

The Value of Color Doppler Imaging In Patients with Primary Open Angle Asymmetric Glaucoma

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Summary:

Background: Open angle primary glaucoma is a bilateral disease, but is often asymmetric. It is reported that this disease shows impaired retrobulbar blood flow.

Objectives: The aim of this study was to assess the value of color Doppler imaging (CDI) & spectral analysis in the evaluation of ocular vascular abnormalities in patients with primary angle glaucoma as compared to normal volunteers to determine whether lower blood velocities & high resistive index (RI) in the retrobulbar arteries are primary or secondary to glaucomatous damage in these patients.

Patients & Methods: During the period from September, 2000 to June 2001, 126 eyes of 32 patients with primary open angle glaucoma & 31 age matched normal volunteers were studied by CDI & spectral analysis to assess the ocular blood flow velocity. The examination was done at Specialized Surgical Hospital, Dept of Radiology using Seimens Sonoline Versa pro ultrasonic & Doppler unit using 7.5 MHz linear array transducer.

Results: This study showed lower blood flow velocity in glaucomatous patients involving the central retinal artery (CRA) & short posterior ciliary arteries (SPCA), lower both peak systolic & end diastolic blood flow velocity with high RI. No significant correlation was found between gender, Rt & Lt eye & blood velocities, a finding similar to those described by other studies.

Conclusion: This study shows that eyes with advanced disease had slower blood flow in the CRA & SPCA than did less damaged or undamaged eyes. Eyes with normal visual fields in patients with asymmetric disease also had decreased blood velocities & increase in resistivity in their retrobulbar vessels suggesting that these circulatory changes probably precede detectable damage.

Key Words: Glaucoma, Doppler, Retinal arteries

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Introduction

Suzaki & Satomura (1959) first described an ultrasonic Doppler flowmeter for the measurements of ocular blood flow (1). In 1969, Sehlegel & Lawrence used an ultrasonic detector to measure the flow through a vortex vein in rabbits. Tookora, in 1972, described a miniature ultrasonic transducer to measure the blood flow in the confined intra-ocular region (1).

It has been proved that Color Doppler Imaging (CDI) is a useful adjunct to clinical examination & cross sectional imaging for evaluating various pathological conditions in the orbit (2). Although grey-scale ultrasound, which has been used since the late 1950s displays the anatomy of the orbit well, CDI provides additional information about the vascularity of the lesion. This additional information is particularly valuable when evaluating patients in whom clinical examination is difficult (3).

Recently, CDI has been used to obtain spectral waveforms from the orbital vasculature, however, the orbital vessels are below the resolution of real time ultrasonography & accurate localization of these vessels for angle correction to calculate velocity can not be done using CDI (4).

Open angle glaucoma is usually a bilateral disease, but it is frequently asymmetric. Although a higher intra-ocular pressure (IOP) in the more severely affected eye has been postulated as the cause of asymmetry in some patients with primary open angle glaucoma, probably more than 50% of the patients with asymmetric disease have no IOP differences between both eyes (5). It is therefore likely that other lateralizing factors may exist. With color Doppler, it is now possible to obtain information regarding blood flow velocity in the central retinal artery (CRA), & to a lesser degree, in the short posterior ciliary arteries (SPCA) (4,6). Previous reports using CDI showed that patients with primary open angle glaucoma have lower velocities (peak systolic velocity (PSV) & end-diastolic velocity (EDV)) & higher RI in their retrobulbar vessels compared with normal eyes (Table 1), suggesting an impaired retrobulbar blood flow in patients with glaucoma (7,8,9). This lower blood flow velocity could be a primary change or just secondary to the disease process (10).

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TABLE 1
Normal blood flow velocity of ocular arteries
(3,5,10,,11)

Artery	Velocity cm/sec
Ophthalmic artery	
PSV	35 ± 5.1
EDV	10 ± 4.5
Central retinal artery	
PSV	15.3 ± 2.1
EDV	3.3 ± 1.1
Posterior ciliary arteries	
PSV	12.4 ± 4.8
EDV	3.7

The aim of this study was to assess the value of CDI & spectral analysis in the evaluation of ocular vascular abnormalities in patients with primary open angle asymmetric glaucoma as compared to normal volunteers to determine whether lower blood flow velocity & high RI in the retrobulbar arteries are primary or secondary to glaucomatous damage in these patients.

