AMERICAN JOURNAL OF OPHTHALMOLOGY®

VOLUME 98 NUMBER 3 SEPTEMBER, 1984

ARGON LASER PHOTOCOAGULATION FOR MACULAR EDEMA IN BRANCH VEIN OCCLUSION

THE BRANCH VEIN OCCLUSION STUDY GROUP

The Branch Vein Occlusion Study is a multi-center, randomized, controlled clinical trial designed to answer several questions regarding the management of complications of branch vein occlusion. This report discusses the question, "Is argon laser photocoagulation useful in improving visual acuity in eyes with branch vein occlusion and macular edema reducing vision to 20/40 or worse?" One hundred thirty-nine eligible eyes were assigned randomly to either a treated or an untreated control group. Comparing treated patients to control patients (mean follow-up 3.1 years for all study eyes), the gain of at least two lines of visual acuity from baseline maintained for two consecutive visits was significantly greater in treated eyes (P = .00049, logrank test). Because of this improvement in visual acuity with argon laser photocoagulation of macular edema from branch vein occlusion, we recommend laser photocoagulation for patients with macular edema associated with branch vein occlusion who meet the eligibility criteria of this study.

Retinal branch vein occlusion is a frequent retinal vascular abnormality; from a review of diagnoses for all new patients seen at the Wilmer Institute participating clinic, it is second only to diabetic retinopathy in the frequency with which it produces retinal vascular abnormality. The increasing use of photocoagulation therapy in the late 1960s and early 1970s, along with the increasing expertise in fluorescein angiography, aided recognition of the disease, study of the nature and course, and small trials of photocoagulation therapy for the complications of macular edema and neovascularization, as reviewed in 1978.[1] From these important studies, it became evident that many patients without laser photocoagulation did not develop visual loss from macular edema or neovascularization, increasing the difficulties of evaluating photocoagu-

Accepted for publication July 20, 1984.

For a list of participants in the Branch Vein Occlusion Study see pages 281 and 282.

This study is supported by grants EY02466, EY02467, EY02468, EY02469, EY02470, EY02471, and EY01765 from the National Eye Institute.

Reprint requests to Branch Vein Occlusion Study Coordinating Center, 550 N. Broadway, Suite 301, Baltimore, MD 21205.

lation therapy effect. Consequently, it became clear that a prospective, randomized, controlled clinical trial was required to answer questions of treatment efficacy.

The Branch Vein Occlusion Study is a multi-center, randomized, controlled clinical trial sponsored by the National Eye Institute, Bethesda, Maryland. The Branch Vein Occlusion Study was designed to answer three questions regarding complications of branch vein occlusion:

1. Can photocoagulation prevent the development of neovascularization?
2. Can photocoagulation prevent vitreous hemorrhage?
3. Can photocoagulation improve visual acuity in eyes with macular edema reducing vision to 20/40 or worse?

To answer these three questions, four separate groupings of branch vein occlusions were recruited:

Group I—(Eyes at risk for the development of neovascularization)

Recent (three to 18 months since onset) branch vein occlusion involving a retinal area at least 5 disk diameters in diameter, with no neovascularization present. Eyes in this group were randomized either to "scatter" laser photocoagulation or to no laser treatment. These Group I eyes were recruited, randomized, and followed up to answer question No. 1, "Can photocoagulation prevent the development of neovascularization?"

Group II—(Eyes at risk for the development of vitreous hemorrhage)

Recent (three to 18 months since onset) branch vein occlusion with retinal neovascularization present. Eyes in this group were randomized either to "scatter" laser photocoagulation or to no laser treatment. These Group II eyes were recruited, randomized, and followed up to answer question No. 2, "Can photocoagulation prevent vitreous hemorrhage?"

Group X—(Eyes at high risk for development of neovascularization)

Recent (three to 18 months since onset) branch vein occlusion with capillary nonperfusion involving a retinal area at least 5 disk diameters in diameter, with no neovascularization. Recruitment for Group X was only begun after the minimum sample size required for Group I had been reached and recruitment for Group I had been terminated. Patients in Group X were recruited to maintain a pool of cases that would have a high risk of developing neovascularization and therefore becoming eligible for Group II. Group X patients were also followed up for natural history information.

Group III—(Eyes at risk for vision loss from macular edema)

Recent (three to 18 months since onset) branch vein occlusion with macular edema reducing visual acuity to 20/40 or worse. Eyes in this group were randomized either to a "grid" pattern of photocoagulation within the involved macular region or to no laser treatment. These Group III eyes were recruited, randomized, and followed up to answer question No. 3, "Can photocoagulation improve visual acuity in eyes with macular edema reducing vision to 20/40 or worse?"

Laser photocoagulation was performed with the argon laser. For Groups I and II, scatter photocoagulation was performed throughout the involved fundus segment, but was not to be extended into the macula (no scatter treatment was to be extended closer than 2 disk diameters from the center of the fovea). For Group III, the protocol for laser photocoagulation is detailed below.

