A "throttle" mechanism in the central retinal vein in the region of the lamina cribrosa

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Aims: To demonstrate a constriction in the central retinal vein in the region of the lamina cribrosa.

Methods: A prospective comparative interventional study of 13 controls and 19 patients with central retinal vein occlusion (CRVO) using colour Doppler imaging of the central retinal artery and vein in the region of the lamina cribrosa and optic nerve posterior to the globe.

Results: In controls peak velocities in the vein were higher in the region of the lamina cribrosa than the optic nerve, mean 175 mm/second (mm/s) and 49 mm/s respectively, $p < 0.0001$. The velocities in the artery were also higher in the region of the lamina cribrosa, mean 122 mm/s and 92 mm/s, $p = 0.007$. The variability of the velocities in the region of the lamina cribrosa was 7.4% in the artery and 15.2% in the vein. The mean ratio of the velocities in the vein (4.2 (SD 2.1)) was significantly higher than the mean ratio in the artery (1.4 (SD 0.4), $p < 0.0001$). In CRVO, the mean ratio in the vein was lower in the affected eyes (2.2 (SD 1.9), $p < 0.01$) and fellow unaffected eyes (2.2 (SD 1.0), $p = 0.003$) than controls. The values were stable in eight after radial optic neurotomy.

Conclusion: The presence of a constriction of the vein in the region of the lamina cribrosa can be inferred from the presence of higher blood velocities at this site than further back in the optic nerve. In CRVO there may be a more uniform narrowing of the vein along its course in the nerve. Neurotomy did not affect the measurements.

Retinal circulation is prone to occlusion in the veins.¹ The reasons for this have not been fully explained.² Even the anatomy of the central retinal vein is poorly described. Although a narrowing of the vein is suspected as it passes through the lamina cribrosa, descriptions of this have been scanty in postmortem eyes³ and have never previously been demonstrated in vivo. This narrowing has sometimes been blamed for the propensity of the central retinal vein to block at this point, perhaps by thrombus formation, causing the blinding condition of central retinal vein occlusion.⁴

Anatomically the central retinal vein in the nerve does not have any major branches and receives only a few very small venules draining the inner part of the optic nerve on its passage through the nerve.⁵ In this paper an assumption has been made that equal blood flow exists in all portions of the central retinal vein. Therefore if a narrowing exists in the vein in the region of the lamina cribrosa, the velocity of the blood flowing in the lumen of the vessel should increase at this site in comparison with other parts of the vein. In this study Doppler measurements were obtained from the central retinal artery and vein as they pass through the lamina cribrosa and through the optic nerve more posteriorly. A comparison of the blood velocities at the two sites was made to try to determine the likelihood of the artery or the vein being of reduced calibre at the lamina cribrosa in normal individuals.

In addition, patients with central retinal vein occlusion (CRVO) were examined to try to provide more information on the pathogenetic mechanism in this condition. CRVO results from incomplete blockage of the vein, probably at or just behind the lamina cribrosa, and Doppler blood velocities have been shown in the past to be altered.²

Opremcak described radial optic neurotomy (RON) as a means to decompress the suspected constriction of the vein in the lamina cribrosa by incising the supporting ring of the lamina cribrosa with a knife.⁶ In this he has presumed that there is a constriction of the vein, that it is a potential cause of

CRVO, and that the RON procedure is effective in decompressing the vein. None of these has been proven—indeed the efficacy of RON is uncertain.⁷ Blood velocities were therefore also examined in patients with ischaemic CRVO who received RON.

METHODS

Colour Doppler imaging

The method of CDI has been described previously.⁸ In this study a Medison SA-6000C (Diagnostic Sonar, Livingston, UK) was employed with a 10 MHz transducer. The equipment provides an Ispta of 910 mW/cm² during pulse Doppler acquisition which is well below the levels recorded to cause damage to ocular tissue.^{9–11} The patient was examined in the supine position. The examiner placed his hand on the brow of the patient to avoid pressure on the globe by the transducer. A B-scan was obtained to identify the optic nerve and the central retinal blood vessels located with the colour Doppler modality. Using pulsed Doppler with an examination area of 1.4×1.6 mm, spectral Doppler values were measured from the artery and the vein simultaneously. Measurements were taken of the blood velocities in the central retinal artery and vein in the optic nerve approximately 0.5 cm posterior to the globe and as they passed through the optic nerve head, at the site of the lamina cribrosa. The latter site was often identified as a high signal on colour Doppler imaging before pulsed Doppler was used to obtain blood velocities. In the artery peak systolic velocities (PSV) were obtained. In the vein peak velocity (Vmax) was measured. These were chosen as the relatively low blood velocities of these vessels can result in reproducibility errors in other measures such as Vmin and end diastolic velocities.¹² The reproducibility of these measures in the optic

