limiting membrane dissection (10-22).

In 1988, Osterloh and Charles gave the first description of surgical vein decompression at the AV crossing in a patient with BRVO. During surgery, no changes in vein caliber or blood flow were detected, but 8 months later visual acuity (VA) improved from 20/200 to 20/25 (11). Eleven years later, Opremcak and Bruce reported the first series of patients in whom vein decompression was performed. Following surgery, 67% of patients had improved VA at a mean of four lines (12). Shah et al also found a substantial visual improvement in four of five eyes following vein decompression surgery (13). In 2001, Mester and Dillinger compared the results of surgical vein decompression in 40 patients with 22 controls, finding better VA in treated eyes (14). In the same year, Dotrelova et al reported three cases where VA improved 3.5 lines with the same surgical technique (15). The only authors to have reported no visual improvement following surgery were Le Rouic et al in a study performed on three eyes (16).

However, other authors have reported improved VA following vitrectomy with posterior hyaloid removal without performance of vein decompression (17, 18).

This article reports the results of two prospective pilot studies on two consecutive series of patients surgically treated for BRVO. In the first group, vitrectomy with posterior hyaloid removal was followed by decompression of the vein at the AV crossing, whereas in the second, vitrectomy with hyaloid removal was performed with no maneuvers at the crossing. The results of the two studies were retrospectively compared. To our knowledge, this is the first report to compare the results of these two surgical techniques in patients with BRVO.

PATIENTS AND METHODS

Thirty-five eyes of 35 patients with macular edema and VA worse than 20/100 secondary to BRVO were prospectively evaluated. Vitrectomy with posterior hyaloid removal and vein decompression at the AV crossing was performed on 15 eyes between December 1998 and January 2000 (Group 1); the same technique without vein decompression was performed on 20 eyes between January 2000 and January 2001 (Group 2). Primary outcome was VA and secondary outcomes were resolution of macular edema and development of neovascularization.

Informed consent was obtained from each patient and data accumulation is in conformity with all country laws.

Inclusion criteria were the same for both groups: BRVO cases presented for examination within 1 year of onset of symptoms, best-corrected Snellen VA equal to or worse than 20/100, and macular edema involving the fovea on slit-lamp examination.

Exclusion criteria were the presence of new vessels in the anterior or posterior segment or the presence of diabetic retinopathy or any other disease that could cause loss of vision.

Best-corrected VA was checked prior to surgery and throughout the follow-up period. Color fundus photographs were taken during all visits, and fluorescein angiography was performed before surgery, at 1, 3, 6, 9, and 12 months, and then annually thereafter.

Surgical technique

In Group 1, vitrectomy with posterior hyaloid removal and vein decompression at the AV crossing was performed. Decompression was done with a microvitreoretinal blade bent at the tip to separate the overlying arteriole from the venule, as previously described by Opremcak and Bruce (11). When the tangential force needed to separate the vessels was strong enough to endanger the integrity of the vein, horizontal or vertical scissors were used to complete decompression. In Group 2, vitrectomy with posterior hyaloid removal was performed. In this group, no maneuvers were performed at the AV crossing.

Statistical analysis

The results of the two prospective studies were retrospectively compared. For data analysis, Student t and Mann-Whitney U tests were used. A finding was considered statistically significant at $p<0.05$. The statistical package used was PRESTA PC, version 2.2.

RESULTS

Group 1: Surgical decompression

Fifteen eyes of 15 patients were included, 6 women and 9 men, with a mean age of 63 years (range 51-80). The mean interval between the first symptoms and surgery was 28 days (range 7-75). The first step in surgery was to detach the posterior hyaloid, which was attached in 15/15 (100%) eyes. Decompression was successful in 11/15 (73%) patients. In four cases where the integrity of the vein was endangered owing to strong attachment between the vessels at the crossing, decompression was not completed. During the procedure, no changes in vein caliber or blood flow were detected in any case.

Despite successful decompression, two eyes developed venous collaterals 7 and 15 months after surgery (Fig. 1). Although successful decompression was performed in these two eyes 15 and 19 days after the occlusion, a severe vein stenosis persisted following surgery, making collaterals inevitable.

