21. 未熟児網膜症に対する硝子体手術の検討

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研究要旨 未熟児網膜症（ROP）の stage4B あるいは stage5 に至った 9 例 14 眼に対し、硝子体手術を施行した。対象の内訳は Stage4B が 2 例 2 眼、stage 5 が 7 例 12 眼で出生体重、週数とも既報より小さい傾向があり、また Zone 1, plus disease の症例が多くみられた。全例に硝子体手術を行い、初回手術にて網膜復位は 7 眼（50%）で得られた。初回手術で復位が得られなかった 7 眼中 6 眼に対して再手術を行ったが、これらの症例では最終的に復位を得ることはできなかった。ROP に対する硝子体手術は失明予防、眼球形態温存の点からは有用であると思われるが、さらなる復位率の向上とより良い視機能獲得が必要と思われた。

A. 研究目的

未熟児網膜症（ROP）は小児の失明原因として第一位の重要な疾患である。1950 年代に ROP の発症には高濃度酸素投与が関係していることが明らかとなり、投与酸素濃度の適正化により ROP の発症は一時減少した。しかし、近年の周産期医学の発達に伴い、超低出生体重児の生存率が向上するに伴い、以前より重症の ROP に遭遇する機会が増加している。今回はこの中でも特に重症である網膜剥離を伴った ROP に大して硝子体手術を施行した症例について検討した。

B. 研究方法

対象は網膜剥離を伴う未熟児網膜症に対して大阪府立急性期・総合医療センター、大阪府立母子保健総合医療センター、淀川キリスト教病院、大阪大学医学部付属病院の 4 施設で 2001 年 9 月～2004 年 9 月の間に同一術者（S.K.）によって施行された 9 例 14 眼である。内訳は男児 7 例 11 眼、女児 2 例 3 眼、未熟児網膜症国際分類で stage4B が 2 例 2 眼、あるいは stage5 が 9 例 12 眼である。在胎週数は 22 週 5 日～27 週 6 日（平均 24 週 3 日）、出生時体重は 466～1,055g（平均 659.6g）であった。、初回手術時月齢は 3 ヶ月～12 ヶ月（平均 5.3±標準偏差ヶ月）、術後経過観察期間は 2 ヶ月～3 年 2 ヶ月（平均 16.0±標準偏差ヶ月）であった。

硝子体手術では増殖膜を処理剥離・切除し網膜への牽引を解除することに努め、術中に医原性裂孔が認められなかった場合は硝子体腔内にヒアルロン酸ナトリウムを注入し、裂孔が認められた場合には 液空気置換、ガスタンポナーデ、術前に輪状締結術が施行されていなかった症例では強膜バックリング法を行った。

術後は無水晶体眼となっているため網膜の状態をみながら、可能な限り早期にコンタクトレンズ装用を開始した。

（倫理面への配慮）

対象例の個人情報は明らかにされていない。また、治療法として未だ成功率は低いものの硝子体手術は網膜剥離を伴う ROP に対して確立された有効な治療法であり、これを行わなければ患児はやがて失明、眼球癆に至る。今回の研究は倫理的に特に問題がないと思われる。

C．研究結果

網膜の復位は 14 眼中 7 眼（50%）に得られた。その内訳は stage4B の 2 眼中 2 眼、stage 5 の 12 眼中 5 眼であった。これら網膜復位が得られた 7 眼で症例はすべて初回手術のみで復位が得られた。一方、初回手術後に網膜復位が得られなかった 7 眼中 6 眼に対しては再手術を行ったが、これら 6 眼では、最終的に網膜復位は得られなかった。

初回手術時の裂孔形成は 14 眼中 9 眼に認められた。裂孔が形成されなかった 5 眼のうち 3 眼は網膜の復位を得たが、2 眼は網膜復位が得られなかった。また、初回手術で裂孔が形成された 9 眼のうち、4 眼で網膜の復位が得られ、5 眼では復位が得られなかった。非復位例では平均出生時体重は軽く、在胎週数も短く、手術時の月齢も若い傾向があった。なお、今回の症例では経過観察期間が短いこともあり、患児の術後視機能に関しては未だ評価できていない。

D．考察

今回の対象の特徴として 1 卵生双生児であった 1 症例を除きすべて出生週数 22～24 週、出生体重が 700 g 未満といった超低出生体重児であったことや、また、眼科初診時は Zone 1 、Plus disease の症例が多く見られ、非常に未熟性の強い症例であった。今回、我々は 14 眼中 7 眼の（50%）での症例で網膜復位を得ることができたが、これは既報とほぼ同水準の治療成績と思われる。ROP における網膜剥離の原因は牽引性と考えられており、術中に裂孔が形成されるか否かは予後を大きく左右する因子だと考えられるが、今回の検討では裂孔形成の有無は網膜復位の点ではあまり大きな影響はなかった。しかし、初回手術で網膜復位の得られず再手術を行った全例で網膜の復位を得ることができなかった。再手術でも初回手術後に再増殖した膜を取り除き、網膜への牽引を解除することに努めたが、特に網膜周辺部の硬くなった増殖膜を完全に剥離・切除することはしばしば困難で、同部による周辺部網膜の牽引解除が十分にできなかった十分に取り切る事ができなかったことや、網膜症の活動性の高さ、網膜裂孔の存在した症例では増殖性の変化が強く、増殖膜の完全な除去が困難であったことなどが復位を困難にしたのではないかと考えられた。今後は初回手術から再手術までの手術時期の決定や再手術の方法、適応についても今後の検討が必要と考えられた。

また、今回の検討では症例数が少なく、経過観察期間も短く、機能面からの評価ができていないといった限界があり、今後さらに多数の症例を長期に渡って経過観察していく必要があると思われるが、症例によっては網膜復位が得られても視神経乳頭がすでに蒼白であったり、網膜の変性が強いものがあり、視力予後が懸念されるものがある。未熟児網膜症に対する硝子体手術は眼球の温存といった面ではある程度有効であると思われるが、今後はより良好な視機能

の獲得に向けて治療法の改良が必要であると考えられた。

E．結論

網膜剥離を伴った stage 4B,5 ROP に対して硝子体手術は有効であると考えられたが、より良い視機能の獲得を目指して、手術方法、時期に関してさらに検討を加える必要があると考えられた。

F．健康危険情報

なし

G．研究発表

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2．学会発表

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H．知的財産権の出願・登録状況

1．特許取得

なし

2．実用新案登録

なし

3．その他

なし

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22. 網膜内血管腫状増殖に対する外科治療後の再発

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([1)] 香川大、 [2)] 福島県立医大)

研究要旨　網膜内血管腫状増殖（RAP）に対して、硝子体手術を行なって流出入血管を切断する外科治療が有効であることを Borrillo ら[1)] は報告した。そこで、RAP8 例 9 眼に Borrillo らの手技に準じて、硝子体手術を行なって流出入血管を切断する外科治療を行い、術後、9 眼全てにおいて蛍光眼底造影で新生血管は消失し、網膜色素上皮剥離（PED）を含めて滲出性病変は消失した。その後、頻回に蛍光眼底造影を行い、新生血管の消失、再発について検討したところ、2 例 3 眼（33%）に新生血管の再発がみられ、再発新生血管にレーザー光凝固を行ったところ、1 眼にて術後滲出性病変は消失し再発を認めないが、1 眼で 3 回光凝固を行うも病変部は拡大し、1 眼では網膜の流出入血管は閉塞するも、脈絡膜新生血管が発生し病変部は拡大した。