PATIENTS & METHODS:

During the period from September 2000 to June 2001, a total number of 32 patients with primary open angle glaucoma (20 males & 12 females) were included in this study. The patients were referred from the Ophthalmology Department of the Medical City. All patients were diagnosed clinically after ophthalmologic examination by a consultant ophthalmologist as having primary open angle glaucoma; the patients had no relevant medical or ophthalmic history except for their glaucoma. Only patients with systolic blood pressure below 140 mmHg & diastolic below 90mmHg were included in this study. Patients with closed irido-corneal angle, evidence of secondary glaucoma, or any form of retinal or neuro-ophthalmic diseases that could result in visual field defects were not included in this study.

The results obtained from glaucomatous patients were compared with those of an age matched control group of apparently healthy volunteers. None had any clinical evidence of retinal vascular disease such as hypertension or diabetes mellitus. The normal control subjects had normal optic discs & visual fields, in addition to IOP below 21mm Hg in both eyes.

Technique : The sonographic unit used was Siemens Sonoline Versa pro, having color Doppler facility. A linear array transducer (7.5 MHz) was also used.

The patient was placed in supine posture and the examination was performed through closed eye lid.

The patients were instructed to keep still during the examination. Contact lenses were removed to avoid inaccurate vascular recording & patient discomfort. Grey-scale examination was performed first to obtain an overview of the anatomy in the orbit, then color Doppler was done to identify appropriate blood vessels. Once the arteries were optimally identified, pulsed Doppler & spectral analysis were performed. Because the angle between the ultrasonic beam & the artery is very low in ocular arteries, velocity measurements were made without angle correction. PSV & EDV were determined by averaging from 3 consecutive waveforms. The patients were asked to deviate their eyes quickly to the Lt & to the Rt & a range of velocities were recorded.

Safety Issues: There are several important issues related to CDI of the orbit. The power output from the ultrasound transducer during pulsed Doppler examination at the setting most commonly used is 5.1m w/cm² which exceeds the limit of 1m w/cm² set by the Food & Drug Administration for ophthalmic examination but is within the 100m w/cm² guidelines suggested by the American Institute for Ultrasound in Medicine for this reason. The time spent obtaining pulsed Doppler recordings should be minimized (11).

RESULTS:

The general characteristics of the glaucoma patients & normal subjects are shown in table 2.

TABLE 2
General characteristic of patients with glaucoma and control subjects

	Glaucoma Patients(N:32) No.(%)	Control subjects (N:31) No.(%)	P-value
Male	20(62.5)	16(52)	0.005
Female	12(37.5)	15(48)	0.01
Age (years) Mean ± S.D	65.8 ± 11.2	61.0 ± 15.6	0.196

The highest IOP recorded before treatment was significantly higher in the severely affected eyes of glaucoma patients than in the fellow eyes 27.87±/7.77 versus 24.56±/6.35mmHg (P<0.001). The severely affected eyes were also treated with more pressure reducing medication than the fellow eyes (p=0.011). As a result of selecting these patients, the cup/disc ratio was statistically larger in the more eyes (p<0.001) (Table 3).

Table 3
Clinical data from worse and better eyes of patients with asymmetric glaucoma (mean ± S.D mmHg)

Patients with asymmetric glaucoma (N=32)			
	Worse eye	Better eye	P-value
Highest untreated IOP	27.87 ± 7.77	24.56 ± 6.35	<.001
IOP during follow up	18.42 ± 3.35	18.46 ± 3.32	0.94
IOP during CDI	16.77 ± 4.28	18.15 ± 4.82	0.09
Vertical cup/disc ratio	0.84 ± 0.12	0.48 ± 0.16	<.001
No-ocular medication	1.38 ± 0.99	1.09 ± 0.84	<.01
Eye receiving topical B-Blocker No. (%)	23 (71.9)	21 (65.6)	0.59

The results of CDI of patients with glaucoma & control subjects is shown in table 4 (Figures 1-4). Both the severely & less severely affected eyes of glaucoma patients had significantly lower PSV & EDV in the CRA & SPCA & higher RI in the CRA than in the normal subjects. The RI in the SPCA was also higher in both severely & less severely affected eyes of glaucoma patients than in the normal eyes of control subjects but achieved statistical significance only in the superior SPCA of the less severely affected eye & in the temporal superior & mean value of four SPCA of the better eyes.