The mean improvement in Snellen acuity at 3, 6, 9, 12, and 18 months was 1.7±1.2 lines, 2.3±1.8 lines, 3.5±2.4 lines, 3±2.7 lines, and 2±2.1 lines, respectively (Tab. I). The mean time for macular edema resolution (ophthalmoscopically and angiographically) and VA improvement was 9 months. By that time macular edema had resolved in 13/15 (86%) eyes and VA had improved by two lines or more in 11/15 (73%), one line in 2/15 (13%), and remained unchanged in 2/15 (13%) eyes. No relationship was found between the duration of the preoperative interval and visual results. Indeed, the patient with greatest VA improvement also had one of the longest preoperative intervals (45 days). The Wilcoxon test showed a statistically significant difference between the preoperative and postoperative visual finding (p=0.002).

The presence of intraretinal hemorrhages did not lead us to preoperatively classify macular edema as either ischemic or nonischemic. Throughout the follow-up, as hemorrhages resolved, 5 of 15 eyes showed nonischemic macular edema (Fig. 2). Following surgery, the edema resolved in all of them and vision improved by a mean of 5.2 lines (range 3-7 lines) and a median of 6.17. Ten eyes showed ischemic macular edema. Following surgery, macular edema resolved in 8/10 and vision improved two lines or more in 6/10

