The effects of carotid endarterectomy on ocular haemodynamics

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Abstract

Purpose To determine the profile of blood flow velocities and resistive indices in the ocular vessels of patients with atherosclerotic carotid disease and characterise the effect of endarterectomy on these parameters. Methods Following a preliminary study on healthy volunteers, ophthalmic colour Doppler ultrasound examinations were performed on 27 male and 11 female patients with carotid disease. These measurements were compared with central retinal artery perfusion pressures and intraoperative internal carotid artery stump pressures. Results Significant changes were seen on the endarterectomised side. The peak systolic velocity in the ophthalmic artery, and resistive indices in the ophthalmic artery, central retinal artery and nasal posterior ciliary artery, rose from pre-operative values. No correlation between colour Doppler ultrasound measurements and intraoperative internal carotid artery stump pressures was present. When compared with ophthalmodynamometry readings, a

relationship was noted with maximum velocities in the central retinal vein. *Conclusion* Carotid endarterectomy alters the haemodynamics in selected vessels of the ocular circulation as measured by colour Doppler ultrasound, but more work is required to determine the clinical utility of this investigative modality.

Key words Atherosclerotic, Colour Doppler ultrasound, Endarterectomy

The relationship between atherosclerotic carotid disease and conditions of ophthalmic vascular insufficiency has been recognised since Fisher in 1952 described a short series of patients who had suffered strokes following transient monocular blindness.¹ Amaurosis fugax resulting from a thrombo-embolic event in the eye is a common presenting complaint among patients with carotid disease. More severe but less frequent is the problem of hypotensive retinopathy and the ocular ischaemic syndrome.²

Many techniques have been developed for the measurement of ocular blood flow and velocity. Each has significant disadvantages when used on human subjects and has therefore a limited place in clinical settings.³ Erickson *et al.* in 1989 were the first to report the application of colour Doppler ultrasound (CDU) imaging to retrobulbar vessels.⁴ Since then there has been increasing interest in its use and several groups have been able to confirm its practicability and adequate reproducibility in selected vessels.^{5–9}

Colour Doppler analysis of the ophthalmic circulation in the presence of atherosclerotic carotid disease has been the subject of studies by Wolfgang, Hu and their respective collaborators.^{10,11} Wolfgang *et al.* looked at one patient and concluded that CDU findings correlated with the more established modalities, namely fluorescein angiography and ophthalmoplethysmography. Hu's work suggested that an inverse relationship exists between ophthalmic and central retinal artery velocities and the degree of carotid artery stenosis.

Our study was directed at characterising changes in the velocities and resistive indices of selected retro-orbital vessels following carotid endarterectomy. We also sought correlations between velocity measurements by CDU and ophthalmodynamometry readings, as well as intraoperative internal carotid arterial stump pressures. A component of this investigation compared the reproducibility of ocular CDU between normal healthy volunteers and older vasculopathic patients.

Methods

Prior approval was obtained from the Geelong Hospital Research and Ethics Advisory Committee. Every participant provided written informed consent after full explanation by the principal investigator.

A preliminary study was undertaken to establish the reproducibility of ocular CDU. Twenty healthy volunteers were recruited from among the hospital staff (age 23–60 years, median 26 years; 6 males). In 10 subjects the ophthalmic artery (OA) and central retinal Y.M. Wong 🖂 I.B. Faris Melbourne University Department of Surgery The Geelong Hospital Geelong Victoria 3220 Australia Tel: +61 (03)5226 7899 Fax: +61 (03)5226 7019 I.B. Clark Ophthalmology Unit The Geelong Hospital Geelong Victoria 3220 Australia C.B. Styles IA Kiss Department of Medical Imaging The Geelong Hospital Geelong Victoria 3220 Australia

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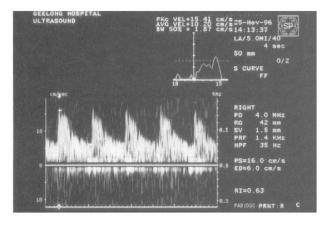


Fig. 1. Spectral analysis of ophthalmic artery on the operated side. Pre-operative peak systolic velocity (PSV) was 16 cm/s.

artery (CRA) were assessed, while in the remainder the central retinal vein (CRV) and the nasal (NPCA) and temporal (TPCA) posterior ciliary arteries were examined. All examinations were performed in the supine position. A brief medical and ophthalmic history was taken and vital signs recorded prior to each scan, since marked fluctuations in systemic blood pressure have an effect on ocular blood flow velocities.^{12,13} The brachial blood pressure and radial pulse rate were checked for variability of less than 20% between the first and second measurements.