A．研究目的

RAP の外科治療後に新生血管が再発した症例に対し、レーザー光凝固を施行し、その有効性について検討した。

B．研究方法

RAP の症例 8 例 9 眼に対し Borrillo らの手技に準じて硝子体手術を行い、網膜の流入動脈、流出静脈を切断した。9 眼全て Yannuzzi の stage 分類[2)] の stage II で、漿液性 PED を伴っていた。新生血管が再発した 2 例 3 眼に対してレーザー光凝固による治療を施行した。照射条件は、波長が赤色、黄色波長、照射径は 200-500 μ m、照射時間は 0.5 秒で新生血管全体が白色化するまで凝固した。術前後に検眼鏡検査、視力検査、フルオレセイン、インドシアニングリーン蛍光眼底造影、光断層干渉計を行った。

（倫理面への配慮）

十分なインフォームドコンセントをとり、手術の合併症の可能性、レーザー光凝固の有効性について同意を得た上で治療を行った。

C．研究結果

外科治療後、9 眼全てにおいて蛍光眼底造影検査で網膜の流出入血管および新生血管は閉塞し、滲出性病変も消失した。その後、新生血管が再発した症例は 9 眼中 3 眼(33%)と高率にみられた。その時期は、術後 3、5、11 ヵ月であった。再発新生血管はいずれも中心窩外であったため、レーザー光凝固による全体凝固を施行した。3 眼のうち 2 眼は滲出性病変が消失し、そのうち 1 眼は 16 か月の経過観察にて再発をみとめていないが（図１）、1 眼でレーザー光凝固 4 か月目に脈絡膜新生血管が発生し、滲出性病変が再発して病変部が拡大した（図２）。1 眼において、レーザー光凝固を施行する

も再発をくり返し、新生血管が網膜色素上皮下に拡大して stage III に進行した。

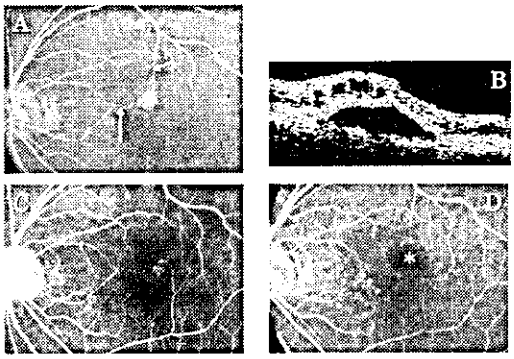

図 1

A　術前フルオレセイン蛍光眼底造影(FA)。長矢印：流入動脈、短矢印：流出静脈。

B　術前光断層干渉計。

C　外科治療後新生血管再発時 FA。

D　レーザー光凝固後 FA。＊：光凝固斑。

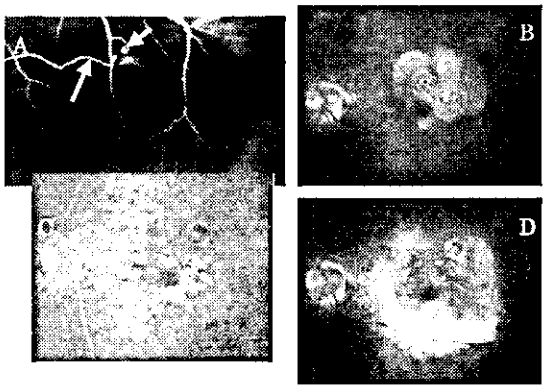

図 2

A　術前インドシアニングリーン蛍光眼底造影。長矢印：流入動脈、短矢印：流出静脈。

B　術後新生血管再発時フルオレセイン蛍光眼底造影(FA)。

C　レーザー光凝固後 FA。＊：光凝固斑。

D　レーザー光凝固後、脈絡膜新生血管発生時 FA。

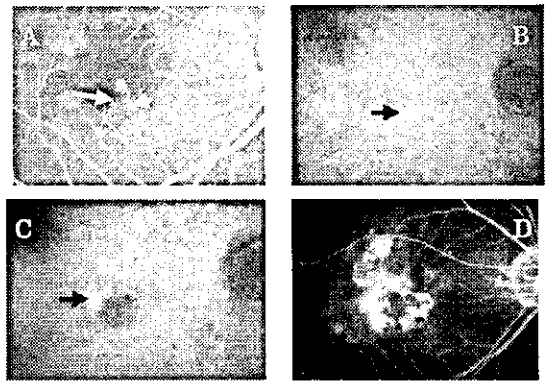

図 3

A　術前フルオレセイン蛍光眼底造影(FA)。長矢印：流入動脈、短矢印：流出静脈。

B　外科治療後インドシアニングリーン蛍光眼底造影(IA)。矢印：再発新生血管。

C　レーザー光凝固後 IA。矢印：再発新生血管。

D　3 回目のレーザー光凝固後 FA。

D．考察

RAP の外科治療を施行した後に再発した 3 眼にレーザー光凝固を施行し、長期経過では 1 眼のみに再発を認めず奏功したが、他の 2 眼は滲出性病変が再燃し、レーザー治療が有効でなかったのは、レーザー光凝固の時、新生血管全体が完全に凝固閉塞できなかった可能性もある。また、レーザー光凝固が過凝固となり新生血管の発生を誘発した可能性も考えられる。レーザーを行う時、新生血管の打ち残しがないようにすることと、過凝固にならないように照射条件に注意を要することが必要と考えられる。

E．結論

RAP に対する外科治療後、新生血管が高頻度に再発した。再発した新生血管に対しては、光凝固が有効な症例もあるが、レー

ザー治療に抵抗を示すものもあった。RAP の再発症例に対するレーザー光凝固の有効性を評価するには、症例の蓄積と長期経過の観察が必要である。

F．健康危険情報

なし

G．研究発表

1．論文発表

なし

2．学会発表

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H．知的財産権の出願・登録状況

1．特許取得

なし

2．実用新案登録

なし

3．その他

なし

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23. 網膜中心静脈閉塞症に対する放射状視神経切開術後視力に影響する因子

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研究要旨　網膜中心静脈閉塞症(CRVO)は現在においても難治な網膜疾患のうちのひとつである。2001 年に Opremcak らは CRVO に対する放射状視神経切開術、radial optic neurotomy (RON)という新しい手術手技を報告した。[1]彼らは CRVO の原因が神経線維、網膜中心動静脈が共有して強膜を貫く強膜篩状板と scleral ring での圧迫であると仮定し、RON によって同部位での減圧が可能であるとした。この報告を踏まえて、われわれはこの術式の効果を網膜循環の観点から評価した。[2] その結果、RON 単独では同部位の減圧効果は認められず、術後発生する網脈絡膜静脈吻合血管を介してうっ帯した静脈血が脈絡膜静脈系に流出することで減圧の効果があると考えている。

今回は同時期に RON を施行した症例の術後 6 か月の視力に影響する因子を統計学的に検討した。

A. 研究目的

CRVO に対する RON の術後視力に影響する因子を統計学的に明らかにすること。

B. 研究方法

対象は 2001 年 12 月から 2004 年 4 月までに CRVO 患者に対して RON を施行した 33 例 34 眼。男性 16 例、女性 17 例、年齢 43-83 歳 (平均 66.2 歳)、発症から手術までの期間は 1-9 か月 (平均 4.0 か月)、術前視力は手動弁-0.4、虚血型 18 眼、非虚血型 16 眼、術前後部硝子体剥離があったものは 20 眼であった。術終了時にトリアムシノロン後部テノン嚢下投与をしたものは 7 眼、硝子体内投与と後部テノン嚢下投与を両方施行したものが 12 眼であった。

手術は Opremcak の術式 [1]に従い core vitrectomy、後部硝子体剥離を作成後、視神経乳頭鼻側を microvitreoretinal blade または CRVO knife™ (Synergetics 社) で穿刺切開した。トリアムシノロンの投与は術終了時とした。