Because the Branch Vein Occlusion Study is evaluating complications of both macular edema and neovascularization, certain cases were eligible for placement in more than one of the above groups. For example, a patient with a quadrant branch vein occlusion and no neovascularization with macular edema could be entered in both Groups I and III. Although the investigators thought that the macular treatment in Group III would not influence neovascularization and that scatter treatment for neovascularization would not influence macular edema, the independent randomization of patients into more than one group provided an opportunity to examine this assumption. The method of grouping and randomizing cases led to an efficient use of cases.

This report will discuss only the results for the patients in Group III, who were recruited to answer the question: "Is argon laser photocoagulation useful in improving visual acuity in patients with visual acuity loss of 20/40 or worse from macular edema secondary to branch vein occlusion?" The answers to the questions regarding management of neovascularization will be presented in a future publication.

A classification of Group III patients according to what other group they may have been assigned and according to treatment allocation is presented in Table 1. Patients who entered the study in Groups I, II, or X were considered eligible to be entered into Group III at a later date even if the duration of the occlusion to entry into Group III was more than 18 months. Consequently, 22 (16%) of the patients described here had a duration beyond 18 months.

The study reported here began in 1976 with close collaboration from the National Eye Institute in planning the design and development of a Manual of Operations. Pilot recruitment and testing of forms at one center began in July 1977, with four additional centers joining in July 1978. No significant changes in protocol occurred during the course of the study, from July 1977 through February 1984.

TABLE 1

GROUPINGS AND ALLOCATIONS OF ALL GROUP III PATIENTS

	Group III Allocation			
	Control		Treated	
Other Groups	No.	%	No.	%
None (Group III only)	24	35	30	42
Group I Control	18	26	15	21
Group I Treated	17	25	19	27
Group II Control	2	3	1	1
Group II Treated	3	4	1	1
Group X	4	6	5	7
Total	68	100	71	100

SUBJECTS AND METHODS

Patient Selection and Entry—To enter the Group III (macular edema) part of the study, eyes had to meet eligibility criteria that included the following: a branch vein occlusion occurring three to 18 months earlier (unless entered in another group within the first three to 18 months), refracted visual acuity of 20/40 or poorer, fluorescein angiographic evidence of macular edema involving the fovea, sufficient clearing of intraretinal hemorrhage to permit evaluation of fluorescein angiography and safe laser photocoagulation, absence of hemorrhage directly in the fovea, absence of other ocular disease threatening visual acuity. No patient was eligible before three months elapsed after occlusion because of the clinical impression that spontaneous improvement often occurs during this period. Patients who were using an anticoagulant for the branch vein occlusion discontinued its use before entry into the study; patients

using an anticoagulant (such as aspirin) for systemic conditions who could not discontinue medication were excluded. If the time of onset of branch vein occlusion was uncertain, the presence of segmental intraretinal hemorrhage was accepted as evidence of a recent occlusion.

The study population of 139 eyes was recruited from patients referred to ophthalmologists at the five participating centers. A visual acuity examiner (certified annually by the Branch Vein Occlusion Study Coordinating Center) performed a refraction according to the standard protocol from the Branch Vein Occlusion Study Manual that is available on request from the Branch Vein Occlusion Study Coordinating Center, Suite 301, 550 N. Broadway, Baltimore, MD 21205. The best corrected visual acuity was measured using the following levels: 20/10, 20/15, 20/20, 20/30, 20/40, 20/50, 20/70, 20/100, 20/160, 20/200, 15/200, 10/200, 5/200, light perception, and no light perception.

Special front-lighted Diabetic Retinopathy Study charts with Snellen letters from 20/15 through 20/100 and Sloan letters for 20/160 and 20/200 were used.[2] The required incident illumination on the chart was specified as 75 to 125 ft-c. The distance from the patient's eyes to the chart was 20 feet. The level of visual acuity corresponding to the smallest line of letters the patient could read with one or no mistakes was recorded as the best-corrected visual acuity.

The protocol specified that the individual who measured visual acuity should be unaware of ("masked" in regard to) the treatment allocation. If the examiner inadvertently became aware of the treatment allocation before visual acuity measurement, this was recorded on the protocol form submitted to the Coordinating Center. According to this reporting procedure for masking, at the third-year visit, for example, 78% of examinations were obtained by a masked examiner.

If a patient met all eligibility criteria and gave informed consent to be randomly assigned to either the treatment group or to the no treatment (control) group, the participating center contacted the Coordinating Center in Baltimore. The study coordinator in Baltimore reviewed all pertinent information to insure the patient met each of the eligibility criteria. If the patient was eligible, the study coordinator issued the patient management assignment as either the treatment or control group from a computer-generated random allocation schedule. Eyes assigned to the treatment group were treated within one month after the date of the fluorescein angiogram.

