TABLE 3 Mean blood flow at the two regions in dieased and fellow eyes after successful retinal detachment surgery

	Neuroretinal disk rim		Macula	
	Diseased eye	Fellow eye	Diseased eye	Fellow eye
Group E				
Superior	285.8 ± 129.1	267.5 ± 97.1	293.5 ± 169.1	240.7 ± 67.0
Inferior	322.9 ± 123.5	270.8 ± 79.6	304.8 ± 151.5	258.3 ± 83.6
Group L				
Superior	287.5 ± 82.8	289.4 ± 111.6	237.9 ± 108.9	249.1 ± 112.0
Inferior	303.7 ± 138.4	256.5 ± 109.8	227.9 ± 78.6	236.4 ± 78.7
Group V				
Superior	283.8 ± 89.8	272.8 ± 86.8	258.4 ± 99.7	257.3 ± 116.5
Inferior	332.2 ± 88.2	284.7 ± 91.6	270.9 ± 139.2	245.5 ± 104.2

Data are shown as mean ± SD (arbitrary unit: AU).

and the averaged MBF at disk rim and at the macular area in diseased eye and healthy fellow eye as the dependent variables. Statistical significance was considered to be $P < 0.05$.

RESULTS

The demographic characteristics of each group are shown in Tables 1 and 2, and the averaged MBFs in the different areas are shown in Tables 3 to 6. The mean coefficients of variation of the three measurements of MBF for the superior and inferior neuroretinal rim and the superior and inferior macula areas were 14.5%, 10.9%, 8.3%, and 6.5% in the operated eye and 15.3%, 9.9%, 6.8%, and 6.8% in the healthy fellow eye. The differences in the MBF for gender, age, IOP, averaged MBF, and *a/f* ratios between three groups were not statistically significant.

Multiple regression analysis showed that the mean MBFs in the superior and inferior disk rim areas in the operated eye were significantly correlated with the use of gas tamponade (Table 7). Thus, the averaged MBF at the neuroretinal rim was lower in eyes that had a gas tamponade compared with that in eyes without gas tamponade. No significant correlation was found between the MBF and age, gender, preoperative visual acuity, refractive error, size of the retinal detachment, presence of macular detachment, surgical procedures, intentional retinotomy, transscleral subretinal fluid drainage, time after surgery, visual acuity, and IOP at the time of MBF measurement. All of these factors were also not significantly correlated with the averaged MBF at macular area in the operated eye and the disk as well as macular MBF in the healthy fellow eye.

In eyes with gas tamponade, the total amount of gas injected was 0.5 to 1.0 ml during scleral buckling surgery (groups E and L) and was around 4.0 ml during vitrectomy as vitreous cavity was fully substrated by gas at the end of surgery (group V). The averaged MBF was compared between group E + L and group V (Table 5), and no significant difference was found.

The macular involvement was found in 13 eyes (Table 2). The involved macular area was part of the upper half in five eyes and part of the lower half in six eyes, and in the other two eyes the retinal detachment covered both upper- and lower-half macular areas. The averaged MBF in 11 eyes is shown in Table 6. No

TABLE 4 The *a/f* ratio of the mean blood flow at the two regions of surgery in dieased and fellow eyes after successful retinal detachment surgery

	Group E	Group L	Group V
Neuroretinal disk rim			
Superior	1.00 (0.23–2.88)	0.97 (0.62–1.54)	0.18 (0.33–1.97)
Inferior	0.24 (0.47–1.74)	0.15 (0.65–2.73)	0.28 (0.57–2.49)
Macula			
Superior	0.97 (0.51–3.43)	0.96 (0.44–2.26)	0.07 (0.35–2.30)
Inferior	0.97 (0.74–2.96)	0.88 (0.57–1.67)	0.32 (0.41–2.54)

Data are shown as median (range).

TABLE 5 Mean blood flow at the two regions in dieased eyes after successful retinal detachment surgery with or without gas tamponade

	Number of eyes tamponade (+)/(−)		Neuroretinal disc rim		Macula	
			tamponade (+)	tamponade (−)	tamponade (+)	tamponade (−)
Group E or L	18/24	Superior	213.2 ± 89.4	324.7 ± 103.7	251.1 ± 175.9	280.0 ± 132.6
		Inferior	211.5 ± 76.5	340.0 ± 137.8	269.3 ± 161.9	266.5 ± 107.0
Group V	11/0	Superior	238.8 ± 89.8		258.4 ± 99.7	
		Inferior	252.3 ± 66.3		260.8 ± 130.7	

Data are shown as mean ± S.D (arbitray unit : AU).

significant difference in the averaged MBF was found between superior and inferior area.