Table 4
Blood flow velocity in patients with glaucoma and control subjects

	Patients with glaucoma (N=32) (Mean ± SD cm/sec)			Control subjects (N=31) (Mean ± SD)	Control subjects vs. patients with glaucoma	
	Worse eye	Better eye	P-value		Worse eye P-value	Better eye P-value
CRA						
PSV	11.55±2.22	12.72±3.11	0.017	14.55±3.68	0.000	0.03
EDV	2.61±0.99	3.03±1.26	0.034	4.58±1.63	0.000	0.000
RI	0.76±0.06	0.76±0.08	0.78	0.69±0.08	0.001	0.001
SPCA (Mean)						
PSV	7.10±1.44	7.22±1.19	0.57	9.73±1.57	0.000	0.000
EDV	2.33±0.63	2.25±0.57	0.46	3.49±0.83	0.000	0.000
RI	0.67±0.05	0.69±0.06	0.09	0.64±0.07	0.11	0.009

Comparison between the severely & less severely affected eyes of the patients with glaucoma showed that the former had a significantly lower PSV in

their CRA (P=0.017) (Table 4). Among the less severely affected eyes of patients with asymmetric disease, 18 eyes had less visual fields defect and less cupping of the optic discs less. Also these eyes had significantly lower EDV & higher RI in the CRA & SPCA than did 18 eyes of age matched control subjects. When analysis was done for 16 patients with the greatest visual field asymmetry between both eyes, it was found that besides a lower PSV, the CRA of the severely affected eyes also had a lower EDV compared with the fellow eyes (P=0.02).

Table 5
Patients with asymmetric glaucoma with and without IOP differences between the two eyes and age-matched control subjects

	More affected eyes of patients with symmetric IOP (N=15) (mean±SD cm/s)	Age matched control subject (N=15) (mean±SD cm/s)	P-value	More affected eyes of patients with asymmetric IOP (N=15) (mean±SD cm/s)	Age matched control subject (N=15) (mean±SD cm/s)	P-value
C						
PSV	12.00±2.22	14.21±5.07	0.13	11.07±2.34	14.90±4.16	0.01
EDV	2.92±1.12	4.07±1.38	0.03	3.24±0.86	3.14±0.72	0.32
RI	0.76±0.06	0.72±0.07	0.02	0.72±0.04	0.71±0.07	0.12
SPCS (Mean)						
PSV	7.39±1.13	9.62±1.38	0.000	6.76±1.71	9.30±1.55	0.003
EDV	2.44±0.47	3.54±0.87	0.001	2.54±0.76	3.14±0.72	0.02
RI	0.67±0.47	0.64±0.07	0.09	0.64±0.04	0.76±0.06	0.48

Analysis was done also for subgroups of patients according to the IOP differences in both eyes. In the first group 15 (46.8%) of 32 patients we included & had a clinically marked asymmetry of IOP (defined as untreated IOP at least 15% higher in the worse eye than in the fellow eye). The second group included 15 patients (46.8%) with equal IOP in both eyes. The vascular changes were more pronounced in the second group, in which IOP was low to account for the asymmetry of the disease, and there was no significant difference between the severely & less severely affected eyes in either group. However, there was a statistically higher RI in the CRA of the severely affected eye of patients with symmetric IOP compared with those of asymmetric IOP (P=0.12). Compared with the matched normal subjects, patients with symmetric IOP had significantly lower EDV & higher RI in the CRA of the affected eye, whereas patients with asymmetric IOP did not. Both groups had a significantly lower PSV & EDV in the SPCA compared with the normal subjects (Table 5).

In this study there was no significant difference in blood flow velocity because of gender, age, & between Rt & Lt eyes.