A Diasonics Master Series colour Doppler scanner (Diasonics, USA) with a 5 MHz linear array transducer placed lightly on the closed upper eyelid was utilised. Coupling gel was applied to optimise contact. The relevant vessel was located and spectral analysis acquired with a 1.5 mm sample gate (1.2 mm when applied to PCA) after correcting for the Doppler angle where necessary. For PCAs, this angle was assumed to be 0° since we were unable to image an adequate length of these vessels. The OA was studied immediately after it crossed the optic nerve on its medial side, CRA and CRV 2–4 mm posterior to the optic disc within the substance of the optic nerve, and NPCA and TPCA within 5 mm of the posterior wall of the globe on the nasal and temporal sides of the optic nerve respectively. Both eyes were assessed in succession over 30 min. This examination was repeated 22-26 h later with reference to the initial scan in order to best approximate the site of measurement and direction of gaze.

Mean values of the peak systolic velocity (PSV) (Fig. 1), end-diastolic velocity (EDV), resistive index (RI), maximum venous velocity (V_{max}), minimum venous velocity (V_{min}) and venous pulsitility index (VPI) were derived from three waveforms in each vessel. The RI was defined by RI = (PSV – EDV)/PSV and the VPI by VPI = ($V_{max} - V_{min}$)/ V_{max} .¹² The coefficient of variation (CV) of those three parameters for all five vessels was calculated based on the equation: CV = (standard deviation of the mean difference/grand mean) 100%.

Subjects for the main body of the study were recruited from patients referred to the vascular surgery unit and ultrasound department. A total of 38 patients (27 men, 11 women; age range 53–83 years), consented to participate of whom 15 were being treated conservatively and classified as the non-operative group. Only one of these patients had symptoms of cerebral ischaemia. The remaining 23 subjects proceeded to unilateral internal carotid artery endarterectomy and one to a common carotid endarterectomy. There were three exclusions from this group. The first withdrew following a postendarterectomy wound infection, a second patient had a more than 20% decrease in blood pressure on the followup visit, and the final subject was excluded after a vessel was misidentified as the OA on the pre-operative scan. Of the 20 patients 9 were asymptomatic, 4 presented with amaurosis fugax and 7 with transient ischaemic attacks.

Each subject in the non-operative group had two ocular CDU scans performed 7 (mean) weeks apart. A protocol similar to that described above was applied on both visits. Every subject had the velocities in the OA, CRA and CRV measured and, in addition, seven had the NPCA assessed. TPCA was excluded as it was the least reproducible in our hands. There was a median of 9 weeks between the carotid duplex scan, which detected an average stenosis of 75%, and the initial ocular scans. In addition, an ophthalmic examination was conducted routinely. Visual acuity was determined with a Snellen chart at 6 m and intraocular pressures measured using a Goldmann applanation tonometer. Fundoscopic examination, and estimation of diastolic CRA pressure by hand-held Bailliart ophthalmodynamometer (Inami, Japan) were performed by an observer who was masked to the results of both carotid and ocular ultrasound. CRA pressure readings were reported as the mean of three measurements. Pupillary dilatation was achieved with 1% tropicamide drops and corneal anaesthesia with 0.4% oxybuprocaine. Automated perimetry (Octopus, Interzeag, Switzerland) and fundal photography (Topcon, Japan) were also included. However, only tonometry and ophthalmodynamometry were repeated at the second visit. In three patients the CRA pressures could not be determined with confidence on the second visit. A further three did not have measurements taken on the initial appointments. Of the 24 visits with reportable CRA pressures, 20 were performed in conjunction with ocular blood flow velocity recordings.