DISCUSSION

The purpose of this study was to detect differences in ocular circulation in two different regions of the fundus in three groups of patient that had major surgical procedures to treat a retinal detachment. To avoid possible nonsurgical variables, patients were selected by strictly defined general and ocular parameters. In addition, only eyes with best-corrected visual acuity ≥20/20 were studied.

Our results demonstrated clearly that neither the scleral buckling procedure nor the vitrectomy affected the ocular microcirculation at 6 months or longer after surgery. However, our findings showed that the use of a gas tamponade was correlated with decreased MBF rate in the neuroretinal rim areas.

The choroidal and retinal blood flow in the eyes of rabbits that had had an encircling buckling has been reported to be significantly decreased.[1] Additional clinical evidence has been accumulated on RRD surgery on the MBF, for example, a 40% decrease in the blood flow velocity in the choroid-retina on the buckled side[5] and a mean decrease of 50% in the blood flow rate[4] through the major temporal retinal arteries in the operated eye to that in the fellow eye after scleral buckling. Moreover, an impairment of choroidal circulation has been reported after scleral buckling.[12–14] The reduced choroidal blood flow after scleral buckling procedures has been attributed to a compression mechanism. However, our findings showed that the blood flow in the neuroretinal rim as well as in the macula was not reduced when measured at 6 months after successful surgery for RRD. The discrepancy between our findings and the previous results might be caused by the relative small sample size in both studies, the characteristics of the eyes studied, measurement methods, measured area, follow-up period, and use of silicone oil for tamponade. Additional investigations must be done to rectify this difference.

We studied only eyes with best-corrected visual acuity of 20/20 or better. We are planning to examine tissue microcirculation in conjunction with perimetry in eyes with best-corrected visual acuity of less than 20/20 after successful surgery for RRD.

Our results showed that the microcirculation only at the neuroretinal disk rim was affected by the gas tamponade and the microcirculation at the macula was not. Blood flow to the inner retina and nerve fiber layer of the optic disk is supplied by central retinal artery or its branches, and the blood flow to the prelaminar region adjacent to nerve fiber layer is supplied by branches of the juxtapapillary choroidal vessels.[15] The MBF values of neuroretinal disk rim obtained by HRF is, therefore,

TABLE 6 Mean blood flow at the two regions in dieased eyes in eyes with macular retinal detachment after successful retinal detachment surgery

Area of macular involvement	Number of eyes		Neuroretinal disc rim	Macula
Superior	5	Superior	293.7 ± 142.1	203.2 ± 26.9
		Inferior	190.3 ± 75.7	200.8 ± 40.8
Inferior	6	Superior	363.0 ± 175.8	363.2 ± 183.4
		Inferior	374.8 ± 142.3	353.8 ± 185.3

Data are shown as mean ± S.D (arbitray unit : AU).

TABLE 7 **Multiple regression analysis of clinical factors influencing the MBF in the operated eye**

	Regression coefficient			
	Neuroretinal disk rim		Macula	
Variable	Superior	Inferior	Superior	Inferior
Gender	N.S.	N.S.	N.S.	N.S.
Age	N.S.	N.S.	N.S.	N.S.
Extent of retinal detachment	N.S.	N.S.	N.S.	N.S.
Macular involvement	N.S.	N.S.	N.S.	N.S.
Surgical procedure	N.S.	N.S.	N.S.	N.S.
Transscleral SFR	N.S.	N.S.	N.S.	N.S.
Gas tamponade	−0.378	−0.421	N.S.	N.S.
Period after surgery	N.S.	N.S.	N.S.	N.S.
Visual acuity				
Before surgery	N.S.	N.S.	N.S.	N.S.
At MBF measurement	N.S.	N.S.	N.S.	N.S.
Refractive error at MBF measurement	N.S.	N.S.	N.S.	N.S.
IOP at MBF measurement	N.S.	N.S.	N.S.	N.S.
Ajusted R^2	0.143	0.177		
p value	0.0179	0.0069		

