

CLINICAL SCIENCE

Colour Doppler imaging and fluorescein filling defects of the optic disc in normal tension glaucoma

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Aim: To investigate the relation between blood flow parameters of the retrobulbar vessels measured by means of colour Doppler imaging (CDI) and fluorescein filling defects of the optic nerve head in patients with normal tension glaucoma (NTG) and control subjects.

Methods: 29 patients with NTG and 29 age and sex matched control subjects were included in this study. Blood flow velocities—peak systolic velocity (PSV), end diastolic velocity (EDV), and resistive indices (RI) of the ophthalmic artery (OA), the central retinal artery (CRA), and of the temporal and nasal short posterior ciliary arteries (TPCA, NPCA)—were measured with CDI. Fluorescein angiograms were performed with a scanning laser ophthalmoscope. The extent of absolute fluorescein filling defects of the optic nerve head in relation to the optic nerve head was assessed.

Results: The PSV of the OA, the PSV and EDV of the CRA, and of the TPCA and NPCA were significantly reduced in NTG ($p < 0.05$). The RI of the CRA, the TPCA and NPCA were significantly increased in NTG ($p < 0.01$). The optic nerve head fluorescein filling defects were significantly larger in NTG ($p < 0.01$). The filling defects were significantly negatively correlated ($p < 0.05$) with the PSV and EDV of the CRA (PSV_{CRA}: $r = -0.41$; EDV_{CRA}: $r = -0.34$), with the PSV and EDV of the NPCA (PSV_{NPCA}: $r = -0.34$; EDV_{NPCA}: $r = -0.38$), and with the EDV of the TPCA ($r = -0.29$). A significant positive correlation ($p < 0.05$) was found with the RI of both PCAs (RI_{NPCA}: $r = 0.28$; RI_{TPCA}: $r = 0.29$).

Conclusion: Patients with NTG had reduced blood flow velocities and higher resistive indices in most retrobulbar vessels. Optic nerve head fluorescein filling defects were larger compared to controls. The filling defects were correlated with end diastolic velocities and resistive indices of the PCAs and with blood flow velocities of the CRA. Capillary loss of the optic nerve head may be related to higher downstream resistance and reduced blood flow velocities of the retrobulbar vessels.

The pathogenic concepts of glaucoma, defined as a progressive optic neuropathy characterised by optic nerve head excavation and glaucomatous visual field loss, enclose mechanical and vasogenic mechanisms.^{1–4} A vascular failure leading to perfusion deficits of the optic nerve head, the retina, the choroid, or the retrobulbar vessels, by means of vasosclerosis, small vessel disease, vasospasms, or autoregulatory dysfunction may contribute to the nerve fibre loss in glaucomatous optic neuropathy.^{2 5–11}

Different techniques are used to describe the vascular situation in glaucoma, but no technology can characterise the perfusion of the optic nerve head in its entirety.^{5 12} Besides, these perfusion parameters give no direct information on metabolic needs and supply of ganglion cells, although ischaemic lesions may trigger an apoptotic cascade in ganglion cells.¹⁰

Colour Doppler imaging is a non-invasive method to measure blood flow velocities of retrobulbar vessels. This ultrasound technique combining a simultaneous B-mode ultrasound image with coloured represented movements based on Doppler frequency shifts allows the assessment of blood flow velocities (peak systolic velocity, end diastolic velocity) in the ophthalmic artery, the central retinal artery and vein, and the temporal and nasal short posterior ciliary arteries. The resistive index describes the peripheral resistance to flow and its calculation is based on the two parameters of blood flow velocity.^{5 12–15} Fluorescein angiographic studies may describe perfusion alterations of the optic nerve head, the retina, and the choroid. Morphological and dynamic parameters demonstrated impaired ocular blood flow in glaucoma in different studies.^{8 16–33} Fluorescein filling defects of the optic nerve head are specific for glaucoma and ischaemic optic neuropathy and

correlate with the functional and morphological damage in glaucoma.^{25 29 34–39}

The purpose of this study was to investigate the relation between absolute fluorescein filling defects of the optic nerve head and flow velocities measured by colour Doppler imaging. The absolute filling defects of the optic disc as a sign of superficial capillary rarefaction may increase downstream resistance. The effects on the retrobulbar vessels are studied and discussed as well as differences between patients with normal tension glaucoma and control subjects.

