Results of Radial Optic Neurotomy with or Without Intravitreal Triamcinolone for Central Retinal Vein Occlusion

Santral Retinal Ven Tıkanıklığında İntravitreal Triamsinolonlu veya Triamsinolonsuz Radyal Optik Nörotomi Sonuçları

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ABSTRACT

Purpose: To evaluate the efficacy of radial optic neurotomy (RON) with or without intravitreal triamcinolone in improving visual acuity in central retinal vein occlusion (CRVO).

Materials and Methods: We performed vitrectomy and RON to 16 eyes of 16 patients with CRVO with a best corrected visual acuity (BCVA) of 20/200 or less. Eight of them received an injection of 4mg intravitreal triamcinolone (IVTA) at the completion of the surgery. The major outcome parameter was defined as an improvement of BCVA of 2 or more lines and final BCVA better than 20/200. Decrease in central macular thickness was our secondary outcome parameter. Intraoperative and postoperative complications were also evaluated.

Results: Eleven (68.8%) of the eyes were evaluated as ischemic based on fluorescein angiography and presence of relative afferent pupillary defect. Only 2 (12.5%) patients had BCVA of better than 20/200 postoperatively. Central macular thickness was significantly reduced from 811±303 μ to 444±276 μ ($p<0.01$). Preoperative visual acuity and age were significant factors in affecting final BCVA of better than 20/200 ($p=0.02$ and $p=0.05$, respectively). One patient underwent trabeculectomy because of intractable open angle glaucoma. One additional patient developed neovascular glaucoma and was treated with diod laser cyclophotocoagulation.

Conclusions: RON surgery with or without peroperative IVTA led to a significant decrease in central macular thickness but its functional success is very limited in eyes with preoperative BCVA of less than 20/200 and probably is not better than the natural history.

Key Words: Central retinal vein occlusion, radial optic neurotomy, triamcinolone, pars plana vitrectomy.

ÖZ

Amaç: Santral retinal ven tıkanıklığında (SRVT) intravitreal triamsinolonlu veya triamsinolonsuz radyal optik nörotominin (RON) görme keskinliğini iyileştirmedeki etkinliğini değerlendirmek.

Gereç ve Yöntemler: En iyi düzeltilmiş görme keskinliği (EİDGK) 20/200 veya altında olan 16 SRVT hastasının 16 gözüne RON uyguladık. Gözlerden sekizine ameliyatın bitiminde 4mg triamsinolon intravitreal olarak uygulandı (IVTA). EİDGK'da 2 sıra veya daha fazla artış ve sonuç EİDGK'nın 20/200 üzerinde olması ana hedef olarak belirlendi.Merkezi retina kalınlığındaki azalma ikincil hedefti. Ameliyat esnasında ve sonrasındaki komplikasyonlar da değerlendirildi.

Bulgular: Floresein anjiyografiye dayanılarak gözlerin 11'i (%68.8) iskemik olarak değerlendirildi. Ameliyat sonrası dönemda yalnızca 2 (%12.5) hastanın EİDGK'sı 20/200'den daha iyiydi. Merkezi retina kalınlığı anlamlı bir şekilde 811±303 μ'dan 444±276 μ'a geriledi ($p<0.01$). ameliyat öncesi EİDGK ve yaş 20/200'den daha iyi sonuç görmeye ulaşmayı etkileyen faktörler olarak saptandı (sırasıyla $p=0.02$ ve $p=0.05$). Bir hastaya tedaviye dirençli glokom nedeniyle trabekülectomi uygulandı. Bir hastada da neovasküler glokom gelişti ve diyod lazer siklofotokoagülasyon ile tedavi edildi.

Sonuç: İVTA'lı veya IVTA'sız RON cerrahisi merkezi retina kalınlığında anlamlı azalma sağladı fakat ameliyat öncesi EİDGK'sı 20/200 altında olan gözlerde fonksiyonel başarısı çok sınırlıdır ve muhtemelen doğal seyirden daha iyi değildir.