Treatment—Photocoagulation was performed in all centers according to a standard protocol. Important features of the protocol include: availability of a fluorescein angiogram less than one month old, treatment performed under topical anesthesia using the argon laser to achieve a "grid" (Fig. 1) pattern over the area of capillary leakage identified by fluorescein in the macular region, photocoagulation extending no closer to the fovea than the edge of the foveal avascular zone, and not extending peripheral to the major vascular arcade. The eye was re-evaluated at four months after treatment with fluorescein angiography. Additional photocoagulation was applied if untreated leaking areas and foveal edema persisted with continued loss of visual acuity. Fifty-three of 69 eyes were treated one time, ten eyes treated two times, two eyes treated three times, and four eyes treated five times.

The pattern of treatment varied depending upon the area involved, the nature of leaking vessels and collaterals, and presence of residual intraretinal hemorrhage (Fig. 1).

Compliance with the treatment proto-

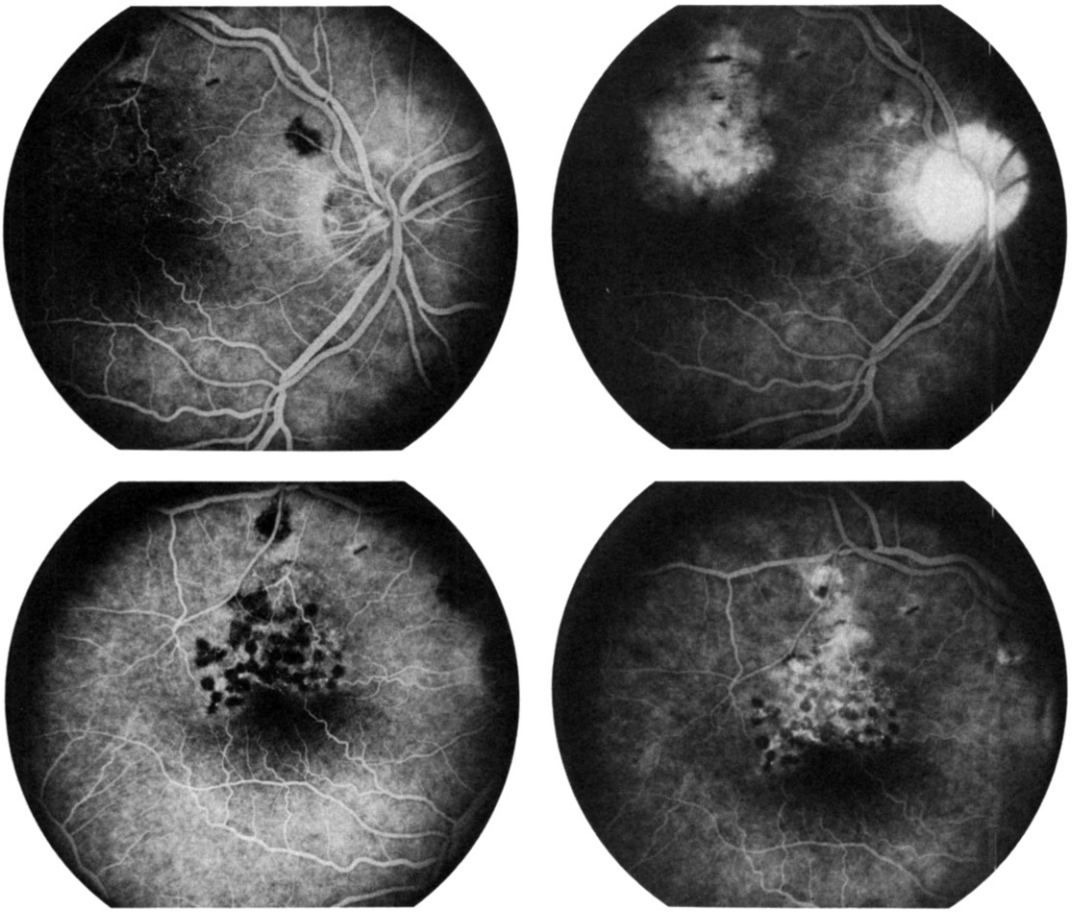

Fig. 1 (Branch Vein Occlusion Study Group). Top left, Pretreatment fluorescein angiogram, transit phase, demonstrating distribution of dilated capillaries superior to the fovea. Top right, Pretreatment fluorescein angiogram, late phase, demonstrating distribution of macular edema, extending into the center of the fovea. Bottom left, Six weeks posttreatment angiogram, transit phase, demonstrating "grid" pattern of protocol argon laser photocoagulation to region of fluorescein-identified edema. Note that the treatment avoids the capillary free zone. Bottom right, Posttreatment fluorescein angiogram, late phase, demonstrating lessening of edema.

col was monitored by the Coordinating Center in Baltimore.