PATIENTS

Twenty nine patients with normal tension glaucoma (NTG) and 29 age and sex matched controls were included in this retrospective clinical study. The fluorescein angiograms and colour Doppler imaging examinations were performed as a matter of clinical practice. All individuals including the control subjects who were examined as volunteers gave informed consent.

All patients with NTG had glaucomatous optic nerve head cupping and glaucomatous visual field defects as defined by the European Glaucoma Society,⁴⁰ in the absence of retinal or neurological disease affecting the visual field. The diagnostic criteria for glaucomatous visual field loss are as follows. Visual field loss was considered significant when (a) glaucoma hemifield test was abnormal, (b) three points confirmed with $p < 0.05$ probability of being normal (one of which should have $p < 0.01$), not contiguous with the blind spot, or (c) corrected pattern standard deviation (CPSD) was abnormal with $p < 0.05$. All parameters were confirmed on two consecutive visual fields performed with Humphrey visual field analyser (full threshold program 24-2). All patients with glaucomatous

visual field loss underwent diurnal curves of intraocular pressure (IOP) measurements (8.00, 12.00, 16.00, 20.00, and 24.00) without any topical or systemic IOP lowering medication. The IOP was never above 21 mm Hg (Goldmann applanation tonometry). Visual acuity was 20/40 or better and no previous laser or surgical treatment had been performed. Patients with refractive aberrations of more than plus or minus 8 dioptres, with diabetic retinopathy and with hypersensitivity to sodium fluorescein were excluded from this study. The control subjects had no significant history of ophthalmological disease.

METHODS

All patients with NTG and control subjects had a detailed ophthalmological examination including diurnal curves of measurements of the IOP at 8.00, 12.00, 16.00, 20.00, 24.00), a colour Doppler imaging examination and a videofluorescein angiogram with a scanning laser ophthalmoscope.

Systolic and diastolic blood pressure and heart rate were measured after a rest of 5 minutes sitting on a chair before colour Doppler imaging and fluorescein angiograms were performed. Mean arterial pressure (MAP) and ocular perfusion pressure was calculated from these data ($MAP = \text{diastolic blood pressure} + \frac{1}{3}(\text{systolic blood pressure} - \text{diastolic blood pressure})$, perfusion pressure = $\frac{2}{3}MAP - IOP$).^{8,9}

Blood flow velocities of the retrobulbar vessels were measured by means of colour Doppler imaging (CDI) using a 7.5 MHz linear phased array transducer (Siemens Sonoline Sienna, Germany). The transducer was gently placed on the closed upper eyelid using a coupling gel, taking care to minimise pressure on the globe. All subjects were in the supine position during the examination. Colour Doppler imaging permits blood velocity measurements of the ophthalmic artery (OA), the central retinal artery (CRA) and vein (CRV), and the temporal and nasal short posterior ciliary arteries (TPCA and NPCA). The peak systolic velocity (PSV) and the end diastolic velocity (EDV) were obtained from the velocity waves of each artery. The resistive index (Pourcelot's ratio) was calculated ($(PSV - EDV)/PSV$) to characterise peripheral vascular resistance of the vessels studied. Finally, the minimum and maximum velocities of the central retinal vein were measured.^{14,15}

Fluorescein angiography of the optic nerve head was performed with scanning laser ophthalmoscopy (Scanning Laser Ophthalmoscope, Rodenstock, Ottobrunn, Germany). The method is described in detail elsewhere.^{25,41,42} All subjects gave informed consent concerning side effects of fluorescein

angiography. To start the angiography, 10% sodium fluorescein dye was injected into an antecubital vein. The angiograms were recorded on videotapes and analysed by means of digital image analysis (Matrox Inspector, Matrox Inc, Quebec, Canada). Images of the early phase (<3 minutes) visualised the superficial capillaries of the optic nerve head. The extent of absolute fluorescein filling defects was measured in relation to the area of the optic nerve head (percentage of the optic disc). Absolute filling defects of the optic nerve head are defined as areas of persisting hypofluorescence during the whole angiogram, and correspond to areas of superficial capillary loss. During the angiogram the focus was changed from the neuroretinal rim to the bottom of the cup to avoid artefacts. The videofluorescein angiograms permit the selection of images with best possible visualisation of the superficial capillaries.