Anahtar Kelimeler: Santral retinal ven tıkanıklığı, radyal optik nörotomi, triamsinolon, pars plana vitrektomi.

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INTRODUCTION

Central retinal vein occlusion (CRVO) is a common retinal vascular disorder with potentially blinding complications.[1-3] The prevalence of CRVO was reported between 0.1% and 0.4% after the fouth decade.[4,5] The natural history is poor. The CRVO Study Group reported that patients with initial visual acuity of less than 20/200 had an 80% chance of having a final visual acuity less than 20/200, whether perfused or nonperfused initially.[2] Also, ischemic CRVO led to iris neovascularization in 45-80% of patients.[6] Panretinal laser photocoagulation was shown to be effective for reducing iris neovascularization and neovascular glaucoma, but macular grid laser photocoagulation was not effective in improving visual acuity. [7,8]

Various medical and surgical treatments for CRVO have been proposed over the last decade. These include anticoagulants, fibrinolytics, acetazolamide, isovolemic hemodilution, intravitreal steroids, intravitreal vascular endothelial growth factor inhibitors, chorioretinal anastomosis with lasers, simple vitrectomy, surgically induced chorioretinal anastomosis, direct venous cannulation with injection of fibrinolytics, and radial optic neurotomy (RON).[9-12] Efficacy of these therapies have not been demonstrated by controlled studies.

Radial optic neurotomy (RON), has been initiated by Opremcak et al. and they postulated that surgical decompression of the optic nerve at the scleral outlet could decrease hemorrhage, edema, and ischemia and could provide better perfusion.[13]

The aim of this study is to evaluate the efficacy of RON in conjunction with PPV in the management of CRVO.

MATERIALS AND METHODS

The study was performed in Beyoglu Eye Training and Research Hospital between January 2004 and January 2005. The study was designed to evaluate the efficacy of RON in eyes with CRVO with or without intravitreal triamcinolone (IVTA) injection. Only cases where no intervention had been performed for one month were included in our study so that the outcome would not be influenced by the occurrence of spontaneous improvement. Patient inclusion and exclusion criteria are shown in table 1.

The study followed the Tenets of the Declaration of Helsinki. The surgical procedure was explained in detail to all patients and informed consent was obtained. Visual acuity testing was done using an ETDRS chart at 2 meters. When the patient was unable to see the largest size letters from 2 meters the ETDRS chart was brought to 1 meter and the test was repeated. Fractional visual acuity data were converted to logarithm of minimum angle of resolution (logMAR) equivalents for statistical analysis. We considered the CRVO ischemic if there was larger than 30 disc areas of nonperfusion in fluorescein angiography. We categorized CRVO as indeterminate if there was sufficient amount of retinal hemorrhage to preclude the angiographic evaluation.

A total of 36 cases with CRVO who met the inclusion criteria were diagnosed in our clinic between January 2004 and January 2005. Sixteen eyes of 16 patients were included in the study. They underwent PPV and RON surgery. IVTA injections were randomly given to 8 eyes at the completion of the surgery. The remaining 20 eyes that were not included in the study were either followed without intervention or underwent IVTA injection and/or laser photocoagulation. All patients underwent careful biomicroscopic evaluation, applanation tonometry, and dilated fundus examination. Fundus photography, fluo-

