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The prognostic value of post-treatment retinopathy after panretinal photocoagulation for proliferative diabetic retinopathy in type 1 diabetes

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PURPOSE. *To study the prognostic value of post-treatment retinopathy after panretinal laser photocoagulation for proliferative diabetic retinopathy in type 1 diabetes mellitus. Proliferative diabetic retinopathy is treated with panretinal photocoagulation, which significantly reduces the risk of visual loss from this complication. However, no parameters are presently known that can be used to define an optimal control interval after the initial panretinal photocoagulation treatment that ensures enhancement of the treatment in cases where this is needed.*

METHODS. *In this retrospective cohort study, 85 eyes from 56 type 1 diabetic patients were identified who had been subjected to panretinal photocoagulation for proliferative diabetic retinopathy before 1990. The patients were divided into two groups: Group 1 had four or fewer microaneurysms only at the first post-treatment examination whereas Group 2 had more retinopathy.*

RESULTS. *At the first photographic examination after treatment the eyes in Group 1 had a significantly lower visual acuity (VA) (mean=0.23, range: 0.01-1.00) than the patients in Group 2 (mean=0.48, range: 0.01-1.6). During the follow-up period the VA was further reduced in Group 2 but not in Group 1. Three eyes out of six in Group 1 had improvement of VA from below to above 0.1, whereas 6 eyes out of 12 in Group 2 experienced progression of retinopathy with a consequent worsening of VA to below 0.1 after a mean of 10.8 years (range: 6.8–15.9) after treatment.*

CONCLUSIONS. *The severity of post-treatment retinopathy can be used to assess the need for enhancing photocoagulation of proliferative diabetic retinopathy in type 1 diabetes. The interval between post-treatment examinations can be increased to several years when the initial treatment has reduced retinopathy to a minimal level. (Eur J Ophthalmol 2004; 14: 538-42)*

KEY WORDS. *Proliferative diabetic retinopathy, Panretinal photocoagulation, Visual outcome*

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INTRODUCTION

Proliferative diabetic retinopathy is treated with panretinal photocoagulation, which significantly reduces the risk of developing visual loss from this complication (1-3). In spite of the general beneficial effect of this treatment, some patients develop visual loss, either because the treatment is started too late, or because it is insufficient. In these cases further progression of retinopathy can often be halted by enhancing the treatment (4, 5). Although several risk factors for developing visual loss are known before the

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treatment is started (6), no parameters are presently known that can be used to identify the patients who will need enhancement after the initial treatment, or when this enhancement should be given. Consequently, there is no evidence available to suggest the optimal control interval after the initial panretinal photocoagulation treatment. The planning of control intervals in patients with early stages of diabetic retinopathy is done on the basis of retinal morphology as seen on fundus photographs (7). Several studies have shown that the number of microaneurysms in early retinopathy has prognostic value by indicating the risk of progression of retinopathy to a vision threatening stage (8-10). It is therefore possible that the microaneurysm count also can be used to foresee the prognosis after treatment.

In the present study the prognostic value of minimal retinopathy of four microaneurysms or fewer after panretinal laser photocoagulation for proliferative diabetic retinopathy in type 1 diabetes mellitus was studied in a retrospective cohort of 85 eyes from 56 patients examined at least twice after treatment.

MATERIALS AND METHODS

Data material

The study is based on data from the database of diabetic retinopathy at the Department of Ophthalmology, Århus University Hospital. This database contains clinical data of all patients who have been screened, examined, or treated for diabetic retinopathy at the department since 1985.

The total population of Århus County is approximately 644,000 citizens. At the time of analysis the database contained information about 7898 (62%) diabetic patients of which 2023 had type 1 diabetes (approximately 90% of the type 1 population), and 5875 had type 2 diabetes (approximately 56% of the type 2 population). The background population consisted of citizens in Århus County (approximately 90% of the treated patients) the remaining being citizens from neighboring counties. All diabetic patients in Århus County are referred to the eye department for specialist evaluation and treatment of diabetic retinopathy, which is registered in the database. Referrals from neighboring counties was discontinued around 1996 because treatment was started locally. The database contains data about panretinal photocoagulation performed in 878 eyes of 525 type 1 diabetic patients. Reporting of anonymized data from the database does not require approval from the local ethics committee.

Evaluation of retinopathy

Regular screening with visual acuity (VA) measurement and 60 degree fundus photography on diapositives was started in 1992. In all fundus photographs retinopathy is evaluated in detail, including a counting of all fundus lesions. In cases with proliferative diabetic retinopathy the presence of fibrosis and dilated vessel fronts are noted, and the grade is evaluated according to the following scale (11).