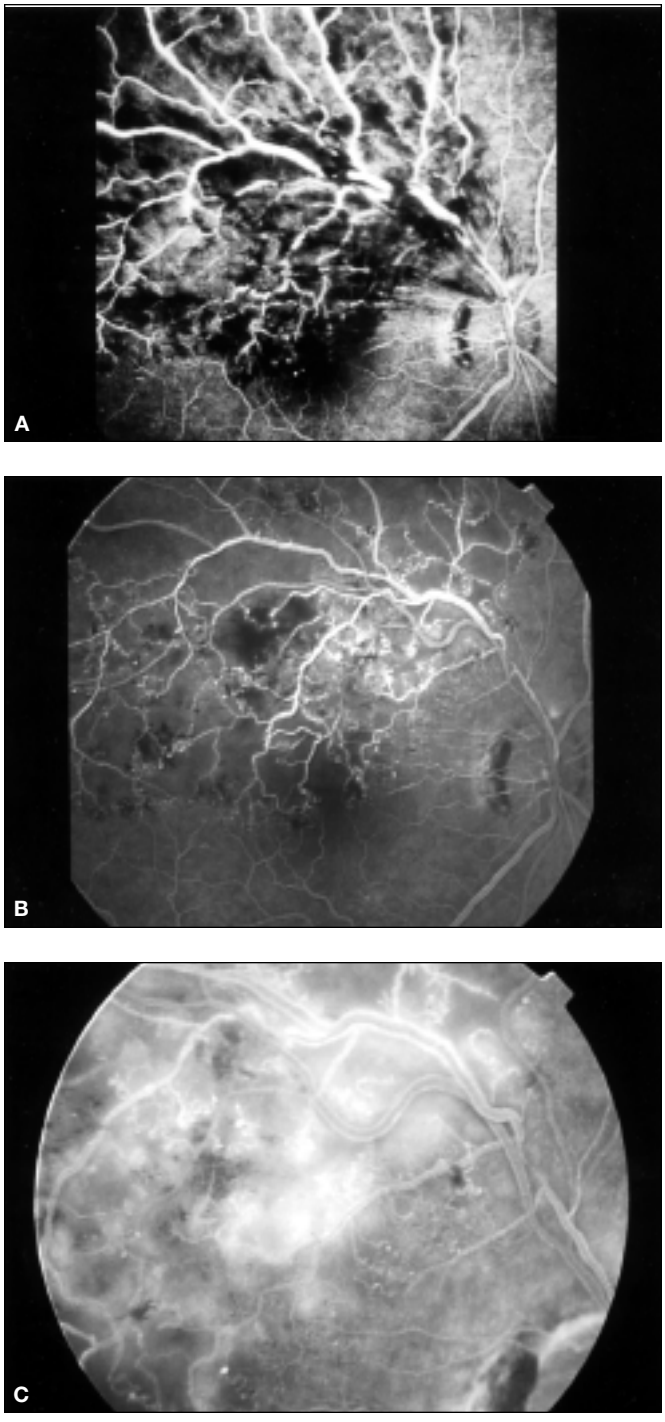

Fig. 1 - A) *Preoperative fluorescein angiography of branch retinal vein occlusion. Artery and vein parallel at crossing. Visual acuity (VA) 20/100.* **B and C)** *Fluorescein angiography 28 months after surgery. Despite successful decompression 15 days after the occlusion, severe vein stenosis persisted, making collaterals inevitable. VA 20/30.*