Treating Physician—Each participating center was administered by the senior staff ophthalmologist designated as the Principal Investigator. Only the Principal Investigator and his co-investigators (also senior staff ophthalmologists) were approved for fundus examination and photocoagulation. Of the 69 eyes treated, 68 were treated by the Principal Investigator.

Evaluation of Fundus Photographs and Fluorescein Angiography—Stereoscopic color photographs and fluorescein angiograms on all patients were forwarded to the Coordinating Center in Baltimore. Eligibility and treatment compliance were assessed; whenever the Coordinating Center determined that compliance was not achieved, the participating center was immediately notified so that the situation could be corrected whenever possible.

Patient Follow-up—Return visits were scheduled for all patients at four-month

intervals. At each visit, the best corrected visual acuity was measured by a certified visual acuity examiner and an ophthalmic examination was performed by the Principal Investigator. For treated and control patients, stereoscopic fundus color photographs were made at each visit, and a fluorescein angiogram was obtained at the initial visit, at the first return visit, and then at annual intervals.

Data Monitoring—The Coordinating Center in Baltimore evaluated and analyzed all data from the clinics, including photographic documentation. Coordinating Center statisticians analyzed the study data. These analyses were provided only to the Data and Safety Monitoring Board (see listing at the end of this article) who met regularly to review the progress of the study and to evaluate the accumulating data with regard to safety and efficacy of treatment.

On April 24, 1984, the Data and Safety Monitoring Board recommended that patients enrolled in the Branch Vein Occlusion Study and the ophthalmic community at large be informed of the Group III study results. The Executive Committee has approved these recommendations of the Data and Safety Monitoring Board.

Statistical Methods—Treatment effects as measured by visual acuity or change in visual acuity from entry into the study (baseline) were evaluated by parametric and nonparametric two-sample tests. For this purpose visual acuity was coded in integers from 0 (20/10) to 14 (no light perception). Treatment effects were also evaluated in terms of the proportion of patients gaining or losing two or more lines of vision at different periods of time after entering the study. The chi-square test or Fisher's exact test was applied. Kaplan-Meier statistics, the logrank test, and the Cox proportional hazards model[3] were also employed to adjust for varying length of follow-up, for the effect of covariables, and for loss to follow-up and death.

RESULTS

This report is based on all information received at the Coordinating Center from July 1, 1977, to Feb. 28, 1984. As of that date, 139 eyes from 139 patients with branch vein occlusion and reduction of visual acuity to at least 20/40 from macular edema were enrolled. Every eye randomized into the study was included in the following analyses in the group to which the eye was originally assigned.

Of the 139 eyes, 115 eyes had at least two years of follow-up, 86 eyes had at least three years, 41 eyes had at least four years, and 12 eyes had five or more years of follow-up (Table 2). The average dura-

TABLE 2

GROUP III DURATION OF FOLLOW-UP AND OCCURRENCE OF LOSSES

Duration of Follow-up x = yrs	Eyes Followed-up				Dropouts and Deaths	
	Control		Treated		Control,	Treated,
	No.	%	No.	%	No.	No.
$0 \leq x < 1$	2	3	0	0	2	0
$1 \leq x < 2$	10	15	12	17	4	3
$2 \leq x < 3$	16	24	13	18	3	1
$3 \leq x < 4$	27	40	18	25	2	1
$4 \leq x < 5$	8	12	21	30	0	1
$5 \leq x < 6$	5	7	7	10	0	0
Total	68	100	71	100	11	6

tion of follow-up was 3.1 years. Seventeen eyes were lost to follow-up because of death (11 patients) and six patients who missed four consecutive visits. Of the remaining 122 patients, 112 (92%) were seen at least once a year.

Of the 71 eyes assigned to treatment, two were not treated, three were found to be ineligible after randomization, and two received treatment too close to the fovea by study protocol. Two of the 68 control eyes were treated outside the protocol and three were found not to have met the eligibility criteria.

A number of baseline variables were examined for differences between the treated and control groups. These included duration of branch vein occlusion, medications for hypertension, age, initial visual acuity, diabetes, use of anticoagulants between onset of the branch vein occlusion and entry into the study, sex, and study eye (Table 3).