統計学的検討方法は RON 後 6 か月の視力を従属変数とし、矯正視力 0.2 以上を成功群、0.2 未満を不成功群とした。検討した因子は年齢、罹病期間、術前視力(0.1 以上)、虚血型か非虚血型か、術前後部硝子体剥離の有無、手術終了時のトリアムシノロン使用の有無とした。

(倫理面への配慮)

この治療の安全性、効果はまだ確立されていないため、十分な informed consent の後に施行した。

C. 研究結果

単解析による結果を表 1 に示した。術後視力獲得に有意に影響する因子は術前視力 0.1 以上だけであった(P=.003)。

	P
年齢	.823 *
罹病期間	.416 *
虚血	.080 **
後部硝子体剥離	.728 **
術前視力(0.1 以上)	.003 *
トリアムシノロン	.219 **

表 1　単解析

術後 6 か月の視力に有意に影響する因子は術前視力 0.1 以上だけであった(*P*=.003)。(* Mann-Whitney U 検定, ** カイ 2 乗検定)

単解析で p 値の小さかった術前視力、虚血型・非虚血型、トリアムシノロン使用の有無についてロジスティック重回帰分析を施行した(表 2)。ロジスティック重回帰分析においても術後視力獲得に有意に影響する因子は術前視力 0.1 以上だけであった(*P*=.0019 オッズ比 7.873)。

	有意確率	オッズ比	95% 信頼区間
術前視力	.019	7.873	.823
虚血	.295	0.401	.416
トリアムシノロン	.565	1.310	.728

表 2　ロジスティック重回帰分析

術後 6 か月の視力に有意に影響する因子は術前視力 0.1 以上だけであった(*P*=.019, オッズ比 7.873)。

D. 考察

CRVO の自然経過に関して Quinlan ら[3]は虚血型の 93%、非虚血型の 50%が 20/200 以下に、The Central Occlusion Study Group[4]は初診時視力の良好なものは(20/40 以上)最終的ほぼ同等の視力であるが、初診時 20/200 未満の症例では 80%が 20/200 未満になると報告している。

RON の視力予後に関しては、Opremcak ら[1]は術前 20/400 以下の 11 症例に RON を施行し、7 眼(73%)が術後 20/200 以上になったとしている。Garcia ら[5]は術前 20/125 以下の 14 症例に施行し 9 眼(64%)が 20/200 以上になっており、自然経過と比してよい傾向がある。われわれの症例でも非虚血型が半数程度含まれているが、術後 6 か月の時点で 20 眼(59%)が 20/200 以上になっており、自然経過よりもよい傾向があった。

今回、CRVO という疾患で術後比較的良好な視力を 0.2 に設定して術後 6 か月で 0.2 以上になる因子を検討したが、有意な因子は良好な術前視力(0.1 以上)なことだけであった。今回の検討では黄斑浮腫に有効とされる、ケナコルトの併用は術後 6 か月の視力には影響しなかった。

E. 結論

RON 後 6 か月の時点で比較的良好な視力(0.2 以上)の獲得に関与する因子は比較的良好な術前視力(0.1 以上)だけであった。

F. 健康危険情報

なし

G. 研究発表

1. 論文発表

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Ｈ．知的財産権の出願・登録状況

１．特許取得

なし

２．実用新案登録

なし

３．その他

なし

Ｉ．参考文献

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Evaluation of Radial Optic Neurotomy for Central Retinal Vein Occlusion by Indocyanine Green Videoangiography and Image Analysis

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• PURPOSE: To evaluate the effects of radial optic neurotomy (RON) on retinal circulation in patients with central retinal vein occlusion (CRVO) by indocyanine green (ICG) videoangiography and a computer-assisted image analysis.

• DESIGN: An interventional case series.

• METHODS: RON was performed in 15 eyes of 15 patients with CRVO. Within 72 hours before the surgery and at 3 months after the surgery, ICG videoangiography was performed with a scanning laser ophthalmoscope, and the images were transferred to a computer. Two measurement points were selected, one on a main retinal artery close to the optic disk and the other on the corresponding retinal vein. At each point, fluorescence intensities were serially measured, and dye dilution curves were obtained. Retinal circulation times (ΔT_{50}) before and after the surgery were calculated.

• RESULTS: Mean preoperative ΔT_{50} was 6.46 ± 1.36 seconds, and mean postoperative ΔT_{50} was 6.80 ± 2.50 seconds. In 8 of 15 eyes, T_{50} decreased by 6.8% to 29.6% after the surgery. In the seven eyes that developed chorioretinal anastomosis (CRA) at the site of RON, ΔT_{50} decreased after the surgery. In contrast, ΔT_{50} decreased postoperatively in only one of the eight eyes without CRA. Best-corrected visual acuity improved significantly after the surgery in the group of eyes with improvement in ΔT_{50}, but not in the group of eyes without improvement inΔT_{50}.

• CONCLUSIONS: Some degree of retinal circulation improvement occurred in approximately half of these eyes, which appears to be correlated with the development of CRA. (Am J Ophthalmol 2004;138:612–619. © 2004 by Elsevier Inc. All rights reserved.)

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CENTRAL RETINAL VEIN OCCLUSION (CRVO) IS A common retinal vascular disease thought to be caused by thrombus formation in the central retinal vein at the level of the lamina cribrosa.[1] CRVO may lead to severe visual loss because of extensive retinal hemorrhage and edema. The Central Retinal Vein Occlusion Study reported the natural history and visual prognosis of CRVO.[2] In 80% of the eyes with initial visual acuity less than 20/200, visual acuity was unchanged or decreased at the final visit. Eyes with intermediate visual acuity of 20/50 to 20/200 at the initial visit showed only a 19% rate of visual improvement.

Although pan-retinal laser photocoagulation prevents iris neovascularization and grid macular laser photocoagulation decreases macular edema without visual improvement for patients with CRVO, there is no proven treatment that decreases retinal hemorrhage and edema and offers improvement in visual acuity. Several therapies for CRVO, such as tissue plasminogen activator injection into vitreous cavity[3] or directly into major retinal vein,[4] lamina puncture,[5] and intravitreal triamcinolone acetonide,[6] have been proved ineffective in improving the perfusion in the retinal vein with visual improvement. Although laser-induced chorioretinal venous anastomosis[7–9] and surgical-induced chorioretinal anastomosis[10,11] can improve retinal circulation, they may cause severe complications such as vitreous hemorrhage or choroidal neovascularization.

In 2001, Opremcak and associates[12] reported a new surgical procedure for CRVO, radial optic neurotomy

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(RON). They hypothesized that increased pressure within the confined scleral outlet at the optic disk might compress the lumen of the central retinal vein (CRV) and result in occlusion of the CRV in eyes with CRVO. Based on this hypothesis, they performed RON to decompress the scleral outlet via a vitreoretinal approach. If RON alleviates the compartment syndrome that leads to occlusion of the central retinal vein, the perfusion in the retinal vein may improve after surgery. Moreover, the postoperative development of chorioretinal anastomosis (CRA)[13,14] may increase retinal venous outflow. Although several studies on RON have been reported,[12–17] there have been no quantitative studies on changes in retinal circulation after RON. Thus, we quantitatively studied changes in retinal circulation after RON by using indocyanine green (ICG) videoangiography and a computer-assisted image analysis and evaluated the effects of RON on retinal circulation.

METHODS

BETWEEN APRIL 2002 AND MAY 2003, 15 EYES OF 15 PATIENTS with CRVO underwent pars plana vitrectomy with RON at the Kagawa University Hospital. All patients met the following criteria: 1) onset of CRVO less than 12 months; 2) presence of retinal edema and hemorrhages in the macula; 3) initial visual acuity worse than 0.5; 4) absence of CRA identified by biomicroscopic slit-lamp examination, fluorescein angiography, or ICG videoangiography; and 5) willingness to sign informed consent after appropriate explanation of the procedure.