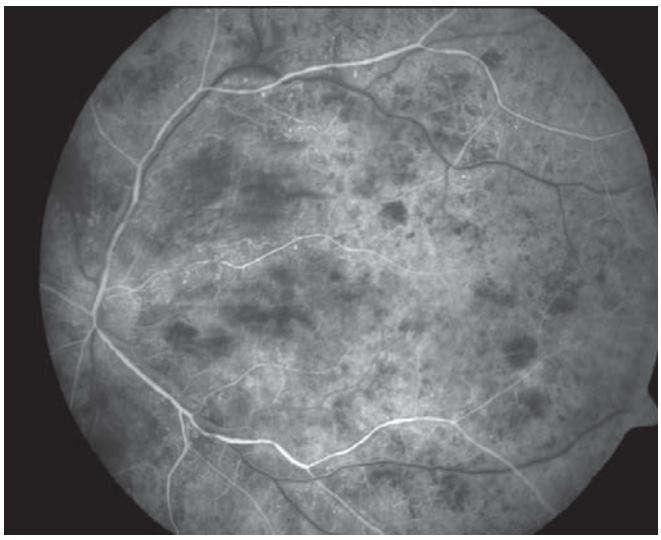

Figure 1a: Preoperative flourescein angiography of a patient in Group 1. Blockage of fluorescence due to superficial and deep hemorrhages, areas of capillary nonperfusion temporal and superior to the macula. Initial visual acuity 20/800

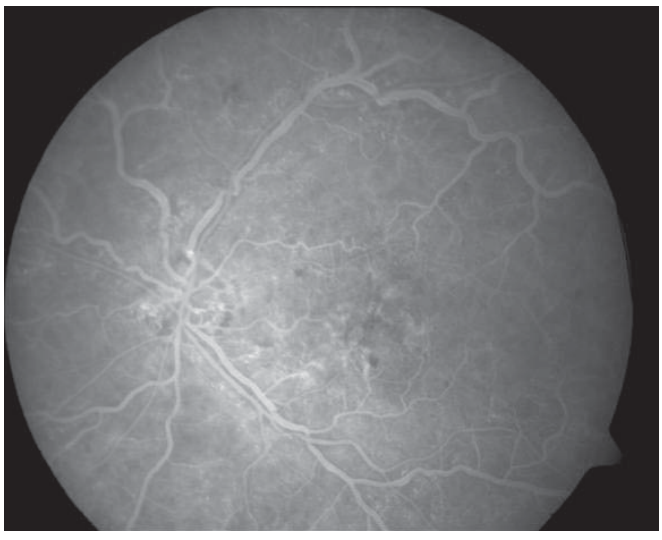

Figure 1b: Postoperative 3rd month, visual acuity increased to 20/400. Hemorrhages decreased significantly. Optociliary shunt is vessel present nasal to the disc.

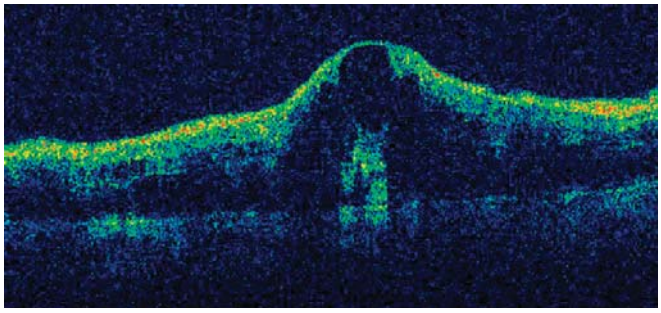

Figure 2a: Preoperative optical coherence tomography of a patient in Group 1. Macular edema with large cystoid spaces.

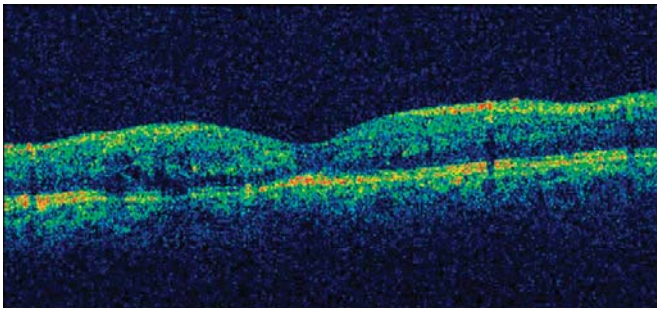

Figure 2b: Macular edema resolved postoperatively with only several tiny cystoid spaces.

rescein angiography, and optic coherence tomography (Stratus 3, Carl Zeiss, Dublin,CA) were performed before surgery and during follow-up.