Abbreviations: CRA, central retinal artery; CRV, central retinal vein; CRVO, central retinal vein occlusion; PSV, peak systolic velocities; RON, radial optic neurotomy

Table 1 The Doppler results are shown from the control population for the two sites (optic nerve behind the globe, optic nerve (ON) and the lamina cribrosa (LC)) in the central retinal artery (CRA) and vein (CRV)

	CRA ON mm/s	CRA LC mm/s	CRV ON mm/s	CRV LC mm/s	CRA ratio	CRV ratio
Mean	92	122	49	175	1.4	4.2
SD	27	36	17	44	0.4	2.1
Lower 95% CI	75	100	38	149	1.1	2.9
Upper 95% CI	109	144	59	201	1.6	5.4
p Value	=0.007		<0.0001		<0.0001	

Ratios of the velocities are shown in the two vessels. p Values are for the comparison of the results in the two columns above.

nerve has been described previously. The variability of the velocities at the lamina cribrosa was tested by performing masked measurements on two occasions, within one hour of each other, on 15 eyes (7 with CRVO, 7 fellow unaffected eyes and 1 control). The results were tested according to the methods of Bland and Altman¹³ and a coefficient of variation calculated as: coefficient of variation = (SD of the mean difference/mean) %.

A ratio of the PSV was calculated to indicate whether the velocities increased at the lamina cribrosa in the artery: arterial lamina cribrosa/optic nerve peak velocity ratio = PSV at lamina cribrosa /PSV at optic nerve

Similarly a ratio of the Vmax was calculated to illustrate whether the velocities increased at the lamina cribrosa in the vein: venous lamina cribrosa/optic nerve peak velocity ratio = Vmax at lamina cribrosa/Vmax at optic nerve.

Controls and patients

Thirteen individuals without ocular disease were examined and measurements were available from all. Twenty one patients

with CRVO were investigated but Doppler measurements were unobtainable from two patients with ischaemic CRVO and these patients were excluded. Four fellow eyes with ocular disorders including previous CRVO were excluded from analysis. The effect of radial optic neurotomy on the blood velocities was examined in a small group of patients with CRVO, preoperatively, at 1–2 months (early postoperative period) and at 4–6 months (the late postoperative period). The definition of ischaemia has been previously described.¹⁴ A description of the surgical procedures has been published.⁷

Statistical analysis

The results were analysed by Student’s two-tailed t test and Spearman rank correlation as appropriate. When no velocities were detectable the results were removed from analysis. Institutional review board/ethics committee approval was obtained. Fully informed consent was obtained and the study adhered to the tenets of the Declaration of Helsinki.

RESULTS

The Doppler velocities were recorded in 13 controls with a mean age of 56 years (SD 17.7 years, range 26–77), 8 males and 5 females, 6 left eyes and 7 right eyes, and the ratios calculated. The results are shown in table 1.

The velocities in the artery were significantly higher at the lamina cribrosa compared with the optic nerve, mean 122 mm/second (mm/s) compared with 92 mm/s respectively, p = 0.007. The velocities in the vein were significantly higher at the lamina cribrosa compared with the optic nerve, mean 175 mm/s compared with 49 mm/s respectively, p<0.0001 (fig 1). The reproducibility of the velocities in the vessels at the lamina cribrosa was 7.4% in the artery and 15.2% in the vein (table 2).

The venous lamina cribrosa/optic nerve peak velocity ratio, mean 4.2 (SD 2.1), was significantly higher than the arterial lamina cribrosa/optic nerve peak velocity ratio, mean 1.4 (SD 0.4, p<0.0001). There were no correlations with the velocities and age of the individual.

Table 2 The values for the reproducibility of the blood velocities obtained in the region of the lamina cribrosa from repeat measurements by the same observer on two occasions are provided for 15 eyes

	CRV	CRA
(n)	15	15
Mean (mm/s)	143	85
Range (mm/s)	34–300	55–142
Mean difference between two examinations (mm/s)	4.7	5.9
SD (mm/s)	21.5	6.6
Coefficient of variation (%)	15.2	7.4

CRV, central retinal vein; CRA, central retinal artery.

Figure 1 The velocities are shown in the central retinal artery (above the baseline) and the central retinal vein (below the line) in the optic nerve posterior to the globe (left scan) and in the region of the lamina cribrosa (right scan) of the same eye. The velocities in the vein in particular are increased in the region of the lamina cribrosa.

Figure 2 A very high velocity in the central retinal vein can be seen in this eye in the region of the lamina cribrosa.