Based on preoperative fluorescein angiograms, we classified eyes as ischemic or nonischemic, as described previously.[2] Eyes with at least 10 disk areas of capillary nonperfusion were categorized as ischemic type.

After a standard three-port pars plana vitrectomy with removal of the posterior hyaloid, RON was performed on the nasal side of the optic disk using 20-gauge microvitreoretinal blade or CRVO knife (Synergetics, St. Charles, Missouri, USA). During and after RON, infusion pressure was increased to avoid bleeding.

ICG videoangiography was performed with a scanning laser ophthalmoscope (Rodenstock Instrument, Munich, Germany) using a diode laser (wave length, 810 nm) within 72 hours before surgery and at 3 months after surgery. Twenty-five mg of indocyanine green (Ophthagreen, Santen, Tokyo, Japan) was dissolved in 1-ml distilled water. The ICG dye was flushed with 10-ml physiologic saline to ensure that the ICG would reach the heart and the eye with as little dye dilution as possible, allowing sharp dye-dilution curves to be obtained.[18] Images were recorded serially (30 frames per second) on S-VHS videotapes. The images were captured with an analog-digital converter board (Dig98; Direct, Tokyo, Japan) and loaded into a computer (PC9821Xa; NEC, Tokyo, Japan). In the superior and inferior region around the optic disk, two pairs of two measurement points were selected, one on a major retinal artery and the other on the corresponding major retinal vein (Figure 1). To minimize the distortion of dilution curves due to spatial distribution and time variation of fluorescence, the fluorescence intensity was collected with a round configuration with a diameter slightly larger than the diameter of the venule.[19] When established measurement points moved because of ocular movement, their points were manually corrected for each frame.

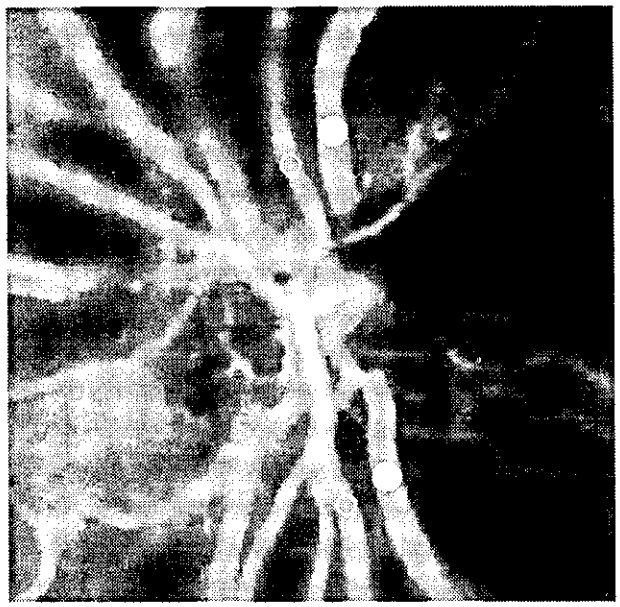

FIGURE 1. Measurement points on indocyanine green videoangiograms. Two points were selected in the temposuperior region and tempoinferior region, one on a main retinal artery close to the optic disk (closed circle) and the other on the corresponding main retinal vein close to the optic disk (open circle).

Fluorescence intensity at each point in each frame (I) was plotted on the ordinate, and time (T) on the abscissa. Using a least-square method computer program, the data were regressed to the following theoretical function, and typical dye dilution curves (time-intensity curves) were obtained.

$$I = K + I_p\mathrm{EXP}[-\alpha\{\log(T - T_0/T_p - T_0)^2\}]$$

K = background intensities before appearance of the dye in blood vessels, Ip = peak fluorescence intensities, EXP = exponent with e as the base, α = coefficients, T_0 = times at the beginning of the regression curves, and Tp = times at which peak intensities were reached.

To determine the differences in fluorescence intensity between the systolic and diastolic phase, the robust estimation method was applied to measurement values.[20]

We calculated the time (T_{50}) from the beginning to 50% of the peak intensity on the ascending part of the dye

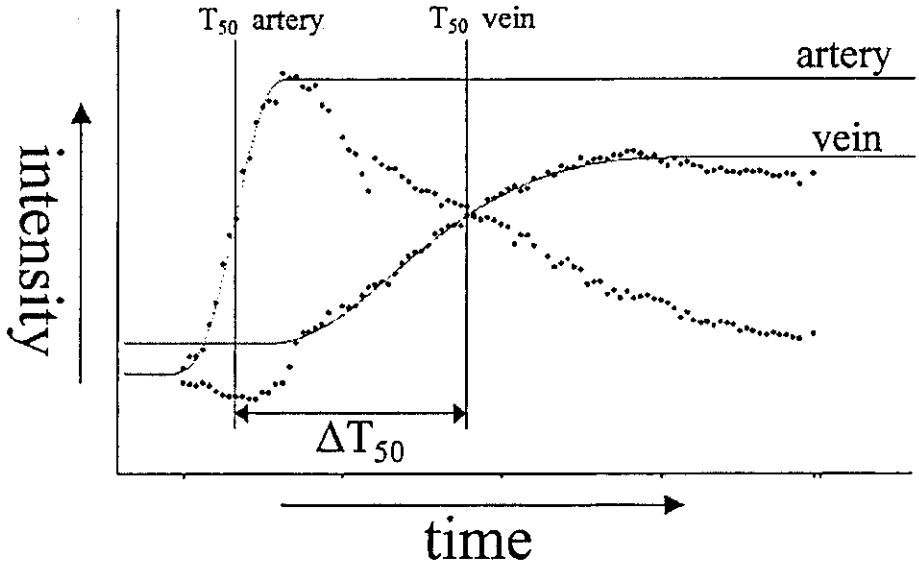

FIGURE 2. Dye dilution curves at the two points. The circulation time (T_{50}) from the beginning of filling to 50% of the peak on the ascending part of dye dilution curves was calculated, and the time difference (ΔT_{50}) between T_{50} at the point on a main retinal artery and that at the point on the corresponding main retinal vein was obtained.

dilution curves. T_{50} showed the highest reproducibility in the measurement of retinal circulation times in the dye dilution technique.[18] The time difference (ΔT_{50}) between T_{50} at the measurement point on the major artery and T_{50} at the measurement point on the corresponding major vein was calculated (Figure 2), representing a retinal circulation time in each region.

RESULTS

PATIENT DATA ARE SHOWN IN TABLE 1. PATIENT AGE ranged from 49 to 79 years (median, 63 years). Of the 15 patients, 6 were men and 9 were women. Onset of CRVO before RON varied from 1 to 9 months (median, 4 months). Seven eyes were classified as nonischemic and 8 as ischemic. Pan-retinal laser photocoagulation had already been performed in 4 eyes with ischemic CRVO, and grid macular laser photocoagulation was not performed in any eye. In 9 eyes, posterior vitreous detachment was present before surgery. Follow-up period ranged from 4 to 14 months (median, 6 months).

Because no retinal breaks occurred during the surgery, intraocular gas was not injected in any eye. In two eyes (patients 3 and 15), a small amount of subretinal hemorrhage occurred around the site of the RON during the surgery, which was spontaneously absorbed by 2 months postsurgery. In four eyes, the enlargement of retinal nonperfusion areas was seen on fluorescein angiography taken at 3 months after the surgery, and pan-retinal laser photocoagulation was performed. One eye (patient 8) developed minimal anterior segment neovascularization without elevation of intraocular pressure.

In seven of 15 eyes, CRAs developed at the site of RON between 1 and 3 months after surgery. Six (86%) of 7 eyes that developed CRA were preoperatively classified as nonischemic type.