MBF, mean blood flow; IOP, intraocular pressure; N.S., not significant.

considered to be a mixture of retinal and choroidal blood flow because the depth of laser penetration is approximately 400 μm[16] so that the scanning depth includes the nerve fiber layer and prelaminar region. There may also be contributions from choroidal blood flow in the foveola where the retina is very thin, approximately 135 μm. However, comparing the diameter of the foveola, 350 μm, with the measurement area of 10° × 2.5 , which is almost 2.7 × 0.7 mm, the contribution of the foveola would be extremely small. Therefore, our results suggest that the choroidal circulation is most likely to be impaired while retinal circulation is relatively intact even after more than 6 months after gas tamponade.

In previous reports,[17,18] a disturbance of the choriodal circulation, at least shortly after scleral buckling surgery, was demonstrated by fluorescein angiography. An alternative explanation for this finding may be that the macular microcirculation is less susceptible to the surgical invasion, which would affect the blood flow in main ocular vessels for longer periods. It has been reported that the retinal microcirculation in the macular area was impaired in patients even without macular involvement and it recovered in 1 month after successful scleral buckling procedures.[6]

This study has several weaknesses that limit the generalization of the findings. There were only a small number of patients studied, the follow-up times were different, and there was a lack of the findings of other tests (e.g., angiography, electrophysiology, and visual fields) that support the choroidal circulation disturbances. Therefore, the findings from this study cannot be used to justify alternative methods to tamponade the retina in the treatment of patients with RRD. The information and data obtained from this study are, however, useful in that they bring to light the possible existence of subclinical adverse effect of gas tamponade on the choroidal circulation. Further investigation focusing on the ocular, especially choroidal blood flow, at different stages of RRD will be helpful to understand the role of the choroidal circulation on the unexplainable visual field defects after successful RRD surgery.

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Letters to the Editor

Clinical Case Notes

Woman with atypical unilateral Leber's hereditary optic neuropathy with visual improvement

ABSTRACT

We describe a patient with Leber's hereditary optic neuropathy (LHON) who had a unilateral involvement and a gradual recovery of vision. A 50-year-old woman was referred to our clinic in December 2004 for the treatment of left optic neuritis. The visual acuity was 0.01 in her left eye and 1.5 in her right eye. The left eye had a central scotoma and a relative afferent pupillary defect. Ophthalmoscopy revealed a hyperaemic optic disc with indistinct margins in the left eye. Fluorescein angiography showed circumpapillary microangiopathy in both eyes and staining of the left optic disc. An nt 11778 mutation was identified and she was diagnosed with LHON. The central scotoma gradually improved, and the visual acuity had recovered to 0.3 in August 2007. LHON should still be considered even in older female patients presenting with unilateral acute visual loss when microangiopathy is seen. In such cases, molecular testing is effective in confirming a diagnosis of LHON.

Key words: Leber's hereditary optic neuropathy, microangiopathy, nt 11778 mutation, optic neuritis.

INTRODUCTION

Leber's hereditary optic neuropathy (LHON) is a maternally inherited disease that is characterized by a permanent and devastating visual loss and usually affects young men. The fellow eye is almost always involved within 1 year from the onset of the disease in the first eye.[1] Approximately 90% of Japanese with LHON have the nt 11778 mutation, which is associated with poor visual prognosis.[2] The incidence of atypical cases of LHON has recently increased because genetic diagnosis has become more widely applied.[3,4]

We report on a woman with LHON with an nt 11778 mutation who had a unilateral involvement and a gradual recovery of vision. A search of Medline did not extract any LHON cases that were unilateral and had visual recovery.