Nerve fibre layer imaging with a red-free laser (argon laser 488 nm) was performed before fluorescein dye was injected. Nerve fibre layer defects confirmed the diagnosis of NTG and the cup to disc area ratio and the area of the optic nerve head were measured in digitised red-free images.

Visual field examinations were performed with the Humphrey field analyser (Model 750, Humphrey-Zeiss, San Leandro, CA, USA) using the white on white 24-2 full threshold program. The visual field global indices mean deviation (MD), pattern standard deviation (PSD), short term fluctuation (SF), and corrected pattern standard deviation (CPSD) were used for statistical analysis.⁴³

For the statistical analysis of this study, one eye of each subject was randomly chosen. Blood flow velocities of the retrobulbar vessels (colour Doppler imaging), fluorescein filling defects (fluorescein angiograms) and functional, morphological, and haemodynamic data of the patients with NTG and control subjects were compared with an unpaired *t* test. Correlations were tested using the Fisher's *r* to *z* test. In all analyses, $p < 0.05$ was regarded as statistically significant.

Adherence to the Declaration of Helsinki for research involving human subjects is confirmed. Informed consent was obtained from all individuals including the analysis of the data.

RESULTS

There was no statistical difference between patients with NTG and control subjects in age, sex, IOP, systolic, diastolic and mean arterial blood pressure, heart rate, and perfusion pressure (Table 1).

The global indices of visual field examinations MD, PSD, SF, and CPSD were statistically significant different in both

Table 1 Demographic and clinical data of the patients with normal tension glaucoma (NTG) and control subjects with corresponding p values (unpaired *t* test)

	NTG	Control subjects	Significance level (p value)
	Mean (SD)	Mean (SD)	
Age (years)	51 (10)	44 (16)	NS
IOP (mm Hg)	15.6 (3)	15.5 (3)	NS
Systolic blood pressure (mm Hg)	123.9 (17)	130.3 (16)	NS
Diastolic blood pressure (mm Hg)	75.2 (11)	74.1 (11)	NS
Mean arterial blood pressure (mm Hg)	91.3 (12)	92.6 (12)	NS
Heart rate (beats/min)	73 (11)	72 (11)	NS
Perfusion pressure (mm Hg)	44.6 (8)	46.1 (7)	NS
MD (dB)	-6.8 (6.7)	-0.99 (1.5)	$p < 0.01$
PSD (dB)	7.2 (4.9)	1.8 (0.4)	$p < 0.0001$
SF (dB)	2.0 (1.2)	1.3 (0.3)	$p < 0.05$
CPSD (dB)	6.9 (4.9)	1.0 (0.8)	$p < 0.0001$
Cup to disc area ratio	0.52 (0.13)	0.28 (0.16)	$p < 0.0001$
Disc area (mm ²)	1.76 (0.39)	1.55 (0.42)	NS

NS = not significant.

IOP = intraocular pressure, MD = mean deviation, PSD = pattern standard deviation, SF = short term fluctuation, CPSD = corrected pattern standard deviation.