1) Post-treatment quiescent proliferative diabetic retinopathy defined as laser scars known to have been directed at new vessels, and no growth of possible remnants of new vessels at two repeated examinations within at least 1 year
2) New vessel elsewhere <0.5 DD and without hemorrhage
3) One of the following:
   New vessel on the disk with a diameter of <0.5 DD
   New vessel elsewhere with a diameter of >0.5 DD
   Preretinal hemorrhage without any visible new vessel
   More than one new vessel elsewhere
4) One of the following:
   New vessel on the disk with a diameter of >0.5 DD
   New vessel on the disk or NVE with preretinal hemorrhage
   New vessel on the disk and NVE
5) Ungradable because of vitreous hemorrhage, retinal detachment, or other complications secondary to proliferative diabetic retinopathy

Data selection

All type 1 diabetic patients were selected in whom treatment for proliferative diabetic retinopathy had started before 1990, who had received more than 2000 laser burns, had been examined with gradable fundus photographs at least twice after the treatment, and had not experienced other diseases or treatment that could affect VA. The patients had been subjected to routine treatment guidelines, which implies the application of 200–500 µm laser scars with one burn size in between. The selection resulted in 85 eyes from 56 patients.

TABLE I - BACKGROUND DATA FOR EACH TREATED EYE IN THE TWO GROUPS

Data	Group 1, N = 28	Group 2, N = 57	p
Age at first treatment, yr	35.0 ± 10.4 (19.9 – 49.7)	38.1 ± 12.3 (20.3 – 70.3)	0.30
Diabetes duration at first treatment, yr	20.8 ± 8.5 (5.1 – 37.0)	18.0 ± 6.4 (0.9 – 29.0)	0.22
Total no.of applications	3180 ± 896 (2004 – 5042)	3567 ± 1322 (2005 – 6452)	0.35
Time from first treatment to first examination, yr	8.1 ± 3.2 (3. – 14.3)	7.7 ± 2.6 (3.8 – 14.8)	0.60
Time from first treatment to follow-up examination, yr	13.6 ± 3.9 (6.7 – 20.0)	13.3 ± 3.6 (6.2 – 21.4)	0.89
Follow-up time, yr	5.5 ± 2.3 (0.5 – 8.8)	5.6 ± 2.3 (0.3 – 9.2)	0.82

Values are mean ± SD (range)

Sixty degree fundus photographs centered on the fovea and VA obtained from the first and the last examination after treatment were used. The images were regraded independently by the two authors, and in case of discrepancy the opinion of the most senior author (T.B.) was used. In six eyes where the images had been lost from the files the original grading data entered into the database were used. Each eye from each patient was assigned to one of two groups according to the presence of retinopathy on the photograph centered on the macula taken at the first follow-up examination after treatment. Retinopathy in the two groups (apart from laser scars and remnants of new vessels) were as follows: Group 1 (n=28): less than or equal to four microaneurysms only; Group 2 (n=57): more than four microaneurysms and/or other retinopathy lesions.

Clinical data of the eyes allocated to the two groups are shown in Table I. The background data and examined effects both depend on interindividual and interocular factors. Therefore, the data were also calculated for each patient using average values from right and left eyes in the cases where both eyes had been included. This did not change the lack of significant difference between the variables shown in Table I. Consequently, in the following only data from individual eyes are considered.

TABLE II - VISUAL ACUITY IN THE TWO GROUPS AT THE FIRST AND THE LAST (follow-up) EXAMINATION AFTER TREATMENT

	Group 1	Group 2	p
First examiniation	0.23 (0.01–1.00), n=28	0.48 (0.01–1.66), n=57	0.03
Follow-up	0.24 (0.01–1.00), n=28	0.28 (0.01–1.25), n=57	0.97

Values are mean (range), number

TABLE III - THE NUMBER OF EYES WITH VISUAL ACUITY LESS THAN 0.1 AT THE FIRST AND THE LAST (follow-up) EXAMINATION AFTER TREATMENT

Examination	Group 1	Group 2
First examination	9	6
Follow-up	6	12

TABLE IV - VISUAL ACUITY IN THE TWO GROUPS EXCLUDING THOSE WHO HAD VISUAL ACUITY < 0.1 EITHER AT THE FIRST OR THE LAST (follow-up) EXAMINATION AFTER TREATMENT

Examination	Group 1	Group 2	p
First examination	0.55(0.19–1.00), n=19	0.65(0.32–1.66), n=45	0.28
Follow-up	0.55(0.16–1.00), n=19	0.50(0.16–1.25), n=45	0.35

Values are mean (range), number

Data analysis

All comparisons of continuous variables between the two groups were done using Wilcoxon's two-sample test for unpaired data. The calculations on visual acuity data were done on log-transformed values. Acuities too low to be measured on the chart (hand movements and less) were set to 0.01 for the numerical calculations.