All operative subjects had had carotid duplex scans on entry to the study with an average stenosis of 81% and a range of 50–95% on the operated side. Doppler grading of carotid stenoses (Table 1) was based on criteria of

Table 1. Carotid duplex ultrasound grading of carotid stenosis

PSV (cm/s)	Stenosis (%)	
<120	30+	
120–150	50+	
150–170	60+	
170–220	60–70	
250	70+	
250-290	70–80	
>300	80+	
Systolic/diastolic blurring	90+	

PSV, peak systolic velocity.

Table 2. Coefficient of variation (%) for PSV, EDV, RI and VPI in normal subjects

	PSV (cm/s)	EDV (cm/s)	RI	VPI
OA	7.0	16.4	4.0	
CRA	10.3	13.3	6.8	-
TPCA	14.8	19.8	12.3	_
NPCA	11.5	14.4	6.8	_
CRV	10.8	11.0	-	9.3

PSV, peak systolic velocity; EDV, end-diastolic velocity; RI, resistive index; VPI, venous pulsatility index; OA, ophthalmic artery; CRA, central retinal artery; TPCA, temporal posterior ciliary artery; NPCA, nasal posterior ciliary artery; CRV, central retinal vein.

Gerraty et al.¹⁴ The time span between the pre-operative carotid duplex and ocular scans ranged from 1 to 39 weeks (median 12 weeks). In 16 patients ocular CDU was done within a fortnight before surgery. Post-operative readings were obtained an average of 6 weeks following the procedure. One patient had had a vitrectomy for phacolytic vitritis 21/2 weeks prior to the second assessment. Every subject had the velocities in the OA (Fig. 2), CRA and CRV measured and, in addition, 13 had the NPCA assessed. Ophthalmic assessment as described above was also conducted. Intraoperative internal carotid artery systolic pressures were determined after the arteries had been exposed and the external and common carotid arteries clamped. A 21G butterfly needle connected to a transducer was then inserted into the common carotid artery distal to the clamp.

Results

Normal subjects

The most reproducible criteria in the normal subjects were the RI and PSV in all vessels except the TPCA (Table 2). In the remaining four vessels, the PSV and RI coefficients were close to or less than the arbitrary 10% threshold. Every vessel was detectable in these participants.

Non-operative vascular patients

Reproducibility in the group of non-operative vascular patients is shown in Table 3. The RI was again the most reproducible parameter, especially when derived from arterial measurements. However, the PSV was only

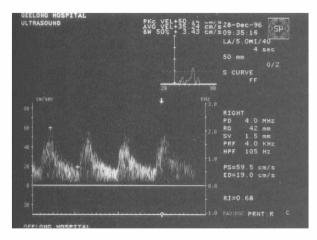


Fig. 2. Spectral analysis of ophthalmic artery on the operated side. Post-operative PSV was 59.5 cm/s.

moderately reproducible, with CV approximating 20%, 2–3 times that of healthy subjects. Calculations for EDV revealed smaller increases when compared with the first group. We were unable to obtain measurements of the NPCA in two of the seven patients in whom this was attempted.

Correlations between measurements

Eleven non-operative and 15 pre-operative subjects were examined for a correlation between pressure readings by ophthalmodynamometry and OA, CRA and CRV velocities in a total of 52 eyes and NPCA in 27 eyes. Spearman's rank correlation demonstrated a significant relationship between ophthalmodynamometry and only one parameter: the V_{max} in the CRV ($r_{\rm S} = -0.293$; p < 0.05).

Operative vascular patients

There was no significant correlation between systolic intraoperative internal carotid artery stump pressures and pre-operative CDU parameters in 18 operative vascular patients.

On the operated side, the median PSV in every vessel studied rose following surgery (Table 4) but was statistically significant only in the OA (Wilcoxon statistic = 186.0; p = 0.003), as depicted in Fig. 3. No significant change was detected in the contralateral ocular vessels (Fig. 4) nor in the EDV on either side.

There was a significant increase in the post-operative RI of the OA (Wilcoxon statistic = 166.5; p = 0.023), CRA (Wilcoxon statistic = 185.0; p = 0.003) and NPCA (Wilcoxon statistic = 28.0; p = 0.022) on the endarterectomised side (Figs. 5–7). As for the other parameters, no changes were seen on the opposite side.