Table 2 Absolute fluorescein filling defects and blood flow velocities of the retrobulbar vessels of the patients with normal tension glaucoma (NTG) and control subjects with corresponding p values (unpaired *t* test)

	NTG	Control subjects	Significance level (p value)
	Mean (SD)	Mean (SD)	
Absolute filling defects of the optic nerve head	0.16 (0.17)	0.01 (0.02)	<0.0001
OA PSV (cm/s)	29.2 (9.4)	36.0 (8.3)	<0.01
OA EDV (cm/s)	8.1 (3.3)	8.1 (3.7)	NS
OA RI	0.73 (0.06)	0.78 (0.07)	<0.01
CRA PSV (cm/s)	7.2 (1.6)	9.8 (2.2)	<0.0001
CRA EDV (cm/s)	1.8 (0.9)	3.2 (0.7)	<0.0001
CRA RI	0.75 (0.10)	0.67 (0.07)	<0.01
CRV minimum (cm/s)	2.6 (0.4)	2.6 (0.4)	NS
CRV maximum (cm/s)	3.8 (0.9)	4.1 (0.6)	NS
Temporal PCA PSV (cm/s)	7.3 (1.3)	8.4 (1.9)	<0.05
Temporal PCA EDV (cm/s)	2.2 (1.0)	3.5 (0.8)	<0.0001
Temporal PCA RI	0.70 (0.12)	0.58 (0.06)	<0.0001
Nasal PCA PSV (cm/s)	6.8 (1.2)	8.5 (1.7)	<0.0001
Nasal PCA EDV (cm/s)	2.1 (0.8)	3.5 (0.6)	<0.0001
Nasal PCA RI	0.70 (0.10)	0.59 (0.05)	<0.0001

NS = not significant.

OA = ophthalmic artery, CRA = central retinal artery, CRV = central retinal vein, PCA = short posterior ciliary artery, PSV = peak systolic velocity, EDV = end diastolic velocity, RI = resistive index.

groups. The cup to disc area ratio was significantly higher in patients with NTG, whereas the area of the optic nerve head showed no statistical difference. The clinical, functional, and morphological data are shown in Table 1.

The absolute fluorescein filling defects of the optic nerve head were significantly larger in patients with NTG (Table 2).

The peak systolic velocity (PSV) of the ophthalmic artery (OA), as well as the PSV and the end diastolic velocity (EDV) in the central retinal artery (CRA), the temporal and nasal short posterior ciliary arteries (TPCA, NPCA) were significantly reduced in patients with NTG. The resistive indices (RI) of the central retinal artery and temporal and nasal short posterior ciliary arteries were significantly increased in patients with NTG, whereas the RI of the ophthalmic artery was significantly higher in the control group. The minimum and maximum velocities of the central retinal vein were not significantly different. The values of the blood flow velocities and the statistical data of the vessels measured by means of colour Doppler imaging are listed in Table 2.

The absolute fluorescein filling defects of the optic nerve head were statistically significantly correlated with the PSV and the EDV of the central retinal artery. The filling defects were correlated with the PSV, EDV, and RI of the nasal short posterior ciliary arteries, as well as with EDV and RI of the temporal short posterior ciliary arteries. The blood flow velocities and resistive indices of the ophthalmic arteries and the velocities of the central retinal vein were not significantly correlated with the filling defects. The results are shown in Table 3.

Further analysis was performed to investigate correlations of the fluorescein filling defects of the optic nerve head and the parameters measured by colour Doppler imaging with visual field global indices and morphological data (Table 4).

The fluorescein filling defects were correlated with the extent of the visual field defect and with the glaucomatous optic disc cupping. The absolute filling defects were correlated with the global indices MD, PSD and CPSD, and with the cup to disc area ratio.

The PSV and the EDV of the ophthalmic artery were significantly positively and the RI negatively correlated with the visual field parameter SF. The RI of the ophthalmic artery was negatively correlated with the visual field parameter MD.

The PSV, EDV of the central retinal artery and of the nasal short posterior ciliary arteries were significantly correlated with the parameters PSD and CPSD, as well as the EDV of the

temporal short posterior ciliary arteries. A significant correlation with the PSV of the temporal short posterior ciliary arteries was not apparent. The calculated RI of the central retinal artery and of the nasal and temporal short posterior ciliary arteries were positively correlated with the parameters PSD and CPSD.