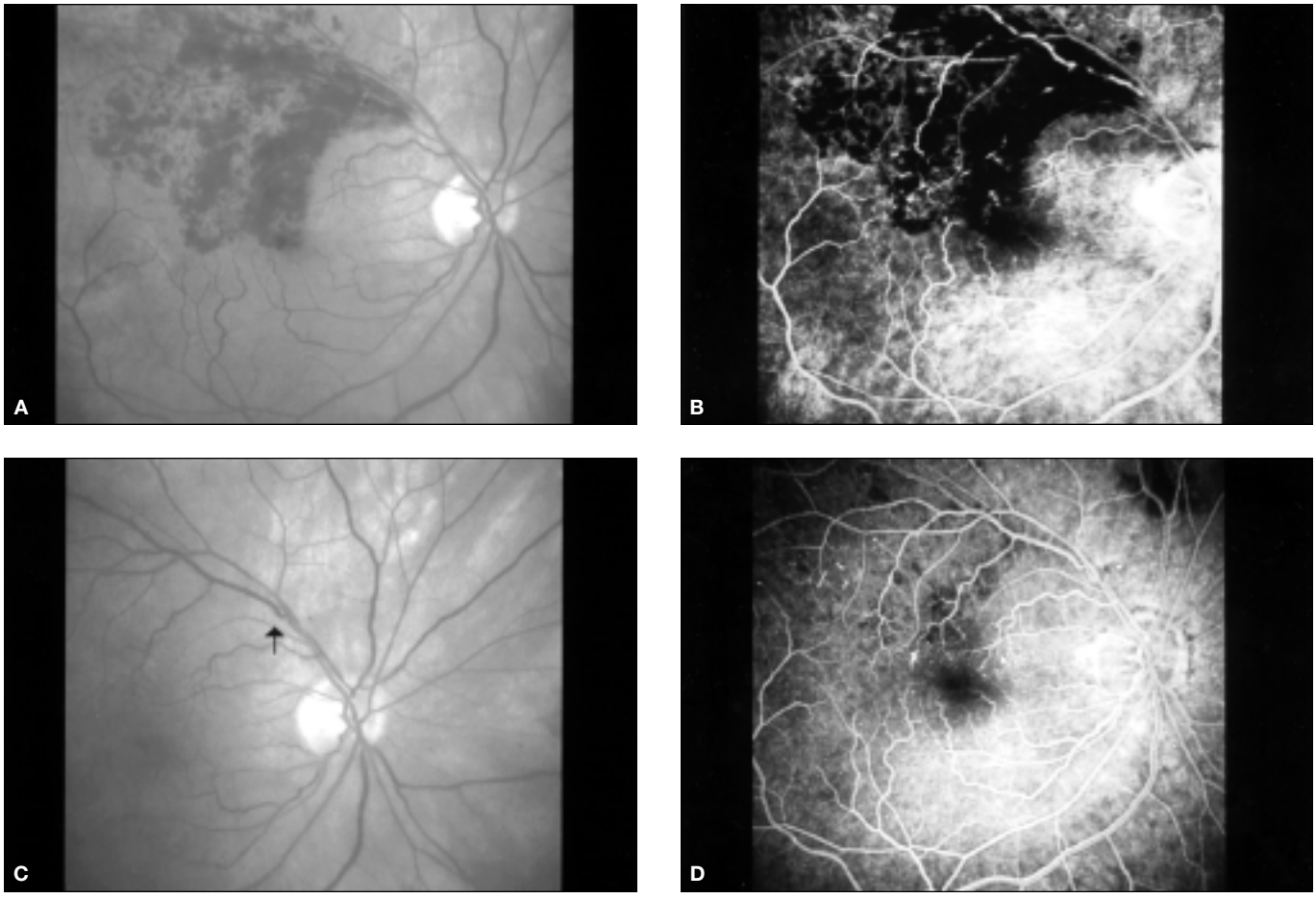

Fig. 2 - A and B) *Preoperative fluorescein angiography and color photographs. Visual acuity (VA) 20/100.* **C and D)** *Postoperative appearance 15 months after surgery. Following decompression, point of contact between the vessels is now visible (arrow). VA 20/20.*

(60%), one line in 2/10 (20%), and remained unchanged in 2/10 (20%) eyes. The mean visual improvement was 2.7 lines and the median was 3.00.

No eyes developed new vessels in either the anterior or posterior segments, although 8/15 (53%) showed retinal ischemia larger than 5 disk diameters.

The following surgery-related complications were observed in this group during and after surgery: mild intraoperative retinal venous bleeding during dissection in two eyes, which resolved by increasing intraocular pressure; a macular hole 36 months after surgery in one eye despite macular edema resolution; and a nuclear cataract progression in 10/15 (67%) eyes.

Group 2: Vitrectomy with posterior hyaloid removal

Twenty eyes of 20 patients were included in this group (8 women and 12 men) with a mean age of 65 years (range 56-71). The mean preoperative interval was 112 days (range 12 days-12 months). During surgery, the posterior hyaloid was detached in 19/20 (95%), whereas one eye showed a preoperative posterior hyaloid detachment.

The mean improvement in acuity at 3, 6, 9, 12, and 18 months was 2±2.5 lines, 2.6±2.7 lines, 3.2±3 lines, 2.8±3 lines, and 2.3±2.8 lines, respectively (Tab. I). The mean time for macular edema resolution and VA improvement was 9 months with a mean improvement

TABLE I - COMPARATIVE STUDY: CHANGES IN VISUAL ACUITY

	Group	n	Mean improvement (lines)	Standard deviation	p (Student's t test)
VA changes 3 months	1	15	1.7	1.2	0.651
	2	20	2.0	2.5	
VA changes 6 months	1	15	2.3	1.8	0.697
	2	20	2.6	2.7	
VA changes 9 months	1	15	3.5	2.4	0.763
	2	20	3.2	3.0	
VA changes 12 months	1	15	3.0	2.7	0.881
	2	20	2.8	3.0	
VA changes 18 months	1	15	2.1	2.1	0.748
	2	20	2.3	2.8	

VA = Visual acuity

of 3.2±3 lines. By that time, macular edema had resolved in 16/20 (80%) and vision had improved by two lines or more in 13/20 (65%), improved one line in 3/20 (15%), remained unchanged in 2/20 (10%), and deteriorated in 2/20 (10%). The Wilcoxon test showed a statistically significant difference between the preoperative and postoperative visual finding (p=0.001).

The presence of intraretinal hemorrhages did not lead us to preoperatively classify macular edema as either ischemic or nonischemic. Throughout the follow-up, as hemorrhages resolved, 6 of 20 eyes showed nonischemic macular edema. Following surgery, the edema resolved in all of them and vision improved by a mean of 5.8 lines (range 1-8) and a median of 7.00. Fourteen eyes showed ischemic macular edema.

Following surgery, macular edema resolved in 10/14 and vision improved two lines or more in 8/14 (57%), one line in 2/14 (14%), remained unchanged in 2/14 (14%), and deteriorated in 2/14 (15%) eyes. Mean visual improvement was 2.2 lines and the median was 2.50.

No eyes developed new vessels in either the posterior or anterior segments after a mean follow-up of 18 months.