The ΔT_{50} is shown in Table 2. In the temposuperior region, mean preoperative ΔT_{50} was 6.15 ± 1.29 seconds (mean ± SD), and mean postoperative ΔT_{50} was 6.78 ± 2.40 seconds. In the tempoinferior region, mean preoperative ΔT_{50} was 6.76 ± 1.59 seconds, and mean postoperative ΔT_{50} was 6.82 ± 2.69 seconds. The change in ΔT_{50} in the temposuperior region was similar to that in the tempoinferior region (Table 2). In eight of 15 eyes, the mean of ΔT_{50} in the temposuperior region and that in the tempoinferior region decreased by 6.8% to 29.6% after the surgery. In all 7 eyes that developed CRA at the site of the neurotomy, mean ΔT_{50} decreased after the surgery, compared with only 1 of the remaining 8 eyes without CRA. ICG videoangiography showed that the ICG dye in the retinal vein flowed into the choroidal vein through CRA (Figure 3). In the 7 eyes with CRA, mean preoperative ΔT_{50} was 6.17 ± 1.37 seconds compared with postoperative ΔT_{50} of 5.28 ± 1.06 seconds, which was a statistically significant difference (paired t test, P = .0087; Figure 4). In contrast, in 8 eyes without CRAs, mean preoperative ΔT_{50} was 6.71 ± 1.40 seconds, compared with postoperative ΔT_{50} of 8.14 ± 2.67 seconds, which was not statistically significant (paired t test, P = .125) (Figure 4).

In 15 age-matched eyes diagnosed as age-related macular degeneration without retinal vascular abnormalities, ΔT_{50} was measured in the temposuperior region and the tem-

TABLE 1. Clinical Characteristics and Preoperative and Final Visual Acuity After Radial Optic Neurotomy

Patient	Age	Sex	Duration (months)*	Type	PVD	PRP	VA	
							Pre	Final
1	77	F	5	Ischemic	+	Pre	0.07	0.09
2	77	F	2	Nonischemic	+	—	0.2	0.2
3	62	M	6	Nonischemic	+	—	0.04	0.09
4	62	F	9	Ischemic	+	Pre	0.02	0.04
5	60	F	9	Ischemic	+	Post	0.01	0.1
6	62	F	6	Nonischemic	+	—	0.1	0.1
7	63	M	8	Ischemic	−	Post	0.3	0.15
8	68	F	4	Ischemic	−	Pre	0.01	0.01
9	72	M	4	Nonischemic	+	—	0.3	0.3
10	56	F	9	Nonischemic	−	—	0.2	0.4
11	55	F	2	Nonischemic	−	—	0.07	0.1
12	49	M	4	Nonischemic	+	—	0.2	0.8
13	68	M	4	Ischemic	−	—	0.01	0.05
14	66	F	1	Ischemic	−	Post	0.02	0.05
15	79	M	1	Ischemic	+	Pre	0.03	0.3

F = female; M = male; pre = before surgery; post = after surgery; PRP = pan-retinal laser photocoagulation; PVD = posterior vitreous detachment before surgery; VA = best-corrected visual acuity.

*Duration (month) = duration from the onset of visual impairment to surgery.

TABLE 2. Changes in Retinal Circulation Times (ΔT_{50}) and Development of Chorioretinal Anastomosis After Radial Optic Neurotomy

Patient	Temposuperior		Tempoinferior		Mean		% Change	CRA
	Pre	Post	Pre	Post	Pre	Post		
1	5.49	6.38	5.08	5.07	5.29	5.73	8.3	−
2	5.50	5.08	5.60	5.07	5.55	5.08	−8.5	+
3	8.10	6.92	8.54	5.73	8.32	6.33	−24.0	+
4	7.48	12.8	8.97	13.8	8.23	13.30	61.7	−
5	5.19	4.99	5.03	4.24	5.11	4.62	−9.7	+
6	5.10	5.70	5.12	5.97	5.11	5.84	14.2	−
7	5.87	8.64	6.02	6.96	5.95	7.80	31.2	−
8	5.86	10.47	7.97	10.81	6.92	10.64	53.9	−
9	7.41	7.28	7.93	7.02	7.67	7.15	−6.8	+
10	5.54	4.91	6.37	4.30	5.96	4.61	−22.7	+
11	4.57	4.10	4.44	4.29	4.51	4.20	−6.9	+
12	5.97	4.56	6.20	5.37	6.09	4.97	−18.4	+
13	9.14	5.89	8.87	6.79	9.01	6.34	−29.6	−
14	5.14	5.77	6.65	7.52	5.90	6.65	12.7	−
15	5.88	8.22	8.69	9.40	7.29	8.81	20.9	−

Mean = the mean of ΔT_{50} (seconds) in the temposuperior region and ΔT_{50} (seconds) in the tempoinferior region.

CRA = chorioretinal anastomosis; pre = ΔT_{50} (seconds) before surgery; post = ΔT_{50} (seconds) after surgery.

poinferior region using the same method. The mean of ΔT_{50} in the temposuperior region and that in the tempoinferior region was 4.17 ± 0.55 seconds (mean ± SD).

Preoperative best-corrected visual acuity ranged from 0.01 to 0.3 (logarithm of the minimum angle of resolution [logMAR], 0.52 to 2.00) with a mean of 0.11 (logMAR,