The cup to disc area ratios were significantly correlated with the PSV and the RI of the ophthalmic artery, with the PSV and EDV of the central retinal artery, with the EDV and RI of the nasal short posterior ciliary arteries and with the EDV of the temporal short posterior ciliary arteries.

The minimum and maximum blood flow velocities of the central retinal veins failed to reach statistical significant correlations with any of the morphological and functional data.

The correlations of the fluorescein filling defects and CDI parameters with functional and morphological data are presented in Table 4.

Table 3 Correlations of the absolute filling defects of the optic nerve head with blood flow velocity parameters of the retrobulbar vessels (Fischer's *r* to *z* test, p values, correlation coefficient *r*)

	Correlations of the fluorescein filling defects of the optic nerve head with	
	Significance level	Coefficient of correlation
OA PSV	NS	
OA EDV	NS	
OA RI	NS	
CRA PSV	p<0.01	r=-0.41
CRA EDV	p<0.01	r=-0.34
CRA RI	NS	
CRV minimum	NS	
CRV maximum	NS	
Temporal PCA PSV	NS	
Temporal PCA EDV	p<0.05	r=-0.29
Temporal PCA RI	p<0.05	r=0.29
Nasal PCA PSV	p<0.05	r=-0.34
Nasal PCA EDV	p<0.01	r=-0.38
Nasal PCA RI	p<0.05	r=0.28

NS = not significant.

OA = ophthalmic artery, CRA = central retinal artery, CRV = central retinal vein, PCA = short posterior ciliary artery, PSV = peak systolic velocity, EDV = end diastolic velocity, RI = resistive index.

Table 4 Correlations of the fluorescein filling defects and blood flow velocities of the retrobulbar vessels with functional and morphological parameters (Fischer's r to z test, p values, correlation coefficient r)

	MD	PSD	SF	CPSD	Cup to disc area ratio
Absolute filling defects of the optic nerve head	$p < 0.01$, $r = -0.43$	$p < 0.01$, $r = 0.44$	NS	$p < 0.01$, $r = 0.56$	$p < 0.01$, $r = 0.74$
OA PSV	NS	NS	$p < 0.05$, $r = 0.36$	NS	$p < 0.01$, $r = -0.49$
OA EDV	NS	NS	$p < 0.01$, $r = 0.53$	NS	NS
OA RI	$p < 0.05$, $r = 0.32$	NS	$p < 0.05$, $r = -0.35$	NS	$p < 0.05$, $r = -0.38$
CRA PSV	NS	$p < 0.05$, $r = -0.33$	NS	$p < 0.05$, $r = -0.35$	$p < 0.01$, $r = -0.63$
CRA EDV	NS	$p < 0.01$, $r = -0.44$	NS	$p < 0.01$, $r = -0.46$	$p < 0.01$, $r = -0.47$
CRA RI	NS	$p < 0.05$, $r = 0.38$	NS	$p < 0.05$, $r = 0.37$	NS
CRV minimum	NS	NS	NS	NS	NS
CRV maximum	NS	NS	NS	NS	NS
Temporal PCA PSV	NS	NS	NS	NS	NS
Temporal PCA EDV	NS	$p < 0.01$, $r = -0.44$	NS	$p < 0.05$, $r = -0.42$	$p < 0.05$, $r = -0.46$
Temporal PCA RI	NS	$p < 0.01$, $r = 0.45$	NS	$p < 0.01$, $r = 0.43$	NS
Nasal PCA PSV	NS	$p < 0.01$, $r = -0.48$	NS	$p < 0.01$, $r = -0.53$	NS
Nasal PCA EDV	NS	$p < 0.01$, $r = -0.51$	NS	$p < 0.01$, $r = -0.52$	$p < 0.01$, $r = -0.52$
Nasal PCA RI	NS	$p < 0.05$, $r = 0.37$	NS	$p < 0.05$, $r = 0.34$	$p < 0.05$, $r = 0.39$

NS = not significant.

OA = ophthalmic artery, CRA = central retinal artery, CRV = central retinal vein, PCA = short posterior ciliary artery, PSV = peak systolic velocity, EDV = end diastolic velocity, RI = resistive index.