There were minor elevations in the CRA perfusion pressure on both sides after surgery, neither of which was statistically significant (Table 5). Measurements were performed on 16 patients but a pre-operative measurement in one eye (non-operated side) was not possible due to active vitritis.

Discussion

The preliminary study involving healthy normal subjects established that it is possible to achieve adequately reproducible results, in especially the RI and PSV. Consistent with other studies we had most difficulty

Table 3. Range, mean, standard deviation (SD) and coefficient of variation (CV) for PSV, EDV and RI in non-operative vascular patients

	Range (cm/s)	Mean (cm/s)	SD (cm/s)	CV (%)
PSV				
OA	14.97-68.13	32.55	11.56	20.30
CRA	4.07-36.4	13.05	6.12	18.44
NPCA	6.43-24.23	12.31	3.97	16.26
CRV (V _{max})	4.27-18.3	7.55	2.49	21.38
EDV				
OA	3.13-28.57	7.72	5.02	28.58
CRA	1.83-8.1	3.73	1.43	15.18
NPCA	2.05-6.03	3.41	0.91	18.73
CRV (V _{min})	3.1–7.53	4.52	1.05	15.05
य				
OA	0.45-0.87	0.76	0.09	3.23
CRA	0.46-0.84	0.69	0.08	3.47
NPCA	0.57-0.78	0.72	0.05	4.15
CRV (VPI)	0.16-0.6	0.38	0.09	12.85

Abbreviations as in Table 2.

with the PCAs due to the anatomical characteristics of this group of vessels.^{6,9} However, a CV of 6.8% for the NPCA resistive index suggests that attempts at measurements in these arteries may provide useful data. The marked difference in reproducibility between the NPCA and TPCA may be explained by the fact that the majority and largest short PCAs pierce the sclera on the temporal side of the optic nerve.¹⁵ Greenfield and associates noted that there was no significant difference between velocities in the NPCA and TPCA.¹³ Therefore, for subsequent stages in our study, we opted to look at the NPCA as it had the better reproducibility. The EDV was generally less reproducible and this concurs with findings by Baxter and Williamson.⁶ It may be due to the technical difficulty in distinguishing the trough of the waveform from background noise, especially at lower velocities.

Vasculopathic patients were a more difficult population to investigate with CDU. The PSV and EDV had increased CV but the reproducibility of arterial RIs was conserved. This suggests that Doppler angle errors, which influence PSV and EDV but not the RI, are a major factor. Such errors probably occur because of variation in the transducer's position from test to test.⁹ It is virtually impossible to re-create the relative positions of a handheld probe in three-dimensional space and an eye which is free to move. Baxter and Williamson hypothesised that the presence of arteriopathic disease in the posterior ciliary arteries would lead to unsatisfactory spectral analysis in spite of adequate colour flow identification of the vessels.¹⁶ The inability to detect NPCA in some patients may be due to stenotic lesions reducing blood

Table 4. Median of PSV (cm/s) before and after surgery on the operated side

	Pre-operative	Post-operative	
OA	23.88	36.68	
CRA	9.92	12.32	
NPCA	9.83	10.50	
CRV	6.72	6.87	

Abbreviations as in Table 2.

flow beyond the sensitivity of current CDU equipment. However, in the subgroup of patients who underwent surgery, the mean pre- and post-operative PSVs on the non-operated side remained the same. The variation appeared to be less than in the reproducibility studies. There was little difference in the mean velocities between this group and the healthy participants in our study and that of Greenfield *et al.*¹³ The RI was higher in the CRA, NPCA and CRV.

An isolated *negative* correlation between diastolic perfusion pressures in the CRA as measured by ophthalmodynamometry and maximum CRV velocities was an unexpected result. If it is true that CRV velocities provide a better indication of retinal perfusion, then this would suggest that an increase in pressure does not

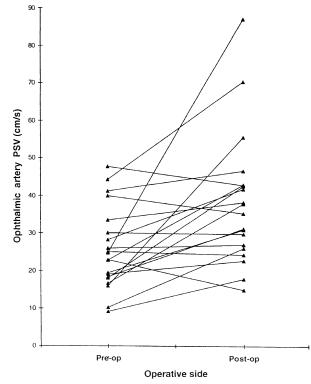


Fig. 3. Changes in PSV in the ophthalmic artery on the operated side before and after surgery.