Analyses of visual results based on the

TABLE 3

BASELINE CHARACTERISTICS

Characteristic	Treatment Allocation				P Value*
	Control		Treated		
	No.	%	No.	%	
Duration of occlusion at entry into study (mos)					
0-12	38	56	41	58	
13+	23	34	24	34	.93
Unknown	7	10	6	8	
Hypertension†					
Yes	31	46	30	42	.69
No	37	54	41	58	
Age, yrs					
40-49	3	4	4	6	
50-59	14	21	18	25	
60-69	26	38	29	41	.73
70-79	24	35	19	27	
80-89	1	1	1	1	
Initial visual acuity					
20/40-20/50	30	44	34	48	
20/70-20/100	24	35	22	31	.69
20/160-20/200	11	16	9	13	
15/200 or worse	3	4	6	8	
Diabetes					
Yes	4	6	1	1	.16
No	64	94	70	99	
Anticoagulant usage before entry into the study					
Yes	25	37	25	35	.85
No	43	63	46	65	
Sex					
Male	33	49	37	52	.67
Female	35	51	34	48	
Study Eye					
Left	29	43	36	51	.34
Right	39	57	35	49	

*Based on χ^2.

†Defined as on medication for the treatment of increased blood pressure.

TABLE 4

SUMMARY OF CHANGE IN VISUAL ACUITY SINCE INITIAL VISIT FOR EYES THAT WERE EVALUATED AT THE THIRD-YEAR VISIT

	Control (No. = 35)	Treated (No. = 43)	
Percent gaining two or more lines at two consecutive visits	37% (13)*	65% (28)	P =.01386
Percent losing two or more lines at two consecutive visits	17% (6)	12% (5)	P =.48641
Percent with visual acuity 20/40 or better at third-year visit	34% (12)	60% (26)	P =.02141
Percent with visual acuity 20/200 or worse at third-year visit	23% (8)	12% (5)	P =.18566
Average visual acuity at third-year visit	20/70	20/40-20/50	P<.0001
Average number of lines gained at third-year visit	0.23	1.33	P<.0001

*No. of eyes in parentheses.

78 eyes that were examined at three years of follow-up indicated average visual acuity of 20/70 in the control group and 20/40 to 20/50 in the treated group (Table 4). Of treated eyes 65% gained two or more lines from baseline maintained for at least two consecutive visits vs 37% of control eyes. Of control eyes 17% lost two or more lines from baseline maintained for two consecutive visits vs 12% of treated eyes. At the third-year visit, close to twice as large a proportion of treated as control eyes had visual acuities of 20/40 or better and almost twice as large a proportion of control as treated eyes had visual acuities of 20/200 or worse. Treated eyes gained an average of 1.33 lines of vision; the control eyes gained an average of 0.23 lines of vision.

The response variable in the Cox proportional hazards analysis was the gain from baseline of two or more lines of vision for two consecutive visits. Covariables included in the full model were age, sex, duration of occlusion before entry into the study, treatment allocation, on medication for hypertension at entry, anticoagulant use between onset of branch vein occlusion and entry into the study, initial visual acuity, and if the eye had received treatment in Groups I or II. The final model included only treatment allocation, duration of occlusion before entry into the study, and taking medication for hypertension. The probability of increased visual acuity was greater in the treated group (P = .00063), decreased with duration of occlusion (P = .004), and was higher for those not taking medication for hypertension (P = .09). The other covariables, including treatment in Groups I or II, were found to have no significant effect on the change in visual acuity.

The Kaplan-Meier plot (Fig. 2) shows the cumulative proportion of eyes in the treatment and control groups that gained two or more lines of visual acuity since the initial visit for two consecutive visits for all 139 patients (P = .00049). The cumulative proportions in both groups are increasing throughout the entire follow-up period.

An analogous plot (Fig. 3) shows the proportion of eyes in the treatment and control groups who have lost two or more lines of visual acuity since the initial visit for two consecutive visits. Although more untreated than treated eyes have lost two lines of visual acuity or more, the difference is not significant (P = .43044).