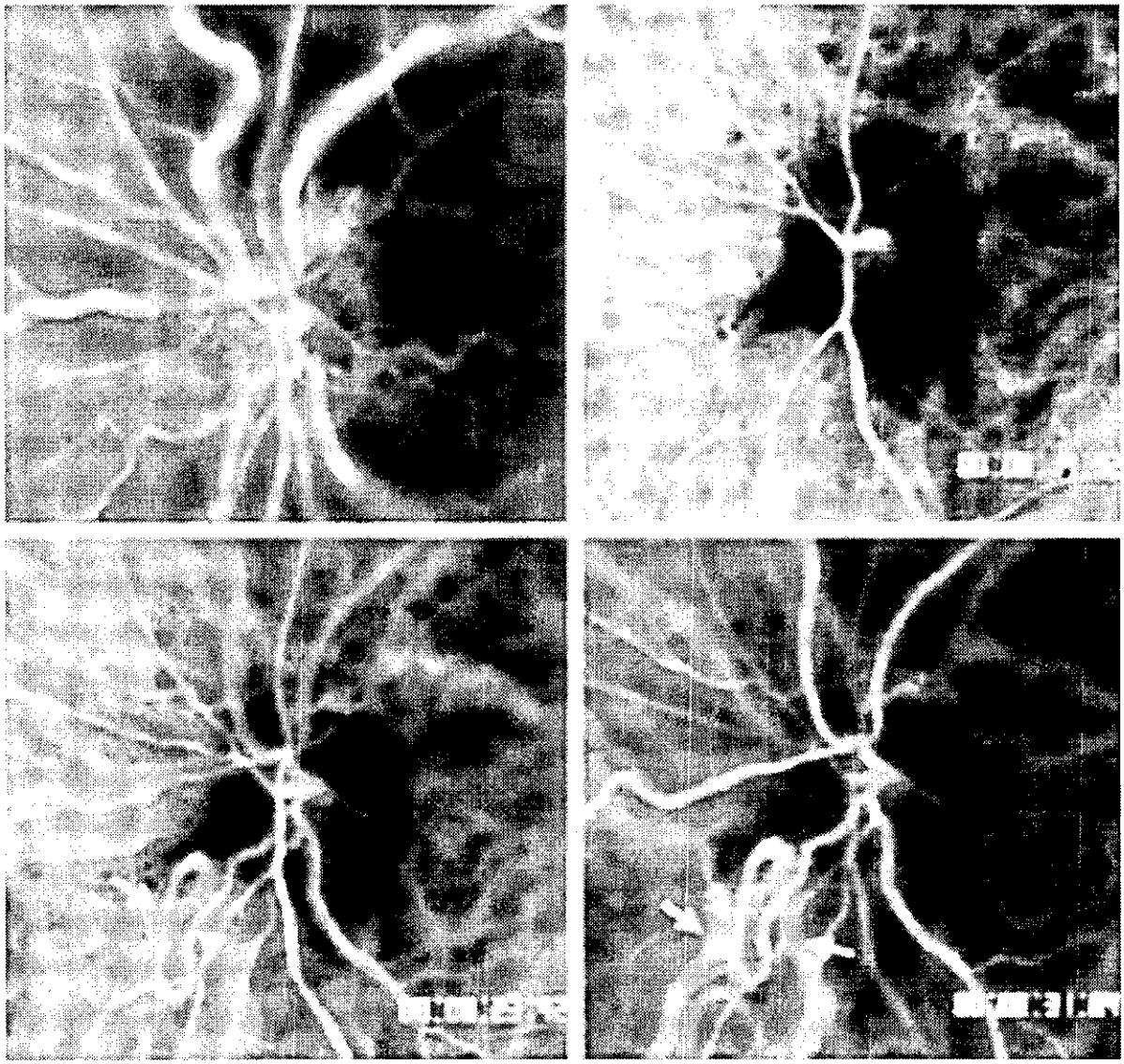

FIGURE 3. Patient 5: Indocyanine green angiography, taken 72 hours before and 3 months after radial optic neurotomy (RON), demonstrates the development of chorioretinal anastomosis after RON. (Top left) Preoperative angiography: no chorioretinal shunt vessel is seen. (Top right) Arterial phase of postoperative angiography. The site of radial optic neurotomy (arrow) shows hypofluorescence. (Bottom left) Arteriovenous phase of postoperative angiography. A chorioretinal shunt vessel (arrow) connects with a retinal vein (an arrowhead). (Bottom right) Venous phase of postoperative angiography. Choroidal veins (arrows) connect with the retinal vein through the chorioretinal shunt vessel at the site of RON.

1.25), whereas the final best-corrected visual acuity ranged from 0.01 to 0.8 (logMAR, 0.10 to 2.00) with a mean of 0.19 (logMAR, 0.94). Although the difference between the preoperative visual acuity and the final visual acuity was not statistically significant (paired t test, $P = .073$), 10 (67%) of 15 eyes improved by 2 or more lines. In 8 eyes showing the decrease in ΔT_{50}, preoperative logMAR visual acuity was 1.15 ± 0.60 (mean ± SD) compared with 0.75 ± 0.40 postoperatively, which was a statistically significant difference (paired t test, $P = .017$). In the remaining 7 eyes without the decrease in ΔT_{50}, preoperative logMAR visual acuity was 1.37 ± 0.51 compared with 1.16 ± 0.47 postoperatively, which was not a statistically significant difference (paired t test, $P = .218$).

DISCUSSION

IT IS WELL KNOWN THAT CRA (RETINOCILIARY OR OPTOCILIARY SHUNTS VESSELS) may develop spontaneously after CRVO. Quinlan and associates[21] noted that CRAs developed in 80 (48%) of 168 eyes with CRVO, and Fuller and associates[22] described CRAs in 49 (46%) of 107 eyes. Development of CRAs may prevent anterior segment

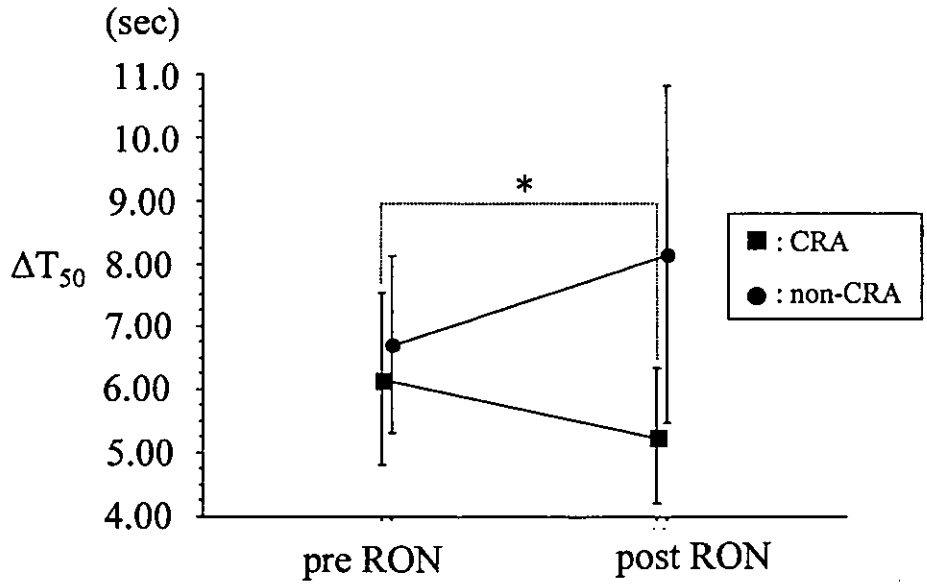

FIGURE 4. Changes in mean retinal circulation times (ΔT_{50}; mean ± SD) between before (pre-RON) and after (post-RON) radial optic neurotomy (RON) in eyes with (CRA) and without (non-CRA) development of development of chorioretinal anastomosis (CRA). There was a significant difference in eyes that developed CRA (* $P = .0087$, paired t test).

neovascularization after CRVO. Conversely, Friedman and associates[13] reported two cases that developed optociliary venous anastomosis after RON. Garciia-Arumii and associates[14] reported that six (42.9%) of 14 patients developed CRA between 3 weeks and 3 months after RON. In our study, new CRAs developed at the neurotomy site between 1 and 3 months after surgery in 7 (47%) of 15 eyes. Although eyes that had spontaneously developed CRAs before the initial visit were excluded from our study, the incidence of CRAs after RON is similar to that of spontaneously developed CRAs. However, RON may cause CRAs earlier than in the natural course of CRVO, leading to improvement in retinal circulation with resolution of retinal edema and hemorrhage occurring before irreversible severe damage to the retina.

According to Opremcak and associates,[12] the purpose of RON is to promote decompression of the central retinal vein in the scleral ring and the lamina cribrosa. If RON can relax venous compression within the scleral outlet, retinal circulation time can be reduced after the procedure. In our study, ΔT_{50} did not decrease after RON in most of the eyes without postoperative CRAs. This suggests that RON may not decompress the central retinal vein within the scleral outlet. In contrast, ΔT_{50} decreased postoperatively in all eyes that developed CRAs in our study. Takahashi and associates[23] noted that ICG dye flow in the retinal veins entered the choroidal veins via spontaneously developed CRAs and drained into the vortex veins on ICG videoangiography in CRVO patients. Okamoto and associates[24] reported that spontaneous CRAs in CRVO shortened retinal circulation time, with recovery to normal demonstrated on fluorescein angiograms. These results suggest that the improvement in retinal circulation after RON may be the result of postoperative CRA development. Mean ΔT_{50} of 15 age-matched eyes with age-related macular degeneration was 4.17 ± 0.55 seconds (mean ± SD), and mean postoperative ΔT_{50} in the 7 eyes with CRA development was 5.28 ± 1.06 seconds. This suggests that the retinal circulation did not recover to normal, even if CRAs developed after RON.