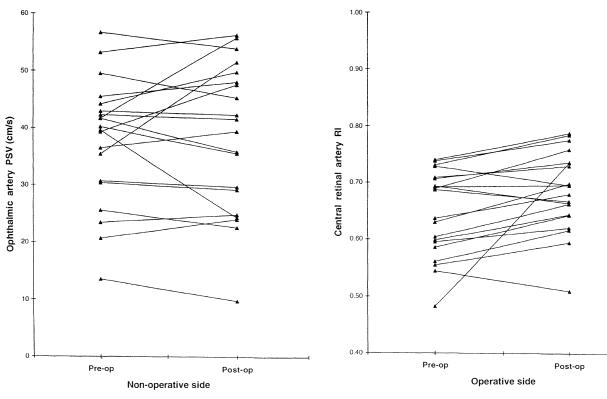


Fig. 4. Changes in PSV in the ophthalmic artery on the non-operated side before and after surgery.

necessarily imply a corresponding increase in arterial flow. The absence of any relationship with arterial velocities is inconsistent with the published results of two previous studies. One by Williamson and co-workers also obtained a negative correlation but with PSVs in the OA.¹⁷ At the same time, they found a positive

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Ophthalmic artery

Fig. 6. Changes in RI of the central retinal artery on the operated side before and after surgery.

correlation with RI values in the same artery. A second study by Hu *et al.*¹¹ discovered a positive correlation with systemic velocities in the CRA but not the OA.¹¹ The above combination of findings underscores the fact that difficulty remains in the interpretation of such indirect measurements of the ophthalmic circulation. As pointed

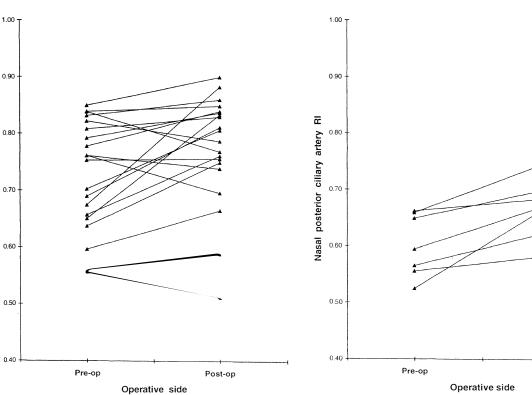
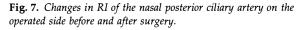


Fig. 5. Changes in resistive index (RI) of the ophthalmic artery on the operated side before and after surgery.



Post-op

Table 5. Median of ophthalmodynamometry measurements

	Operative side		Non-oper	rative side
	Pre-op.	Post-op.	Pre-op.	Post-op.
Median (mmHg)	42.0	45.0	42.5	43.4

There was no significant difference between the pre- and postoperative values.

out by Williamson, this may be secondary to inherent inaccuracies of the techniques utilised (despite good reproducibility, in our study, of ophthalmodynamometry) or highly complex interrelationships between the haemodynamic parameters of flow, perfusion pressure and velocity.

Authors who have looked at patients with carotid stenosis and ocular ischaemia have demonstrated that carotid endarterectomy or bypass has resulted in improved visual symptoms and signs.^{18–20} This provides reasonable evidence that such surgery leads to increased blood flow to the ipsilateral eye. However, Sivalingam and associates,²¹ who reviewed case histories of 52 consecutive patients seen at the Wills Eye Hospital with the diagnosis of ocular ischaemic syndrome, were unable to demonstrate sustained visual benefit of carotid endarterectomy or superficial temporal artery-middle cerebral artery bypass. More recently Ward, Geroulakos, Mawn and their respective collaborators have focused on the effects of such surgery on the ophthalmic circulation using CDU.²²⁻²⁴ Our finding of a statistically significant elevation in the OA PSV but not the EDV agrees with that of Geroulakos et al.²³ Ward et al.,²² in their case reports of only three patients, noted a linear relationship between velocities in the OA, CRA and PCA, that is, as the OA velocities improved so did velocities in the CRA and NPCA. This is an observation not apparent in our work. Although there was a rise in the median values of both the CRA and NPCA, statistical significance was not achieved. Mawn et al.24 noted an increase from preoperative values of mean systolic values in the CRA and PCA, but these did not achieve statistical significance. No comment was made regarding the outcome of OA measurements.