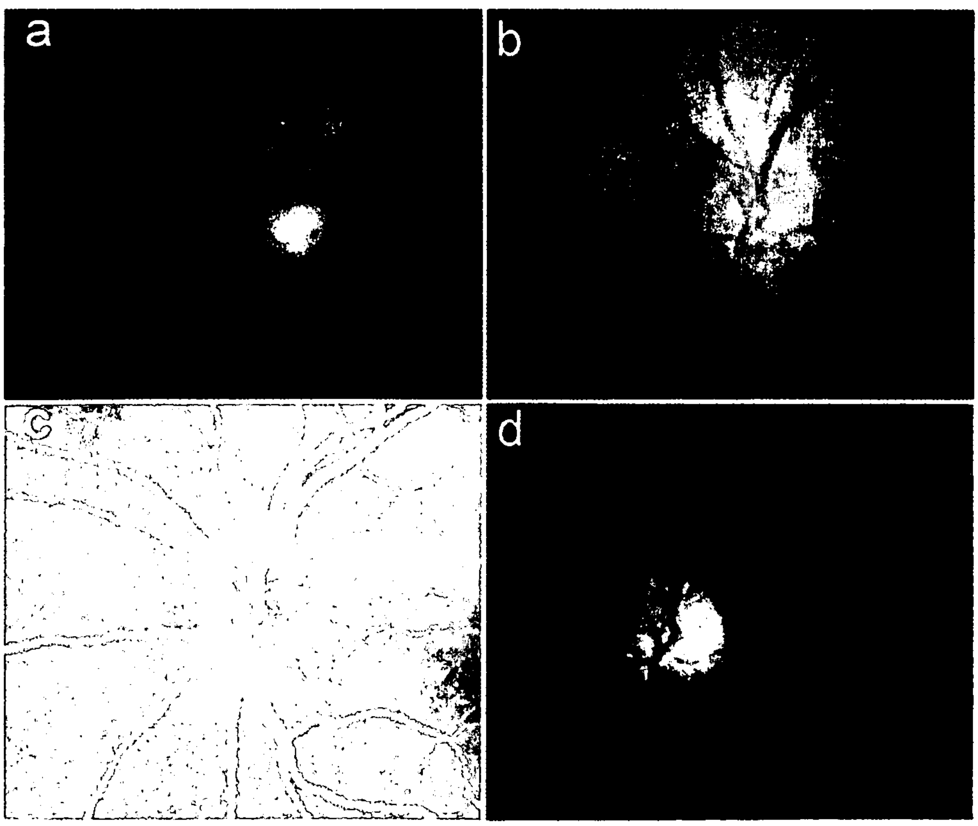

Figure 1. Fundus photographs at an early stage and 25 months after the onset. (a) Right optic disc appears normal on 14 December 2004. (b) Left optic disc is reddish with indistinct margin on 14 December 2004. (c) Fluorescein angiogram of the left eye showing circumpapillary microangiopathy on 29 December 2004. (d) Left optic disc is pale and atrophic 25 months after onset (7 September 2006).

Case report

A 50-year-old woman presented with acute visual loss in the left eye in November 2004. She was diagnosed with optic neuritis, and high doses of intravenous corticosteroids were given by a local eye clinic, but no improvements were noted. When the patient was referred to the Keio University Hospital on 14 December 2004, here visual acuities were 1.5 in the right eye and 0.01 in the left eye. The intraocular pressure was 17 mmHg in the right eye and 18 mmHg in the left eye. A relative afferent pupillary defect was present in the left eye. Fundus examination showed that optic disc appeared normal in the right eye (Fig. 1a), but the left optic disc was hyperaemic with indistinct margins (Fig. 1b). Fluorescein angiography showed circumpapillary microangiopathy in both eyes and staining of the left optic disc (Fig. 1c). A central scotoma was found in the left eye (Fig. 2a), and no visual field abnormalities were found in the right eye. The waveforms of the pattern visually evoked potentials from the left eye were markedly distorted, and the amplitudes and implicit times could not be measured, whereas the response in the right eye was normal.

The cerebrospinal fluid was clear and normal. Neither neurological nor radiological findings suggested multiple sclerosis. Her medical history showed that there were no other features, for example, pain on eye movements, that suggested optic neuritis. She was a non-smoker and consumed alcohol only occasionally. She had no history of head trauma, drug administration and hormone disorder. No family history of eye diseases was found. A genetic study identified an nt 11778 mutation with homoplasmy, and she was diagnosed with LHON. Vitamin C, vitamin B2, high-dose coenzyme Q10 and unoprostone isopropyl eye drops were prescribed.[5] The central scotoma of her left eye gradually improved from the nasal area (Fig. 2b–d), which, as previously reported, is characteristic of LHON patient.[6] The visual acuity gradually improved to 0.1 in February 2006, 0.2 in June 2006 and 0.3 in March 2007. However, the pallor of the left optic disc was still present (Fig. 1d).