Central retinal vein occlusion

Nineteen patients with CRVO were examined mean age 67 years (SD 14 years, range 22–89) which was not statistically different to the age of the controls. There were 12 right eyes and 7 left with 14 males and 5 females with a mean duration from onset of the CRVO of 3.5 (SD 3.2) months. There was a reduction in the velocities in the artery at the optic nerve in the patients with CRVO (mean 67 (SD 25) mm/s) in comparison to their fellow unaffected eyes (mean 83 (SD 27) mm/s, $p = 0.03$) and the controls (mean 92 (SD 27) mm/s, $p = 0.008$) (table 3).

In the vein the velocities in the optic nerve were similar in the eyes with CRVO (mean 46 (SD 31) mm/s), their fellow unaffected eyes (mean 52 (SD 19) mm/s), and the controls (mean 48 (SD 17) mm/s). There were no differences between the arterial lamina cribrosa/optic nerve peak velocity ratios obtained in the controls, the eyes with CRVO and their fellow eyes. The venous lamina cribrosa/optic nerve peak velocity ratios were significantly different in the eyes with CRVO and the controls, mean 2.2 (SD 1.9) and 4.2 (SD 2.1) respectively, $p < 0.01$. Also there was a significant difference in the fellow eyes of those with CRVO (mean 2.2 (SD 1.0)) and the controls (mean 4.2 (SD 2.1), $p = 0.003$).

Effects of radial optic neurotomy

In the eight patients with ischaemic CRVO receiving radial optic neurotomy mean venous lamina cribrosa/optic nerve peak velocity ratio was 1.8 (SD 0.7) preoperatively, 3.9 (SD 3.2, $p = 0.08$) in the early postoperative period and 1.9 (SD 1.2, not

Table 4 The effects of radial optic neurotomy on the ratios in the central retinal vein

Parameter	Preoperatively	1–2 months postoperatively	4–6 months postoperatively
Mean	1.8	3.9	1.9
n	8	8	6
SD	0.7	3.2	1.2
Lower 95% CI	1.3	1.3	0.5
Upper 95% CI	2.4	6.6	3.1

$p = 0.08$ compared with preoperatively

significant) in the late postoperative period. Two patients showed very high postoperative ratios of 8.5 and 9.0 (tables 4 and 5, fig 2).

There was no effect on the blood velocities in the optic nerve in the artery (preoperative mean 68 (SD 31) mm/s, early postoperative mean 62 (SD 21) mm/s, and late postoperative mean 64 (SD 38) mm/s) and vein (preoperative mean 38 (SD 14) mm/s, early postoperative mean 29 (SD 9) mm/s, and late postoperative mean 35 (SD 15) mm/s) after neurotomy. The numbers of patients were too small to relate to visual outcome. No patient developed neovascular glaucoma.

DISCUSSION

The velocities in the central retinal artery and vein were significantly higher at the lamina cribrosa than in the optic nerve in normal individuals and in patients with CRVO. This was particularly noticeable in the vein. A change in the angle of incidence of the ultrasound to the direction of blood flow can affect the velocity calculations in Doppler examinations. The direction of travel of the artery and the vein in the optic nerve is parallel to the ultrasound beam and therefore errors of angulation are likely to be minimal. In addition, angle correction was applied to compensate during the examination. Even so the slight changes in the artery may be due to undetected alterations in the angle of the Doppler signal to the flow in the artery. The disproportionately larger change in the vein compared with the artery suggests that angle error is not the main reason for the large change in velocities in this vessel and therefore suggests that anatomical differences exist in the vein between the two sites (in the optic nerve 0.5 cm behind the globe and in the region of the lamina cribrosa). The increase in the velocities at the lamina cribrosa is likely to be due to a reduction in the calibre of the vessel at this site because blood flow should be constant along the vein. Indeed the results of mean peak velocity in the vein are higher than in the artery at the lamina cribrosa. If it is assumed that inflow equals outflow,

Table 3 The results of the ratio of velocities in central retinal artery and vein in the optic nerve posterior to the globe and in the region of the lamina cribrosa, in controls and patients with central retinal vein occlusion (CRVO)

	Central retinal artery ratio			Central retinal vein ratio		
	Control	CRVO affected eye	CRVO fellow eye	Control	CRVO affected eye	CRVO fellow eye
Mean	1.4	1.3	1.4	4.2	2.2	2.2
n	13	19	15	13	19	15
SD	0.4	0.4	0.4	2.1	1.9	1.0
Lower 95% CI	1.1	1.1	1.2	2.9	1.3	1.6
Upper 95% CI	1.6	1.5	1.6	5.4	3.1	2.7
	No significant differences				$p < 0.01$ vs controls	$p = 0.003$ vs controls

The ratios in the vein were significantly smaller in the vein in the patients with CRVO compared with the controls.