DISCUSSION

The pathogenesis of glaucomatous optic neuropathy encloses haemodynamic alterations of the optic nerve head, the retina, the choroid, and the retrobulbar vessels. Their relevance for progression of the disease is unclear as well as the benefit of a possible therapeutical improvement of such perfusion parameters. As different devices of ocular blood flow assessment with different limitations are available, studies need to investigate the relation between blood flow parameters to further substantiate their significance. In the past, only few studies were performed investigating the relation of the various methods to assess blood flow of the eye.

A blue field and scanning laser ophthalmoscope comparison of macular capillary particle velocities revealed a discrepancy of the measured velocities. The blue field phenomenon seems to correspond to leucocyte motion through capillaries in the microvasculature in front of the photoreceptors. The precise location of these images remains unclear. In contrast, the scanning laser ophthalmoscope (SLO) enables the visualisation of erythrocytes within the capillary lumen of the fovea as hypofluorescent dark spots.⁴⁴ A comparison of retinal haemodynamics as measured by videofluorescein angiography with SLO and colour Doppler imaging parameters in patients with normal tension glaucoma (NTG) showed a correlation of the arteriovenous passage time with end diastolic velocities and resistive indices. No relation was found to the mean dye velocities in retinal arterioles. This suggests the impact of microvascular alterations in the pathogenesis of NTG.⁴⁵ In patients with central retinal vein occlusion, low blood flow velocities of the central retinal vein were related to longer retinal transit times in fluorescein angiograms. The amplitude of the intraocular pressure (measured with a pneumotonometer) rose with higher blood flow velocities in the ophthalmic artery. In contrast with the authors' expectations, a negative correlation was found for the diastolic perfusion pressure (ophthalmodynamometry) with the end diastolic velocity of the ophthalmic artery. The assumption of higher blood flow velocities related to higher perfusion pressure seems to oversimplify the situation, at least in central retinal vein occlusion, if one considers that vessel diameters are not measured in colour Doppler imaging.⁴⁶ The parameters "volume," "flow," and "velocity" of the Heidelberg retina flowmeter showed significant correlations with the blood flow velocities of the ciliary arteries, but not with any resistive index of the retrobulbar vessels. In contrast, the resistive index of the retrobulbar vessels measured by means of colour Doppler imaging tends to be the most striking parameter in

the assessment of disturbances in retrobulbar blood flow in glaucoma.⁴⁷

Various studies investigated blood flow velocities of the retrobulbar vessels in patient with NTG as well as in primary open angle glaucoma (POAG). Altered retrobulbar circulation is a constant finding in glaucomatous optic neuropathy. Most of the studies confirmed reduced end diastolic velocities associated with elevated resistive indices in the central retinal artery and the posterior ciliary arteries. Reduced peak systolic velocities of these vessels tended to be a less obvious phenomenon.⁴⁸⁻⁵⁶ Concerning the ophthalmic artery, the results are less evident. Though reduced blood flow velocities and increased resistive indices have been reported,^{51-53, 57} elevated as well as normal peak velocities were found in POAG.^{56, 58, 59}

The studies comparing patients with NTG and POAG confirmed no significant difference.^{14, 53, 56, 58} The differentiation of glaucoma patients by their optic nerve head appearance showed greater circulatory abnormalities of the retrobulbar circulation in patients with senile sclerotic optic discs compared to myopic, focal ischaemic, or generally enlarged discs—that is, higher resistive indices as a sign of higher downstream resistance.^{49, 60, 61} Several investigators found more striking alterations of blood flow velocities in patients with more advanced visual field loss and progressive disease.⁶²⁻⁶⁹