Table 5 shows the effect of hyperten-

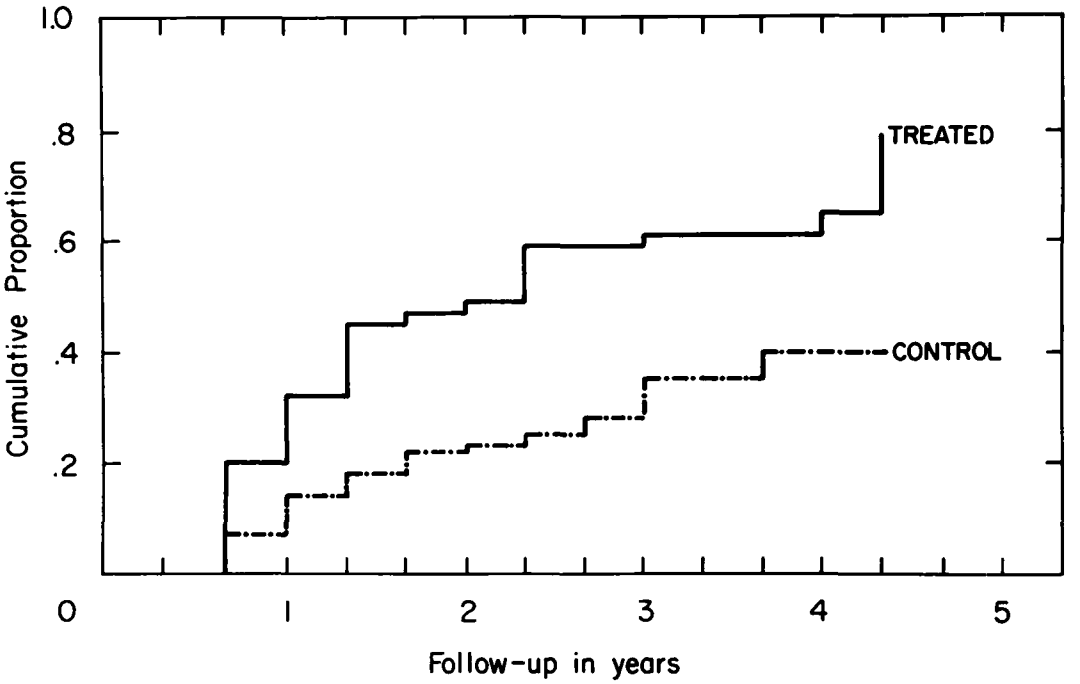

Fig. 2 (Branch Vein Occlusion Study Group). Kaplan-Meier plot of cumulative proportion of eyes gaining two or more lines of visual acuity for two consecutive visits, by follow-up time, treated and control patients. Logrank test P = .00049.

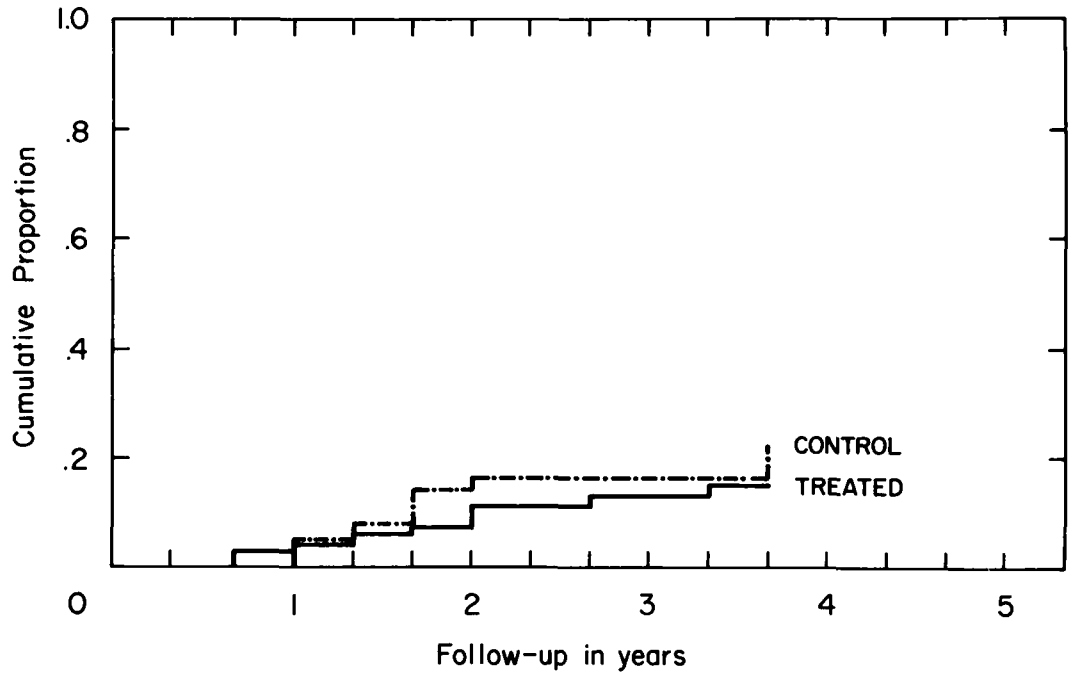

Fig. 3 (Branch Vein Occlusion Study Group). Kaplan-Meier plot of cumulative proportion of eyes losing two or more lines of visual acuity for two consecutive visits by follow-up time, treated and control patients. Logrank test P = .43044.

TABLE 5

PERCENTAGE OF EYES GAINING TWO OR MORE LINES OF VISUAL ACUITY FOR TWO CONSECUTIVE VISITS, EVALUATED AT THREE YEARS OF FOLLOW-UP, BY ALLOCATION AND BY HYPERTENSION

	Control			Treated		
	Total No. of Eyes	No. Gaining	%	Total No. of Eyes	No. Gaining	%
Hypertensive	13	2	15	18	11	61
Nonhypertensive	22	11	50	25	17	68

sion. In this study, hypertension is defined as taking antihypertensive medication before entry. The eyes of control patients taking medication for hypertension fared worse with respect to visual acuity (with only 15% of the hypertensive patients gaining two or more lines of visual acuity for two consecutive visits vs 50% of the nonhypertensive patients [P = .04]). However, there is a weak suggestion than laser treatment (vs no laser treatment) is more beneficial for hypertensive than nonhypertensive patients; 61% of the treated hypertensive patients gained two or more lines of visual acuity at two consecutive visits vs 15% of the hypertensive controls, whereas 68% of the treated nonhypertensive patients gained vs 50% of the nonhypertensive controls (P = .25).