The visual acuity and visual field of the right eye remained normal throughout the more than 2.5 years follow-up period.

Discussion

This case had several clinical features, for example, age, gender, laterality, pupillary reflexes and partial visual recovery, that sug-

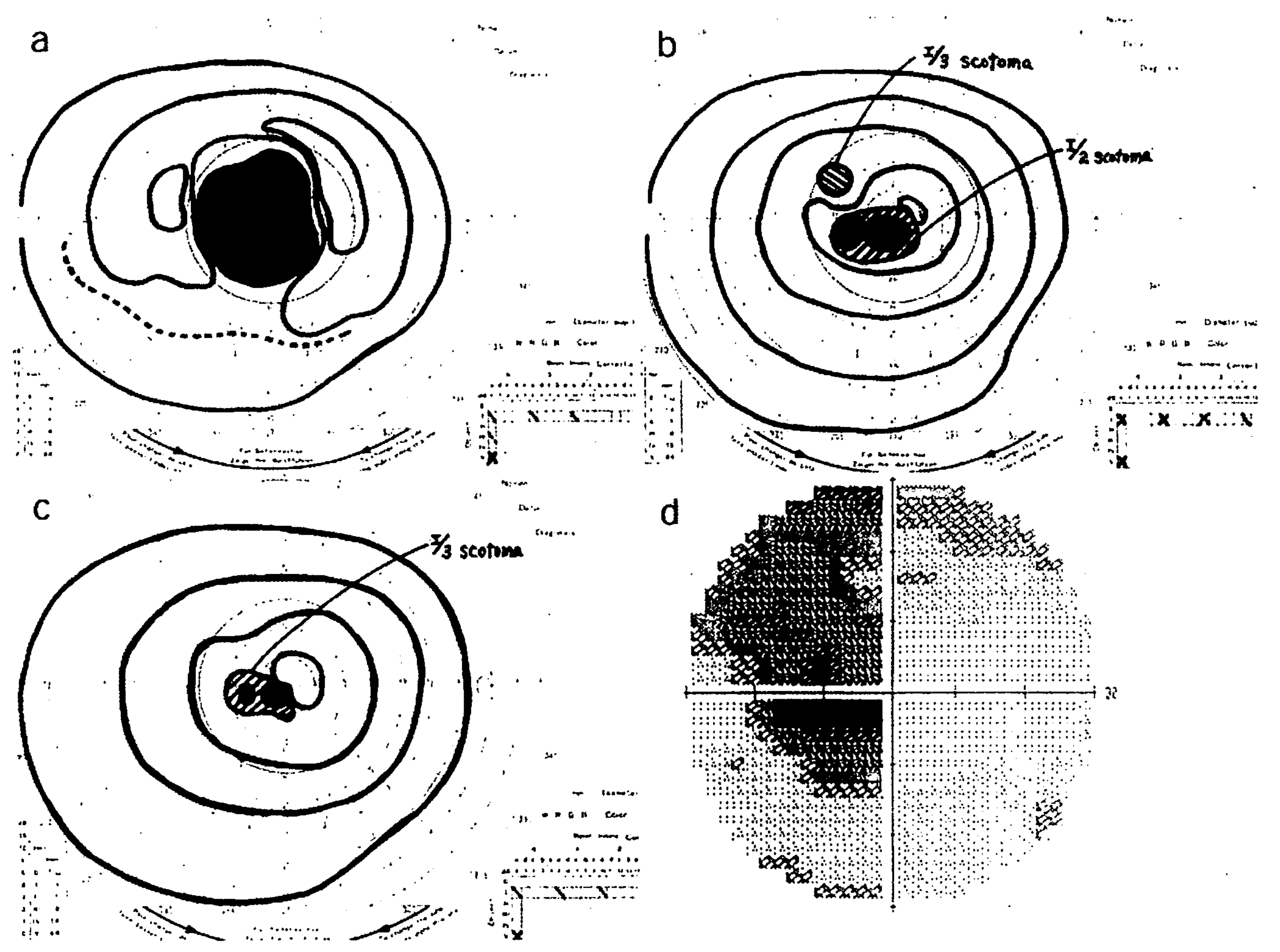

Figure 2. Goldmann's perimetry and Humphrey visual field. A central scotoma is present in the left visual field (a) which improved from the nasal side of the visual field (b, c, d). (a) On the same day as the photographs on the first examination on 14 December 2004. (b) After 8 months from the onset on 20 August 2005. (c) 24 months from the onset (9 December 2006). (d) Thirty-one months from the onset (6 July 2007).