Surgical technique:

Three-port PPV was performed and posterior cortical vitreus was removed with active aspiration in all patients. RON surgery was performed with the technique described by Opremcak.[13] The RON site was carefully selected by examining optic nerve heads and fluorescein angiography images in order to place the incision away from the major vessel branches and hemorrhages. The incisions were always located on the nasal side of the optic discs. The direction of the incision was parallel to the nerve fibers entering the optic disc. We used a one-sided blunt microvitreoretinal (MVR) blade developed for RON (Synergetics,Inc., St. Charles, MO). The blade was positioned at the margin of the disk and then directed posteriorly into the optic nerve and a single incision was performed. The depth of the incision was 2 mm according to the mark on the special blade. The height of the infusion bottle was increased to minimize bleeding during the procedure. Neither ILM peeling nor gas tamponade was used. Eight eyes received an intraocular injection of 4mg/0.1cc triamcinolone at the completion of the surgery (Group 1), and the remaining 8 eyes received no intraocular steroid injection (Group 2). All surgeries were performed by a single surgeon (Z.K.).

After the surgery, control examinations were performed on the first day, after the first week, the first month, the third month, the sixth month, and the final visit. At each control visit; BCVA measurement with ETDRS chart, IOP recording with Goldmann applanation tonometer, detailed anterior segment and fundus examinations were performed. Fundus photography, fluorescein angiography, and optic coherence tomography were made at each visit.

Table 1: Patient Inclusion and Exclusion Criteria.

Inclusion	Exclusion
Eyes with CRVO, ischemic or nonischemic Eyes with BCVA of 20/200 or less Preoperative follow-up for more than 1 month	Previous laser photocoagulation Eyes with neovascularization Eyes with spontaneous improvement

CRVO: Central retinal vein occlusion, BCVA: best corrected visual acuity.

SPSS 11.5 for Windows (Chicago, Illinois, USA) was used for statystical analysis. Chi-square test was performed for categorical variables. Wilcoxon signed rank test and Mann-Whitney-U test were used for continuous variables. Logistic regression analysis was performed to evaluate the predictors of visual outcome in a multivariate fashion.

RESULTS

The mean age of the patients was 61.3±8.4 (range 47-76). Eleven patients (69%) were male and 5 were female (31%). Hypertension was present in 8 patients (50%) and type 2 diabetes mellitus in 5 patients (31%). None of them had previously diagnosed glaucoma. The mean interval between the onset of CRVO and surgery was 13.5±7.3 weeks (range 4-32). The average postoperative follow-up was 15.5±9.2 months (range 6-36). All patients had areas of blocked fluorescence due to hemorrhage and edema in all four quadrants in fluorescein angiography and all eyes had leakage at the fovea in the late phases of angiography. Eleven (69%) eyes had ischemic, 2 (12%) eyes had indeterminate and 3 (19%) eyes had nonischemic CRVO.

Preoperative and postoperative findings are presented in Table 1. The median preoperative BCVA was counting fingers and only 2 of the study eyes had BCVA of 20/200. Mean age was identical in both groups (61 years). Visual acuity improved more than 2 lines in six (75%) eyes in Group1 and in 4 (50%) eyes in Group 2 (total 10 eyes, 62.5%, $p=0.6$, chi-square). Visual acuity remained stable in 4 (25%) eyes, and decreased in 2 eyes (12%). One eye in group 1 and one eye in group 2 (total 2 eyes,12%) met the main outcome criteria postoperatively.