Autoregulation may be responsible for maintaining these parameters at the stable levels that we have observed. It may be that there is no requirement for increased flow as only in one of these patients was there a question of chronic ocular ischaemia. The fact that the CRA diastolic perfusion pressure also remained statistically unchanged seems to support this idea. It is possible that perfusion via the CRA and NPCA, which only supply the globe, is more tightly regulated than flow in the OA. Velocity measurement in the CRV is thought to be a more reliable indicator of ocular perfusion because of its inability to autoregulate.⁷ If this is true, then the lack of significant alteration to the CRV velocities is also consistent with the above hypothesis. However, the study by Geroulakos et al.²³ showed improvements in retinal arteriole PSV and macula photostress recovery times, which suggest that ocular

blood flow is augmented by surgery. It would have been helpful to know the reproducibility of CDU when applied to the retinal arterioles. Using ocular pneumoplethysmography, Araki and co-workers²⁵ demonstrated elevated retinal and choroidal pulse pressures post-operatively, which would also point to a possible increase in ocular perfusion. We must emphasise that the situation might be entirely different in patients with established hypotensive retinopathy or the ocular ischaemic syndrome (OIS). It seems likely that in these patients ocular volumetric blood flow does indeed increase with surgery, as evidenced by resolution of clinical features of OIS and the well-recognised postoperative elevation in intraocular pressure in some patients with rubeosis iridis that is thought to be secondary to hyperperfusion of the ciliary body.¹⁸⁻²⁰ The effect of endarterectomy in this population merits further investigation by CDU.

Ho and associates²⁶ have shown that subjects with OIS have reduced CRA and PCA PSV. Every patient in their series also had confirmed severe unilateral or bilateral atherosclerotic carotid disease. In our sample population (28 eyes), the mean NPCA PSV was similar to that of our healthy participants (20 eyes), who had a mean of 10.4 cm/s. Similarly, the mean CRA PSV was not reduced in our vasculopathic subjects. In that same study, Ho et al. noted that three OIS sufferers who experienced visual loss were the only subjects in whom neither the temporal nor nasal PCAs were detectable. On this basis, they suggested that PCA hypoperfusion was a major prognostic factor and might be useful in determining the most appropriate form of treatment. If carotid endarterectomy improves PCA blood flow, then these patients stand to benefit the most. On the other hand, those in whom the PCA PSV is preserved may not require surgery. In our sample of seven patients with paired pre- and post-operative values, there was no significant elevation of the NPCA PSV with surgery. However, one patient demonstrated a 75% and 70% increase on the operated and non-operated sides respectively. In another, the NPCA on the side of surgery that was not detectable before the procedure, was easily seen with normal PSV following surgery.

Hu and co-workers¹¹ noted that RI values decreased (although not to a statistically significant degree) as the degree of carotid stenosis worsened. Our findings have shown that the converse is true, that is, relieving carotid stenosis actually results in an increase in the arterial RI on the operated side. This lends support to the suggestion that alterations in resistance upstream from the site of measurement do influence the RI. However, the CRV RI seems to be spared from this effect.

In conclusion, our findings suggest that reproducibility of ocular CDU in patients with arteriopathic disease is probably not as good as in healthy subjects studied by ourselves and at other centres. Carotid endarterectomy in patients without signs of pre-existing ocular ischaemia, causes an increase in the OA PSV and RI of the OA, CRA and NPCA. Further study is needed to assist in defining the category of patients with ophthalmic hypoperfusion secondary to carotid artery stenosis or occlusion who will benefit most from a surgical approach. The changes in RI suggest that it is determined not only by the downstream vascular bed but also by upstream events, and therefore interpreting changes in RI and its relationship with the ocular and retinal circulation is fraught with difficulty.

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