Following intraoperative posterior hyaloid detachment, one case showed two peripheral retinal tears, which were treated with retinopexy and fluid/gas exchange. No other surgery-related complications were observed during or following surgery except for the progression of nuclear cataracts in 10/20 (50%).

Comparative study

No differences were found between the groups in terms of patients' age (p=0.566; Mann-Whitney U test). Nor were any differences found between the groups in terms of preoperative VA (p=0.505; Mann-Whitney U test). No differences were found in final VA at 3 (p=0.651; Student t-test), 6 (p=0.697; Student t-test), 9 (p=0.763; Student t-test), 12 (p=0.881; Student t-test), or 18 (p=0.748; Student t-test) months (Tab. I).

At 9 months, a comparison was made between ischemic and nonischemic eyes in terms of resolution of macular edema and results in VA. This difference was not statistically significant in Group 1 (p=0.064; Mann-Whitney U test), but it was significant in Group 2 (p=0.02; Mann-Whitney U test), which showed better VA in the nonischemic form.

No new vessels developed in either group.

DISCUSSION

BRVO is the second most common cause of retinal vascular disease. This type of occlusion is most frequent in the superotemporal arcade because of the high density of AV crossings.

In December 1998 we began a prospective pilot study to determine whether BRVO was reversible by AV decompression and what effect surgery had on the secondary complications of the disease. To analyze the effectiveness of decompression, the procedure must be performed very early in the course of the disease, because experimental histologic studies have shown irreversible capillary closure 4 days after the occlusion (23). Thus we performed surgery on patients with macular edema and 20/100 vision or worse as soon as possible, regardless of the type of edema.

In our series, complete decompression could not be performed in four eyes because a strong adherence between the vessels at the AV crossing posed a serious risk of vein damage. Results for these patients were included in Group 1 because maneuvers at the crossing were performed even though decompression was not completed. Although decompression was not successful in these four eyes, macular edema resolved in all of them, leading us to the conclusion that sheathotomy was not the mechanism for resolution of macular edema. Moreover, it is worth noting that neither our study nor the one by Opremcak and Bruce have found any relationship between the duration of the preoperative interval and the resolution of macular edema following surgery when performed within the year after branch vein occlusion (12). In our series edema resolved both in eyes that were operated on as soon as 7 days after the occlusion and in eyes operated on as late as 75 days after the occlusion. This seems to provide additional support to the idea that decompression is not the cause of resolution of edema and improvement of VA. Detaching the posterior hyaloid and removing the vitreous gel may have been sufficient to resolve edema and prevent development of new vessels. We therefore undertook a second study where vitrectomy with posterior hyaloid removal was performed (Group 2), with the same inclusion and exclusion criteria as in the first study.

One of the weaknesses of the study is that the two groups were not randomized but instead retrospectively compared. This comparison showed no statistically significant differences either in terms of patients' age or preoperative VA. There were no differences between the groups in VA following macular edema resolution (p=0.763), nor were any differences found between the groups in VA during follow-up (Tab. I).

The substantial visual improvement in both groups may have been due to the high proportion of patients with ischemic macular edema. Although we were unable to determine the state of the foveal capillary net preoperatively owing to intraretinal hemorrhages, 24 of 35 eyes showed ischemic macular edema during follow-up. The study by Finkelstein showed that the ischemic type tends to resolve spontaneously with an improvement in 90% of patients and a mean final VA of 20/30 without receiving any treatment. In contrast, the nonischemic form in his series showed resolution of edema and improvement of VA in 30% of cases; that is, 70% showed a persistence of edema with a final VA of 20/100 with no treatment (24).

Of the 35 eyes operated on in our series, 11 showed the nonischemic form (five in Group 1 and six in Group 2). Macular edema resolved and vision improved in all at a mean of 5.5 lines (range 1-8 lines), in a clear contrast with the natural evolution described by Finkelstein, where 70% showed a persistence of edema (24). This improvement was also quite significant compared to that described in the BRVO study, where the mean improvement in treated eyes was 1.3 lines (8). It must be noted that the improvement in vision in our series was greater in patients with nonischemic macular edema than those with the ischemic form of the disease. This would suggest that either the natural evolution of the disease may be better than has been described in previous studies, or that the response of nonischemic edema to surgery was better than ischemic edema.