The preoperative ΔT_{50} in the group with postoperative CRAs was less than that in the group without postoperative CRAs. Six (86%) of the seven eyes in the CRA group had nonischemic CRVO, and one (13%) of the eight eyes in non-CRA group had nonischemic CRVO. This may explain the difference in the preoperative ΔT_{50} between both groups. Friedman and associates[13] reported that two patients who developed CRAs after the RON were classified as nonischemic. Garcia-Arumi and associates[14] reported that five (83%) of six eyes that developed CRAs were classified as nonischemic CRVO. CRA may develop more frequently in nonischemic CRVO than in ischemic CRVO, but the mechanism of this process is unknown.

In only one (Patient 13) of eight patients without CRAs, ΔT_{50} was shortened after RON. This change may be due to decompression by RON or spontaneous improvement. Considering that ΔT_{50} increased in most of the eyes without CRA, RON may be harmful to the retinal circulation in eyes with no postoperative CRAs. Further studies with larger sample sizes are needed to determine whether RON without postoperative CRA development is harmful.

The videoangiography and dye dilution method has been used widely in studies on retinal circulation.[18,25–30] Because ΔT_{50} shows the highest reproducibility as a

parameter to evaluate the mean retinal circulation time using the dye dilution method[18] and has been used in several studies on ocular circulation,[26,29,30] we measured this retinal circulation time and used it as a parameter to evaluate the effect of RON on retinal circulation. In fluorescein angiography, papilloedema and retinal hemorrhage and edema block fluorescence intensities in major retinal vessels. In contrast, ICG angiographic images of retinal vessels are influenced much less by papilloedema, retinal hemorrhage, and retinal edema. We thus used ICG videoangiography for the measurement of retinal circulation times.

To assess the difference in retinal circulation between the superior region and the inferior region, the measurement points were selected in both the temposuperior and tempoinferior regions. There was no difference in ΔT_{50} between two regions. Thus, we assessed changes in retinal circulation with the mean of ΔT_{50} in the temposuperior region and that in the tempoinferior region.

In the original report by Opremcak and associates,[12] best-corrected visual acuity improved in eight (73%) of 11 eyes with a mean gain of 5 Snellen lines. In our study, best-corrected visual acuity improved in 10 (67%) of 15 eyes with a mean gain of 4.7 Snellen lines. Garciia-Arumii and associates[14] described that the median postoperative visual acuity was better in eyes with newly formed CRAs than in the remaining eyes without them (20/60 vs 20/110). In our study, the mean postoperative logMAR visual acuity in the group with CRA was better than that in the group without CRA (0.68 vs 1.17). There was a statistically significant difference between preoperative and postoperative logMAR visual acuity in the 8 eyes that showed shortening in retinal circulation times (ΔT_{50}), and there was no significant difference between them in the remaining 7 eyes without reduced retinal circulation times. These results suggest that the development of CRAs may lead to improvement in retinal circulation and result in visual improvement after RON. Methods to increase the incidence of CRA, such as the surgery at an early stage of the disease or pleural radial cuts on the nasal aspect of the optic disk, should be considered.

Regarding postoperative complications, peripapillary retinal detachment extending from the RON site has been reported.[15] We had no severe complications such as retinal detachment, laceration of major retinal and optic vessels, or postoperative vitreous hemorrhage. The only complication that we experienced was a small subretinal hemorrhage located nasally to the optic disk in 2 eyes, but this disappeared spontaneously within 2 months after surgery.

In conclusion, some degree of improvement in retinal circulation after RON occurred in approximately half of our patients, which appears to correlate with the postoperative development of CRA. RON does not appear to decompress the central retinal vein directly. Further research, including randomized controlled studies, are needed to confirm the effect of RON on anatomic and functional improvement.

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Evaluation of Arteriovenous Crossing Sheathotomy for Branch Retinal Vein Occlusion by Fluorescein Videoangiography and Image Analysis

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• PURPOSE: We quantitatively evaluated the effects of arteriovenous (A/V) crossing sheathotomy on retinal circulation in patients with branch retinal vein occlusion (BRVO) accompanied by macular edema.
• DESIGN: Interventional case series.
• METHODS: In 18 consecutive patients (18 eyes) with BRVO accompanied by macular edema who underwent A/V crossing sheathotomy between August 1999 and April 2002, changes in retinal circulation after the surgery were evaluated by fluorescein videoangiography with a scanning laser ophthalmoscope and by image analysis using dye dilution technique. At a venule distal to the responsible A/V crossing site and a normal venule, the circulation time (T50) from the beginning of filling to 50% filling of the peak intensity was calculated. The time difference (ΔT50) between T50 at the point on the affected venule and that at the point on the normal venule, which represents the filling delay at the venule distal to the A/V crossing site, was compared between before and early after the surgery.
• RESULTS: The preoperative ΔT50 was 1.36 ± 1.15 seconds (mean ± SD), and the postoperative ΔT50 was 0.72 ± 0.77 seconds ($P = .035$, paired t test). In 11 of the 18 eyes, ΔT50 decreased by 20% or more after the surgery. In the other 7 eyes, ΔT50 was unchanged or slightly increased after the surgery.
• CONCLUSIONS: Although a randomized controlled study is needed to confirm the effectiveness of A/V crossing sheathotomy on visual function, this technique could be effective for improving the delay in perfusion in the affected venule. (Am J Ophthalmol 2004;137: 834–841. © 2004 by Elsevier Inc. All rights reserved.)

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MACULAR EDEMA IN BRANCH RETINAL VEIN OCclusion is considered to be caused by circulatory impairment in the arterial system due to stagnation of venous blood resulting from venous compression at an arteriovenous (A/V) crossing site.[1] Release of venous compression at the A/V crossing site may be effective for improving macular edema. Indeed, Opremcak and associates[2] reported the effectiveness of A/V crossing sheathotomy for decreasing macular edema and hemorrhage and improving visual acuity. However, improvement in macular edema and visual acuity is often encountered in the natural course and is observed after laser photocoagulation or vitrectomy.[3–6] Therefore, to confirm the effectiveness of A/V crossing sheathotomy, improvement in retinal circulation should be clarified early after this technique. Opremcak and associates[2] reported improvement in venous perfusion during the operation and also improvement in findings of fluorescein angiography but did not quantitatively evaluate the improvement in the perfusion. There have been no studies that quantitatively evaluated improvement in circulation so far. Therefore, the effectiveness of this technique for improving venous perfusion early after operation has not been demonstrated. Thus, we quantitatively studied improvement in the delay in perfusion in the occluded venule after A/V crossing sheathotomy using fluorescein videoangiography and an image analysis.

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METHODS

THE SUBJECTS WERE 18 CONSECUTIVE PATIENTS (18 EYES) consisting of seven males and 11 females with BRVO accompanied by macular edema who underwent vitreous surgery with A/V crossing sheathotomy at the Okayama University Hospital between August 1999 and April 2002. All patients enrolled gave informed consent. The 18 eyes met the following criteria: 1) presence of blood flow (including backflow) observed in venules proximal to the A/V crossing site by preoperative fluorescein videoangiography, 2) preoperative best-corrected visual acuity of 0.5 or worse, 3) absence of apparent collateral circulation, and 4) dilation and tortuosity of venules distal to the A/V crossing site. The mean age of the patients was 63.3 years, with a range of 47 to 84 years.

Three-port pars plana vitrectomy was performed, and the posterior vitreous cortex was removed. An incision was made using a bent microvitreoretinal blade (Alcon Laboratory, Fort Worth, Texas) at the vicinity of the responsible A/V crossing site, which was identified using fluorescein videoangiography. The incision was continued parallel to and slightly under the retinal arteriole with a gentle lifting motion until the A/V crossing site was encountered. The purpose of the operation was the separation of the arteriole from the venule at the responsible A/V crossing site.