Table 6 demonstrates that eyes are more likely to improve in the first year after the occlusion than afterward; for eyes entered in the first year after the occlusion, 70% gained two or more lines of visual acuity for two consecutive visits vs 32% of those entered after one year (P = .00249). This effect was similar for treated and control groups (P = .92).

The treatment effect was not found to differ in patients with times of onset before and after one year (P = .92); therefore, it should not be inferred that late treatment is not effective. This study was not designed to study early vs later treatment.

In order to examine, in part, the visual significance to the patient of improvement in the eye with branch vein occlusion, we have determined the number of patients whose fellow eye had worse vision than the study eye. For seven of our 99 patients (7%) at two years of follow-up, vision was better in the study eye than the fellow eye.

The consistency of the treatment effect

TABLE 6

PERCENTAGE OF EYES GAINING TWO OR MORE LINES OF VISUAL ACUITY FOR TWO CONSECUTIVE VISITS EVALUATED AT THREE YEARS OF FOLLOW-UP, BY ONSET TIME FROM DATE OF OCCLUSION UNTIL ENTRY INTO THE STUDY

Time (mos)	Control			Treated			Total		
	Total No. of Eyes	No. Gaining	%	Total No. of Eyes	No. Gaining	%	Total No. of Eyes	No. Gaining	%
0-12	20	12	60	23	18	78	43	30	70
13 +	13	1	8	15	8	53	28	9	32
Unknown	2	0	0	5	2	40	7	2	29
Total	35	13	37	43	28	65	78	41	53

was examined within each of the five participating clinics. Although the number of eyes in each clinic was small, each clinic showed a larger percentage of treated eyes than untreated eyes with a gain of two or more lines of visual acuity for two consecutive visits.

Complications of treatment were recorded by the treating ophthalmologist and the Coordinating Center. There was one apparent perforation of Bruch's membrane that did not affect visual acuity. No other complications were noted.

Discussion

The Branch Vein Occlusion Study demonstrates that argon laser photocoagulation improves the visual outcome to a significant degree in eyes with branch vein occlusion and visual acuity reduced from macular edema to 20/40 or worse. We recommend treatment for this category of patient. (The results do not apply to eyes with visual loss from intraretinal hemorrhage in the fovea or foveal capillary nonperfusion; these eyes were not studied.)

Only 41 eyes were followed up longer than four years; consequently, definitive long-term follow-up beyond four years is not available from this study.

The study was not designed to determine how long after branch vein occlusion a patient should be treated. There is no evidence in this study that the benefit of laser photocoagulation varies with the duration of occlusion; consequently, we have no basis for recommending early treatment.

This study did not investigate patients whose visual acuity was better than 20/40. Consequently, we cannot comment on treatment of patients with macular edema and visual acuity better than 20/40.

Although complications appear minimal, we emphasize the care that was taken to avoid treating over intraretinal hemorrhage and, by careful study of fluorescein angiography, to identify the leaking area to be treated, with avoidance of direct treatment of collateral vessels and avoidance of treatment within the capillary free zone. All treatments were performed by senior staff members of the participating centers.

The treatment effect is significant; however, we do not know whether the majority of patients with visual improvement recognize an overall benefit in visual acuity when using both eyes. Approximately 7% of patients in this study did have reduction of visual acuity in the fellow eye from ocular disease, and these patients may directly benefit from the therapy.

The Branch Vein Occlusion Study Group is also investigating the effect of a different form of laser photocoagulation (segmental scatter ablation) on the management of the branch vein occlusion complication of neovascularization. These data will be presented in a future publication.

Acknowledgment

The Branch Vein Occlusion Study Group is grateful for the contributions of the many referring ophthalmologists without whom this study could not have been carried out and to the study patients whose faithfulness to the study has led to conclusions that promise hope for others with branch vein occlusion.