A reduction in the area with hemorrhages were observed in all patients during postoperative visits. There was statistically significant reduction in average macular thickness as measured by OCT. It decreased from 811±303 μ to 444±276 μ (Wilcoxon signed ranks test, $p<0.01$). Decrease in central macular thickness was not different between Group1 and Group 2 (p=0.44, Mann-Whitney-U). Although macular thickness was reduced, the angiographic macular edema persisted in 3 eyes in

Table 2: The summary of preoperative and postoperative findings of 16 patients.

	Patient no	Age/Sex	Preop follow-up (months)	RAPD	Preop logMAR	Postop logMAR	Preop CMT (μ)	Postop CMT (μ)	Optociliary shunt	Follow-up (months)
Group 1	1	59/F	8	0	1.4	1.6	670	148	-	22
	2	67/M	2	1	1.7	1.3	458	325	1	19
	3	76/F	6	1	3.0	2.3	880	699	-	32
	4	57/M	1.5	0	1.7	1.0	720	360-	1	36
	5	68/M	4.5	1	2.5	1.6	1021	896	-	10
	6	47/M	3	0	1.1	0.7	970	300	-	6
	7	69/M	3	1	2.1	3.0	601	590	-	13
	8	48/F	1.5	1	1.7	1.0	620	195-	1	22
	9	57/F	5	1	1.8	1.0	970	345	-	15
	10	59/F	2.5	0	1.0	1.0	468	146-	-	22
Group 2	11	58/M	2	1	2.0	2.0	605	296	-	10
	12	58/M	4	1	2.3	1.7	840	170	-	12
	13	60/M	2.5	1	1.7	1.7	550	580	-	8
	14	55/M	1	0	1.0	0.6	613	330	-	6
	15	72/M	2.5	1	2.1	3.0	1050	810	-	6
	16	72/M	4	1	2.1	1.2	950	495	1	9

RAPD: Relative Afferent Pupillary Defect, Preop: Preoperative, Postop: Postoperative, CMT: Central Macular Thickness, logMAR: logaritm of minimum ngle of resolution.

group 1 and in 5 eyes in group 2. Optociliary shunt vessels were developed in 4 patients. Logisitic regression analysis showed that logMAR equivalent of preoperative visual acuity and age were significant factors in determining final BCVA of better than 20/200 ($p=0.02$ and $p=0.05$, respectively).

Intraocular hemorrhage developed in 3 eyes but cleared spontaneously. Cataract developed in 1 eye and persistent cystoid macular edema was detected in 4 eyes. We encountered no complications such as massive hemorrhage, retinal tear formation, and/or retinal detachment. One (12%) patient in group 1 developed intractable open angle glaucoma 1 month after surgery (Patient no. 8), leading us to perform a trabeculectomy. Primary open angle glaucoma was diagnosed in the other eye of that same patient during follow-up. Iris neovascularization and neovascular glaucoma developed in another patient in Group1 one month after surgery and was treated with external cyclophotocoagulation.

DISCUSSION

CRVO is a common retinal vascular disorder that can lead to blindness. The natural history and visual prognosis for patients with CRVO was studied by The Central Vein Occlusion Study Group.[2] This study concluded that visual acuity outcome was largely determined by the presenting acuity. Patients who had a BCVA less than 20/200 at the first visit had an 80% chance of having BCVA less than 20/200 at final visit, whether perfused or nonperfused initially. Macular grid laser photocoagulation was found to be effective in reducing macular edema; however, it did not improve visual acuity.[8] Many other treatment modalities for this disorder have been tried, but none of them has demonstrated proven benefit. PPV combined with removal of posterior cortical vitreus alone may contribute to resolution of macular edema in eyes with CRVO. Persistent macular edema may be associated with the presence of an attached posterior hyaloid.[14,15] Vitrectomy may increase retinal oxygenation and relieve macular traction. A few retrospective case series have reported improved anatomical and functional outcomes in macular edema associated with CRVO after vitrectomy.[16-18] Tachi has reported resolution of macular edema and improvement in visual acuity following PPV in 29 cases with branch retinal vein occlusion (BRVO) and in 14 cases with CRVO.[19] Sekiryu showed a decrease in macular edema by OCT in 5 eyes with CRVO following PPV.[18] Although PPV seemed to be somewhat effective to increase visual acuity, the increase in visual acuity was