In this study, decreased blood flow velocities and higher resistive indices were found in all retrobulbar arteries of patients with NTG. The velocities and resistive indices were correlated with the visual field indices PSD and CPSD in the central retinal artery and the posterior ciliary arteries. As most patients with NTG had an early to moderate glaucomatous visual field loss as defined by the European Glaucoma Society, correlations with the parameters PSD and CPSD, that are especially increased in early glaucomatous visual field loss, appear comprehensible. The positive correlations with morphological parameters such as the cup to disc area ratio confirm similar findings by other investigators.^{14, 62} The ophthalmic artery interestingly had higher resistive indices in the control group and correlations with the MD and SF were inverse to our expectations. The interpretation of haemodynamic findings in this major retrobulbar vessel seems to be more complex, even more as the coefficient of reliability in a test/retest study revealed best values for the ophthalmic artery.¹³

Absolute fluorescein filling defects of the optic nerve head have been investigated since the 1970s. Filling defects in fluorescein angiograms, as a sign of capillary rarefaction of the superficial optic nerve head region, are correlated with

morphological and functional defects in glaucomatous optic neuropathy.^{24 25 34-36 38 70-86} The filling defects occur in patients with NTG and POAG and are highly specific compared to normals or patients with ocular hypertension.^{25 36 38 39 71 76 80} These results, corroborated by our study in NTG, confirm histological findings of the optic nerve head in glaucoma with a rarefaction of the capillary structure.⁸⁷⁻⁹⁰ A constant relation between nerve fibre loss and capillary density possibly indicates a secondary loss, although we found absolute filling defects in patients without visual field loss.⁹⁰

The absolute filling defects in the presented study were larger in patients with NTG compared to controls and correlated with functional and morphological data, as demonstrated in a previous study in NTG and POAG.²⁵ In addition, the absolute filling defects of the optic disc were correlated with velocity measurements of the central retinal artery and the posterior ciliary arteries assessed by colour Doppler imaging. The resistive indices of both posterior ciliary arteries were increased as the filling defects of the optic disc enlarged.

A higher downstream resistance in ocular blood flow may be caused by an elevated IOP, peripheral vasoconstriction particularly at the lamina cribrosa, vasospasms, vasosclerosis, or reduced cross section of the vascular bed—for example, capillary loss. Rheological factors contribute to the total peripheral resistance of a vascular segment as well. All these alterations have been postulated as significant to the pathogenesis of glaucomatous optic neuropathy, at least concerning the progression of the disease.^{2 3 5-8 11} Our findings emphasise the downstream resistance of retrobulbar vessels as an important parameter of the circulatory disturbances of the optic nerve head in glaucoma.

Circulatory defects of the optic nerve head—that is, capillary rarefaction lead on the one hand to longer diffusion distances and, as a consequence, limit the nutritional supply of the peripheral tissue. Impaired blood flow and vascular dysregulation may then cause ischaemia and malnutrition and trigger an apoptotic cascade.^{9 10} Ganglion cell death occurs and may cause at least progression of glaucomatous optic neuropathy. On the other hand could capillary rarefaction cause an increase in downstream resistance and, via this mechanism, reduce blood flow velocities of the central retinal artery and the short posterior ciliary arteries and increase their resistive indices?^{9 12}

The short posterior ciliary arteries of healthy subjects are not autoregulated in a way to maintain constant blood flow velocities to acute changes in IOP.¹ Studies with posture changes of healthy and glaucoma subjects revealed a deficient autoregulation of the central retinal artery, but not of the ophthalmic artery in POAG.⁹³ These studies underline the importance of possible alterations in blood flow of the central retinal artery and the posterior ciliary arteries as it relates to the perfusion of the optic nerve head.⁹

Our study implies a circulatory circulus vitiosus of impaired blood flow velocities of retrobulbar vessels and increased downstream resistance as measured by colour Doppler imaging and capillary loss in fluorescein images of the optic nerve head in glaucomatous optic neuropathy. A higher downstream resistance of the optic nerve head measured as fluorescein filling defects and reduced end diastolic velocities and higher resistive indices seems to be a significant factor in glaucomatous vascular pathology.

The consequences of these vascular deficits for visual outcome and progression of the disease, as well as the relation between mechanical and vasogenic pathomechanisms, need to be further investigated.

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