The Branch Vein Occlusion Study Group

Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida: John G. Clarkson, M.D., *Principal Investigator;* J. Donald M. Gass, M.D., Victor T. Curtin, M.D., Edward W. D. Norton, M.D., George W. Blankenship, M.D., and Harry W. Flynn, M.D., *Co-investigators;* Marilyn Mulé, *Clinic Coordinator (1983 to present);* Kathy Leyden, *Clinic Coordinator (1982-1983);* and Ivy Guice, *Clinic Coordinator (1978-1982).*

Estelle Doheny Eye Foundation, University of Southern California, Los Angeles, California: James Liang, M.D., *Principal Investigator (1983 to present);* Kenneth R. Diddie, M.D., *Principal Investigator (1978-1983);* Stephen J. Ryan, M.D., Ronald E. Smith, M.D., James Liang, M.D. (1982-1983), and Richard R. Ober, M.D. (1978-1981), *Co-investigators;* Frances Walonker, *Clinic Coordinator (1979 to present);* and Nancy Borkowski, *Clinic Coordinator (1978-1979).*

EYE RESEARCH INSTITUTE OF RETINA FOUNDATION, Boston, Massachusetts: Clement L. Trempe, M.D., *Principal Investigator;* Charles L. Schepens, M.D., H. MacKenzie Freeman, M.D., and J. Wallace McMeel, M.D., *Co-investigators;* Sherrill F. Anderson, R.N., *Clinic Coordinator (1979 to present);* and Lynda Lane, M.D., *Clinic Coordinator (1978-1979).*

INGALLS MEMORIAL HOSPITAL, Harvey, Illinois: David H. Orth, M.D., *Principal Investigator;* Timothy P. Flood, M.D. (1981 to present), and Charles M. Vygantas, M.D. (1978-1981), *Co-investigators;* Linda June-Arredondo, *Clinic Coordinator (1981 to present);* and Roberta Martia, R.N., *Clinic Coordinator (1978-1981).*

UNIVERSITY OF ILLINOIS EYE AND EAR INFIRMARY, Chicago, Illinois: David H. Orth, M.D., *Principal Investigator;* Morton F. Goldberg, M.D., Mark O. M. T'so, M.D., Timothy P. Flood, M.D. (1981 to present), and Charles M. Vygantas, M.D. (1978-1981), *Co-investigators;* Teri Fitzgerald, *Clinic Coordinator.*

THE WILMER INSTITUTE, Baltimore, Maryland: Daniel Finkelstein, M.D., *Principal Investigator;* Arnall Patz, M.D., Stuart Fine, M.D., and Thomas Rice, M.D. (1978-1982), *Co-investigators;* Dolores Rytel, *Clinic Coordinator.*

Executive Committee: Daniel Finkelstein, M.D., John Clarkson, M.D., Kenneth R. Diddie, M.D. (1978-1983), James Liang, M.D. (1983 to present), David Orth, M.D., Clement Trempe, M.D., Allyn W. Kimball, Ph.D. (Biostatistician); and Israel Goldberg, Ph.D. (Ex Officio).

Data and Safety Monitoring Board: James S. Kelley, M.D. (Chairman, 1979 to present), Director of Retinal Services, Greater Baltimore Medical Center; Arnall Patz, M.D. (Chairman, 1978), Professor of Ophthalmology, Director, Wilmer Eye Institute, Johns Hopkins Hospital; Ronald E. Carr, M.D., Professor of Ophthalmology, New York University; Everett F. Goldberg, LL.B., Associate Dean and Professor, University of Maryland School of Law; Allan D. Jensen, M.D., Chief of Ophthalmology, Union Memorial Hospital, Assistant Professor, Johns Hopkins School of Medicine; Curtis Meinert, Ph.D., Professor, Johns Hopkins School of Public Health and Hygiene; Allyn W. Kimball, Ph.D. (Non-voting), Professor, Johns Hopkins School of Public Health and Hygiene; Israel Goldberg, Ph.D. (Non-voting), Chief, Retinal and Choroidal Diseases Branch, National Eye Institute; Daniel Finkelstein, M.D. (Non-voting); Frederick Ferris, M.D. (Non-voting), Senior Surgeon, U.S.P.H.S., Office of Biometry and Epidemiology, National Eye Institute.

Central Coordinating Center, Baltimore, Maryland: Daniel Finkelstein, M.D., *Principal Investigator;* Allyn W. Kimball, Ph.D., *Biostatistician;* Argye Hillis, Ph.D., *Biostatistician (1978-1981); Michele Melia, Biostatistician and Central Coordinator (1984 to present);* Lucy Mead, Sc.M., *Biostatistician and Central Coordinator (1981-1984);* Darcy Massof, *Central Coordinator (1978-1981);* Chestina H. Marquart, *Assistant Central Coordinator (1979-1981);* Dolores Rytel, *Site Visitor;* and Janet Bowman, *Data Secretary.*

REFERENCES

1. Orth, D., and Patz, A.: Retinal branch vein occlusion. Surv. Ophthalmol. 22:357, 1978.

2. Diabetic Retinopathy Study Research Group: Diabetic Retinopathy Study. Invest. Ophthalmol. 21 (Part 2):1, 1981.

3. Gross, A. J., and Clark, V. A.: Survival Distributions. Reliability Applications in the Biomedical Sciences. New York, John Wiley and Sons, 1975, pp. 45-48; 254-255; 320.