not clinically significant. The etiology and pathogenesis of CRVO are not fully understood. Opremcak et al. proposed a compartment syndrome hypothesis for the mechanism of CRVO in 2001.[13] He alleged that an increased pressure within nonelastic scleral outlet might preferentially compress the lumen of the nonmuscular vein and result in occlusion of the central retinal vein.[13] Hayreh opposed this hypothesis. He stated that the occlusion site in CRVO was behind the lamina cribrosa in the majority of patients and RON would be of no benefit in these cases.[14] He also added that cutting the blood vessels in the optic nerve head would seriously interfere with the blood supply of the optic nerve head and result in acute ischemia.[14] There is still debate on the exact mechanism of action, safety, and efficacy of RON.The observed improvements may be due to effects of vitrectomy alone or natural history. Opremcak published the results of 117 RON cases and reported anatomical improvement in 95% of the patients and increased visual acuity in 71% cases.[20] Nagpal reported improved visual acuity in 83% of 24 RON patients but denied that RON had a better visual prognosis than the natural history would suggest.[21] Horio stated that RON might cause further decrease in retinal blood flow and chorioretinal anastomosis could be inadequate.[22]

We reported our experience with RON in patients with CRVO and compared the visual outcomes in eyes with and without IVTA injection. Visual acuity measurements may give variable results in eyes with CRVO. Because all eyes with CRVO have central scotoma, measured visual acuity change may not reflect genuine improvement but may be due to learning of eccentric fixation. To avoid this bias, we established more strict criteria for success. According to our criteria only 2 patients (12.5%) had visual acuity improvement. Because this was not different from the natural history reported by the CRVO Study Group we stopped recruitment to the study.

Optociliary shunt vessels are rarely seen in CRVO patients and show good prognosis.[23] Although optociliary venous anostomosis can be a result of natural progression of the disase it has been shown that RON can increase their occurance. Garcia-Arumi reported chorioretinal anotomosis in 42% of 14 cases.[24] Nomoto has evaluated 15 RON patients with indocyanine videoangiography, and he found chorioretinal anotomosis and increased blood flow in 7 patients (46.7%).[25] In our study 4 patients (25%) had chorioretinal anotomosis near RON site and all 4 eyes had more than 2 lines visual acuity improvement. However, none of them had BCVA better than 20/200.

We compared the eyes with and without IVTA injection. Although not statistically significant, eyes which had IVTA injection had more retinal thinning. Also the visual acuity outcome did not differ between both groups. However an intractable open angle glaucoma developed in an eye in the IVTA group. Primary open angle glaucoma was detected in the other eye of the same patient during follow-up. Glaucoma is associated with retinal vein occlusions.[26] The risk of elevated intraocular pressure is significantly high in eyes which received IVTA injections for CRVO.[27] Opremcak et al. reported that adjunctive use of intraocular triamcinolone provided no additional benefit to RON alone, instead it was associated with a higher incidence of elevated intraocular pressure and endophthalmitis. In the light of these findings, we think that it is better not to use triamcinolone injection to eyes which undergo RON surgery.

Visual field defects, frequently in the form of wedge-shape temporal visual field loss, were reported as a result surgery.[29] As we were unable to perform kinetic perimetry and electrophisiologic testing, we cannot comment on the effect of RON surgery on these other components of visual function

In conclusion, we found that RON surgery with or without IVTA produced no significant improvement in BCVA in this relatively small series of patients. We did not observe any serious intraoperative complication. We think that larger studies that randomize patients to vitrectomy alone, vitrectomy plus RON, and standard care are needed. We also think that the results of these studies shoud be awaited before performing RON.

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