RESULTS

At the first examination after treatment the eyes with mild post-treatment retinopathy in Group 1 had a significantly lower VA than had the patients with more severe retinopathy in Group 2 (Tab. II). The eyes in Group 1 also had a significantly lower grade of proliferative diabetic retinopathy (1.36±0.95) as opposed to Group 2 (1.96±1.20) (p=0.02). At the follow-up examination there was no significant difference between the VA in the two groups, which was due to a significant decline in VA in Group 2 to reach the VA level of Group 1 (Tab. II).

During the follow-up period three eyes out of nine in Group 1 experienced an improvement of VA from below to above 0.1, whereas 6 eyes out of 12 in Group 2 developed social blindness related to proliferative diabetic retinopathy, such as recurrence of new vessels and extension of laser scars to the foveal area. Social blindness developed averagely 10.8 years (range: 6.8–15.9) after the treatment was started (Tab. III).

After omission of the eyes with VA<0.1 at either the first or the follow-up examination there was no difference between VA in the two groups at the two examinations (Tab. IV).

DISCUSSION

Diabetic patients are encouraged to enroll in screening programs with the purpose of detecting sight-threatening diabetic retinopathy, and after photocoagulation treatment regular post-treatment examinations are recommended in order to detect possible worsening indicating that the treatment should be enhanced. Based on knowledge of the natural history of diabetic retinopathy, guidelines have been defined for optimizing the screening intervals before treatment (12). These general guidelines only to a minor extent consider parameters such as diabetes duration, blood pressure, and blood glucose that might be used to individualize the control interval. Earlier studies have proved the beneficial effect of panretinal photocoagulation in proliferative diabetic retinopathy (1, 3, 4), and prognostic factors for visual outcome before treatment have been characterized (6). However, there is a lack of detailed knowledge about the natural history and risk factors for progression of the disease after treatment. This implies that no evidence exists that can be used to settle the optimal examination interval after the initial treatment so that unnecessary examinations are avoided while ensuring that progression of retinopathy in need of enhanced treatment is detected.

The present study compares the visual prognosis in type 1 diabetic patients in whom panretinal photocoagulation for proliferative diabetic retinopathy had reduced retinopathy to the presence of four microaneurysms or fewer, and patients in whom retinopathy after treatment was worse. The conclusion was that patients in whom treatment has resulted in minimal background retinopathy also have less severe proliferative diabetic retinopathy and a lower VA than those patients who have more background retinopathy after the initial treatment. None of the patients in whom treatment had reduced retinopathy to a minimal level experienced deterioration of VA to a level below 0.1, whereas three patients experienced improvement of VA to above this level. On the other hand, among the patients with more retinopathy at the first post-treatment examination there was a doubling (from 6 to 12) of the number of patients having VA < 0.1 in the follow-up period, the first patient experiencing visual loss due to progression of proliferative diabetic retinopathy 6.8 years after the treatment. At the end of the follow-up period the visual acuity had become similar to that in patients in whom treatment has reduced retinopathy to be minimal initially. There was no difference in the number of laser applications and other background parameters in the two groups. Therefore, the difference in retinopathy level after treatment may either be due to differences in retinopathy before treatment or differences in the response to the treatment.

The findings have implications for recommending the optimal control interval after panretinal laser treatment for proliferative diabetic retinopathy in type 1 diabetes. Since the follow-up period varied substantially,

it is possible that some of the patients who were only followed for a short time would later develop visual loss. However, there was a clear difference between the two groups indicating that patients in whom retinopathy has been reduced to four microaneurysms or fewer could be followed with longer intervals, probably several years.

Altogether, the findings suggest that type 1 diabetic patients in whom photocoagulation for proliferative diabetic retinopathy does not reduce retinopathy to less than four microaneurysms should receive enhancement of the treatment until retinopathy has become minimal. Once retinopathy is minimal the interval between controls can be increased without any risk of overlooking progression of retinopathy in need of enhanced treatment.

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