Surgery did not only improve VA, but it also prevented the development of new vessels in both groups, which is the second most common complication following BRVO. The reason for the absence of neovascularization in Group 2 could be a positive selection due to the longer preoperative interval in the vitrectomy group and the exclusion of those eyes that already showed neovascularization. Nevertheless, is not uncommon to develop neovascularization between 6 and 12 months after the occlusion, that is, at a later stage in the course of the disease. Moreover, no eyes in Group 1 developed neovascularization despite the shorter preoperative interval in this group. This may be caused by the sheathotomy itself, but in our series no visible changes in vein caliber either during surgery or in the follow-up were detected, which means that perfusion was not effectively preserved. We be-

lieve that the absence of new vessels in this group was also due to the detachment of the posterior hyaloid and the removal of the vitreous gel.

Therefore, our findings suggest that posterior hyaloid detachment and vitreous removal might be sufficient to resolve macular edema, improve VA, and prevent the development of new vessels in patients with BRVO, thereby making maneuvers at the crossing unnecessary. Recent reports by Tachi et al and Saika et al support our findings on vitrectomy with hyaloid removal. Tachi et al reported 27 patients in whom macular edema resolved and VA improved following phacoemulsification and pars plana vitrectomy with posterior hyaloid detachment (17). They found that VA improvement was better in those eyes that had higher VA before surgery. Saika et al combined this technique with a gas/air tamponade and found that VA improved substantially when surgery was performed no later than 11 months after the occlusion (18).

But what might be the mechanism for resolution of macular edema and improvement of vision following a vitrectomy with hyaloid removal? It should be emphasized that nearly all the eyes in this study showed an attached posterior hyaloid during surgery. Detaching the posterior hyaloid and removing the vitreous gel may improve the oxygen supply to ischemic inner retina by way of fluid currents in the vitreous cavity, as Stefánsson et al reported in 1990 (25). The improvement in the preretinal oxygen tension levels may cause vessel constriction and lower intravascular pressure, thereby reducing edema formation, according to Starling's law (26). This may cause resolution of macular edema in BRVO in a manner similar to the resolution of diabetic macular edema following vitrectomy.

But it is also possible that the removal of vitreous gel causes resolution of macular edema owing to elimination of intravitreal cytokines. Vascular endothelial growth factor (VEGF) is a cytokine produced by hypoxic retina in central retinal vein occlusion and diabetic retinopathy that induces capillary permeability and angiogenesis (27, 28). It has recently been reported that VEGF leads to endothelial cell hypertrophy and capillary luminal narrowing, causing more ischemia and more VEGF production (29). Vitreous removal, by eliminating this cytokine, and perhaps other cytokines as well, may induce the resolution of macular edema and the improvement of VA found in our study. Nevertheless, these are only hypotheses that must be tested by future studies.

Although there are numerous potential complications associated with these surgical techniques, including retinal tears or detachment, vitreous hemorrhage, retinal gliosis at the incision site, or nerve fiber layer defects, these were uncommon in our series. During surgery, only one eye showed retinal tears, which were successfully treated with retinopexy and fluid/gas exchange, whereas another developed a macular hole 3 years after surgery. Our most common complication was the acceleration of nuclear sclerotic cataract formation, a problem that is inherent to vitrectomy.

In summary, our study suggests that vitrectomy with posterior hyaloid removal resolves macular edema, improves VA, prevents development of new vessels in patients with BRVO, and makes maneuvers at the crossing unnecessary. However, there are major limitations to the present study: it is a case series with no controls that would serve only as a pilot study to report the clinical outcome of a rather limited number of patients undergoing pars plana vitrectomy for BRVO. A randomized, multicenter study is necessary to confirm these findings.

ACKNOWLEDGEMENTS

The authors thank Alfonso Muriel and Victor Abraira of the Department of Statistics, Ramón y Cajal University Hospital, for statistical assistance.

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