gested that the patient had optic neuritis. However, the diagnosis of LHON was established by the presence of microangiopathy on the discs and the nt 11778 mutation. The clinical features of this 50-year-old woman is atypical for LHON. Three female patients with atypical LHON were reported, and the authors reported difficulties in making a diagnosis.[3] Because a delayed onset of LHON has been reported in patients over 60 years old,[1,7] diagnostic confusion may occur in older subjects. Borruat *et al.* reported[4] on the importance of genetic and radiological investigations in a 63-year-old LHON patient whose diagnosis was confused with ischaemic optic neuropathy.

Only a few unilateral cases of LHON have been reported.[3] Although limited information is available concerning LHON cases with visual improvement, most patients with visual recovery develop the disease in their teens.[5] Clinician should keep in mind that not only multiple sclerosis/retrobulbar neuritis but also LHON should be considered in older patients presenting with unilateral acute visual loss and circumpapillary microangiopathy in fluorescein angiography. In such cases molecular testing is effective in making a diagnosis of LHON.

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Assessment of the spontaneous pulsations of the central retinal vein in daily ophthalmic practice

ABSTRACT

The purpose of this study is to assess the frequency of eyes with a spontaneous pulsation of the central retinal vein in the setting of a busy daily ophthalmic practice. The clinical observational case series study included 690 eyes (345 subjects). The optic disc was ophthalmoscopically assessed using a non-contact ophthalmoscopic lens at the slit lamp. Out of the study population, 526 eyes (76.2%) of 265 (76.8%) subjects showed a detected spontaneous pulsation of the central retinal vein (prevalence rate: 76.2 ± 1.6% [mean ± standard error] per eye, and 76.8 ± 2.3% per subject). In univariate analysis, the presence of a detected spontaneous central retinal vein pulsations was statistically associated with systolic systemic blood pressure ($P = 0.04$) and with the ocular perfusion pressure ($P = 0.03$). The results suggest that as examined in the setting of a busy daily ophthalmic practice, the central retinal vein was found to show a spontaneous pulsation in about 80% of the subjects.

Key words: brain pressure, central retinal vein pressure, central retinal vein pulsation, glaucoma, ophthalmodynamometry.

Modified ophthalmodynamometry using a contact lens with a pressure sensor in its holding grip is a new technique to indirectly and non-invasively estimate the pressure in the central retinal artery and vein.[1,2] The first step of the modified ophthalmodynamometry is to assess in a non-contact manner whether there is a spontaneous pulsation of the central retinal vein. For that purpose, a hand-held non-contact ophthalmoscopic lens has usually been used. In a previous hospital-based study, the frequency of spontaneous pulsations of the central retinal vein was about 90%.[3] As most patients are examined and treated in ophthalmic practices, it was the purpose of the present study to examine the frequency of ophthalmoscopically detected spontaneous pulsations of the central retinal vein in a busy ophthalmic practice.

The observational case series study included 345 patients (690 eyes) (age: 69.4 ± 13.0 years; range 16.7–89.0 years) consecutively attending the ophthalmic practice for various reasons such as prescribing of glasses, dry eye symptoms, regular ophthalmic check-up examination, and control examination of cataract and age-related macular degeneration. Eyes with glaucoma, intracranial lesions or other conditions associated with elevated intracranial pressure, retinal vein occlusions, ischaemic optic neuropathies and other disorders associated with papilloedema were excluded. Mean refractive error was −0.68 ± 3.41 dioptres (median: 0 D; range: −20.25 to 7.25 D). The systemic arterial blood pressure was assessed using the conventional Riva-Rocci method. After measuring the intraocular pressure by Goldmann applanation tonometry, the pupil was dilated. The optic disc was examined using a slit lamp and a hand-held 78 D ophthalmoscopic lens for at least 20 s. Any small pulse synchronous movement of the central retinal vein or its major branches inside of the optic disc was noted as spontaneous pulsations. All examinations were performed by the same examiner (UL) in his ophthalmic practice.