• QUANTIFICATION OF DELAY IN PERFUSION: *Fluorescein Videoangiography* Within 72 hours before the surgery and within 7 days after the surgery, fluorescein videoangiography was performed with a scanning laser ophthalmoscope (SLO, Rodenstock Instrument, Munich, Germany) using argon blue (wavelength 488 nm), and serial images (30 frames/second) were recorded on S-VHS videotapes. The gain was set at 7, and early phase of the angiography was observed with a 40-degree field size. Five ml of 10% fluorescein sodium (Alcon, Fort Worth, Texas) was injected into the antecubital vein. To more sharply obtain an ascending part of the dye dilution curve, this solution was pushed into the antecubital vein by flash of 10 ml saline so that a bolus of ICG dye could reach the ocular fundus.

Image Analysis Obtained fluorescein videoangiographic images were captured with an analog–digital converter board (Dig98; Ditect, Tokyo, Japan) loaded into a computer (PC9821Xa; NEC, Tokyo, Japan). Two measurement points were selected, one on a venule distal to the responsible A/V crossing site and the other on a normal venule, so that their distances from the optic disk become similar (Figure 1, A). At each site, fluorescence intensities were serially measured. To minimize the distortion of dilution curves due to spatial distribution and time variation of fluorescein, the fluorescent intensity was collected with a round configuration with a diameter slightly larger than the diameter of the venule.[7] When established measurement points moved due to ocular movements, the position was manually corrected. The upper limit of measurement intensities was 255 pixels, and there was no case in which the intensity exceeded this value.

Fluorescence intensity at each point in each frame (I) was plotted on the ordinate, and time (t) on the abscissa. With a program of least-square fitting running on the computer, the data were regressed to the following theoretical function, and typical dye dilution curves were obtained.

$$I = K + IpEXP[- \alpha\{\log(T - To/Tp - To)2\}$$

K = Background intensities before appearance of the dye in blood vessels;
Ip = Peak fluorescence intensities;
α = Coefficients;
To = Times at the beginning of the regression curves;
Tp = Times at which peak intensities were reached;
EXP = Exponent with *e* as the base.

With respect to differences in fluorescence intensity between the systolic and diastolic phase, a robust estimation method was applied to measurement values.[8]

In the dye dilution method, because the circulation time (T50) from the baseline of the ascending part of the dye dilution curve to 50% of the peak has the highest reproducibility among circulation time parameters,[9] the time difference (ΔT50) between T50 at the normal site and that at the point distal to the A/V crossing site was calculated (Figure 1, B), and delay in venular perfusion was compared between before and after the surgery.

RESULTS

THE DATA ON ALL EYES ARE SHOWN IN TABLE 1.

The duration from the onset of visual impairment due to BRVO to surgery was 2 to 9 months (mean, 4.2 months). Posterior vitreous detachment was already present before the operation in two eyes. In all eyes, the arteriole could be separated from the venule at the responsible A/V crossing site. In one eye, hemorrhage due to retinal vascular damage was observed during A/V crossing sheathotomy but could be immediately stopped by high perfusion pressure. No severe intra- and postoperative complications, such as vascular rupture, vitreous hemorrhage, or retinal detachment, were observed.

The mean preoperative ΔT50 was 1.36 ± 1.15 seconds (mean ± SD), and the mean postoperative ΔT50 was 0.72 ± 0.77 seconds. There was a significant difference (P = .035, paired t test) between them. In 11 of the 18 eyes, ΔT50 decreased by 20% or more after the surgery. Five of the 11 eyes showed recovery to an almost normal state (Figures 2, 3). However, ΔT50 was unchanged or slightly

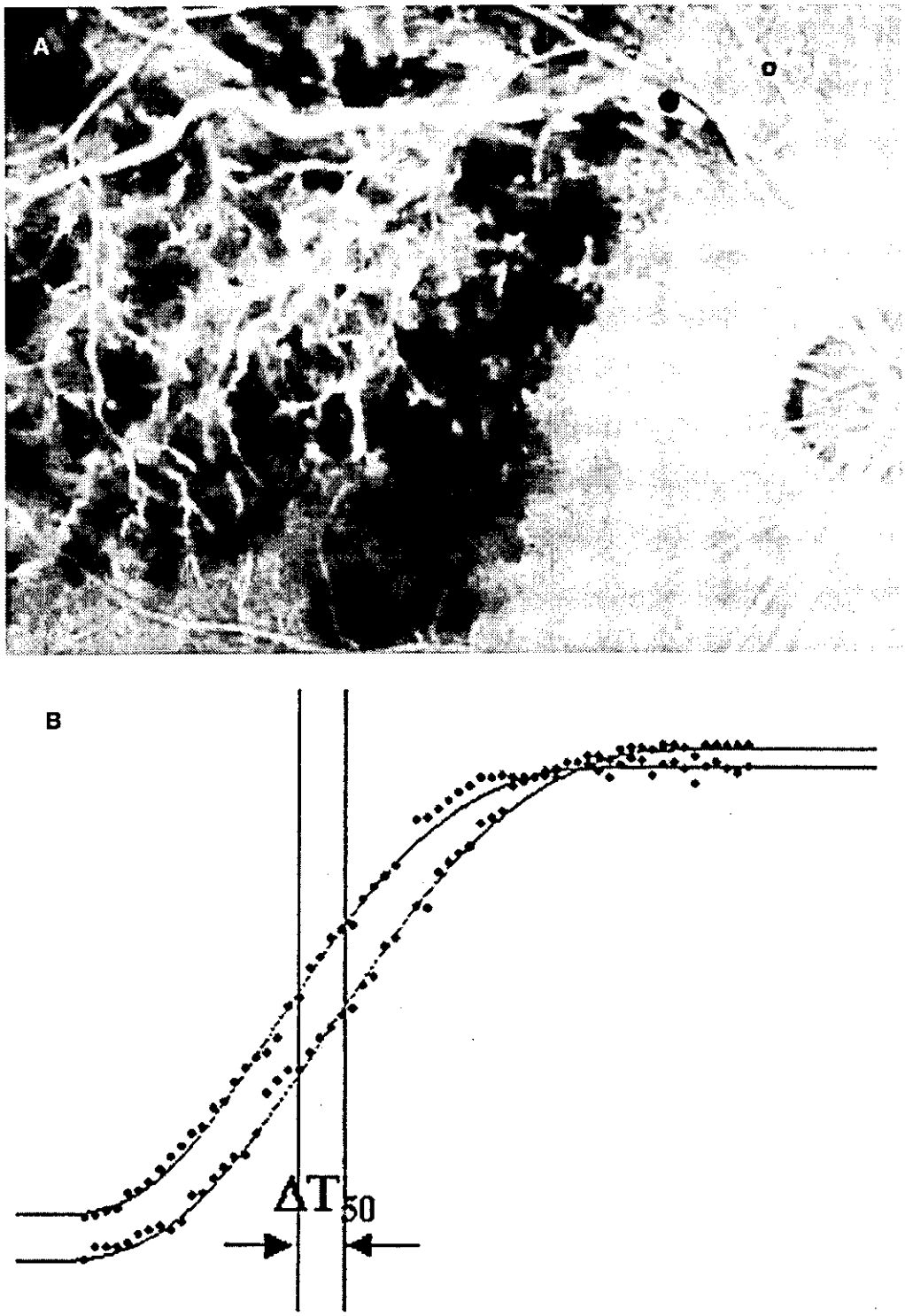

FIGURE 1. (A) Measurement points on fluorescein videoangiograms. Two points were established, one on a venule distal to the responsible arteriovenous crossing site (closed circle) and the other on a normal venule (open circle). (B) Dye dilution curves at the two points. The circulation time (T50) from the beginning of filling to 50% filling of the peak was calculated, and the time difference (ΔT50) between T50 at the point on the affected venule (red) and that at the point on the normal venule (blue) was obtained.