Table 5 The ratios from the central retinal vein before and after radial optic neurotomy

Patient	Preoperatively	1–2 months postoperatively	4–6 months postoperatively
1	1.7	4.5	1.1
2	1.2	1.2	0.9
3	1.4	1.2	Missing data
4	1.7	2.8	2.0
5	2.4	8.5	4.1
6	2.8	9.0	1.1
7	2.5	1.0	Missing data
8	1.0	3.3	1.9

the diameter of the vein must be smaller than the artery at the lamina cribrosa. This illustrates that the vein is subject to greater shear stress than the artery at this site. The increased shear stresses could cause endothelial damage and explain the presence of endothelial proliferation with or without thrombus formation in CRVO. The results in this study appear to be the first demonstration in vivo of a constriction in the vein in the region of the lamina cribrosa.

The reproducibility of the velocities, as measured by intraobserver coefficient of variation, at the lamina cribrosa (15.2% for the vein and 7.4% for the artery) were similar to other sites in the orbit (ophthalmic artery of 5.2%, central retinal artery in the optic nerve 12.1% and central retinal vein in the optic nerve 13.5%¹²). However the results show greater variation than is desirable and demonstrate a potential flaw in the technique reflecting the technical difficulty of obtaining readings from a small site in the eye. Despite the variability the measure was readily detectable in the normal individuals and may be useful for future study of eyes with and without disease.

To illustrate the degree of constriction and allow comparison between groups ratios of the values, venous lamina cribrosa/optic nerve peak velocity ratio and arterial lamina cribrosa/optic nerve peak velocity ratio were calculated. The observation that the values were higher in the controls than in the patients with CRVO suggests that the narrowing in the vein is a normal feature and that it may be important for normal function of retinal circulation. One possibility is that the constriction is present to allow a drop in internal pressure in the vein as it exits from the relatively high pressure environment of the eye to the lower pressure extraocular environment. Without the constriction the blood leaving the eye would accelerate as the change in pressure would induce an increase in kinetic energy according to the Bernoulli principle: $\text{Pressure} \times (\text{kinetic energy/volume}) = \text{Constant}$.

This acceleration of blood could cause collapse of the intraocular vein. This could be undesirable because a collapsed tube requires extra energy to reopen. Collapse may also damage the endothelium leading to the adherence of thrombus as indicated by Green *et al* in CRVO.⁴ Reducing the diameter of the vein as the pressure drops—that is, in the region of the lamina cribrosa—would maintain the intraluminal pressure of the vein inside the eye, preventing acceleration of the blood from the eye while reducing the intraluminal pressure in the vein outside of the eye.

In CRVO the venous lamina cribrosa/optic nerve peak velocity ratio was lower in the affected eye. It is possible that eyes affected by CRVO might have alteration in the anatomy of the vein at the LC—for example, early collateral formation—which would affect the results. However the results were also lower in the fellow unaffected eyes. Since fellow eyes are at risk of CRVO it suggests an association with a lower venous lamina cribrosa/

optic nerve peak velocity ratio and CRVO. Therefore a constriction of the vein far from being detrimental to the vein and a potential cause of the CRVO is more likely to be a feature of a healthy eye. In an anatomical study of serial sections of healthy eyes removed postmortem for the harvesting of corneas, the CRV in a young patient narrowed at the lamina cribrosa and then increased in cross-sectional area more posteriorly, while in an older group the vein narrowed and remained narrow.³ A normal CRV may have the former configuration causing a high venous lamina cribrosa/optic nerve peak velocity ratio and vasculopathic individuals may possess the latter providing a lower venous lamina cribrosa/optic nerve peak velocity ratio. In this study no correlation was found with age but the number of individuals examined was small.

Opremcak described the method of radial optic neurotomy to release the pressure on the vein in the lamina cribrosa in a putative compartment syndrome. In our study of eight patients the venous lamina cribrosa/optic nerve peak velocity ratio was dramatically increased in some patients in the short term postoperatively suggesting that the constriction of the vein was increased after RON temporarily. This would be consistent with the findings of an animal model of RON in which the effect of the surgery was to induce swelling of the optic nerve head thereby exacerbating any potential compartment syndrome in the nerve.¹⁵ Such changes in the venous lamina cribrosa/optic nerve peak velocity ratio may not be beneficial to the eye. The results tend to refute the idea that RON decompresses the vein at this site.

In conclusion, it is possible to detect and measure the effects of a constriction of the central retinal vein in the region of the lamina cribrosa in normal individuals. This constriction may be less in eyes at risk of CRVO. The constriction is not relieved by RON.

Competing interests: None.

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