DISCUSSION:

Open angle glaucoma is usually a bilateral disease, but it is frequently asymmetric. Although a higher IOP in the severely affected eye has been postulated as the cause of asymmetry in some patients with primary open angle glaucoma, probably more than 50% of the patients with asymmetric disease have no IOP differences between both eyes (5). It is therefore likely that other lateralizing factors must exist. In this study, the previous findings of lower PSV & EDV & higher RI in the retrobulbar vessels of eyes with open angle glaucoma were confirmed. However, the contralateral eyes with normal or less visual field & disc defects, had the same lower blood flow velocity & higher RI in their vessels. This suggests that these circulatory changes occur early in the disease, even before the visual field defects can be detected. The vascular changes might be considered as one of the risk factors associated with glaucoma.

Recent studies of color Doppler imaging in patients with open angle glaucoma with cup disc asymmetry did not show differences between the severely & less severely affected eyes (12). In the present study, the severely affected eyes of patients with asymmetric disease had a significantly lower PSV in their CRA compared with the less severely affected eyes. Furthermore, in the 16 patients with the greatest asymmetry of visual field defects, their severely affected eyes also had a significantly lower EDV in their CRA. These results are inconsistent with the findings of others (7,8) and suggests that low blood flow velocities in the CRA might be associated with worse glaucomatous damage in some patients with asymmetric disease.

The mean of the highest untreated IOP was statistically significantly higher in the more affected eye compared with the fellow eye, confirming previous reports that IOP is an important lateralizing factor (5).

In the present study, there were more men among the patients with glaucoma than among the control subjects. Doppler measurements in the orbit are probably not related to gender (7,9) & therefore the difference in gender distribution presented in this study is unlikely to have influenced the results.

With the current color Doppler imaging technique, the measurements obtained from the CRA are more reliable than those from the short PCAS, because the CRA is much easier to locate allowing better Doppler measurements (4,8,13), & this may explain why there were differences between eyes of patients with marked asymmetric disease in the CRA, but not in the PCAS.

The effects of topical therapy on blood flow are still a controversial subject. Baxter & associates showed that topical timolol had no effect on color

Doppler imaging measurements in healthy subjects (14).

IOP may also influence color Doppler imaging result. Tribble & associates (15) showed that there was an increase in velocity & decrease in resistance in the CRA & short PCAS after trabeculectomy. In the present study, all patients had IOP below 22mmHg during the color Doppler imaging examination & there was no significant IOP difference between the severely & and less severely affected eyes. It is therefore unlikely that the abnormal color Doppler imaging results are due to higher IOP.

Conclusions; This study showed that eyes with advanced disease had slower blood flow velocity in the CRA & SPCA than the less damaged or undamaged fellow eyes.

The above results show that circulatory changes may be associated with disease asymmetry in some patients, even with equal IOP & does not account for the asymmetric damage. It was also detected that the less severely affected eyes & the undamaged eyes from subjects with asymmetric glaucoma had significant slowing of velocities & increase in resistance of the retrobulbar arteries. This suggests that circulatory changes probably precede & therefore predict glaucomatous changes. They may be involved in the pathogenesis of the disease in some patients, and are not secondary to the glaucomatous damage.

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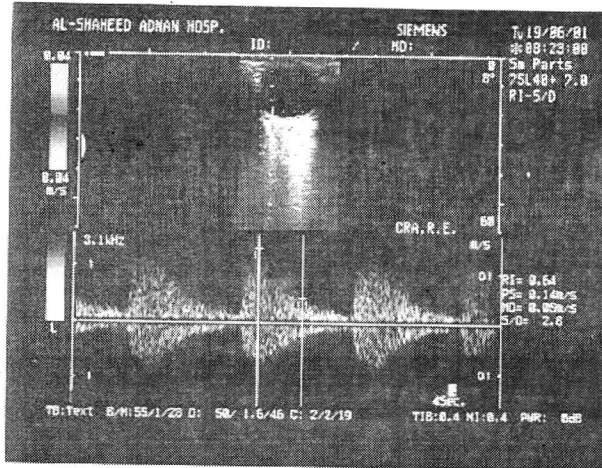


Figure 1: Central retinal artery (Normal pulsated Doppler waveform).

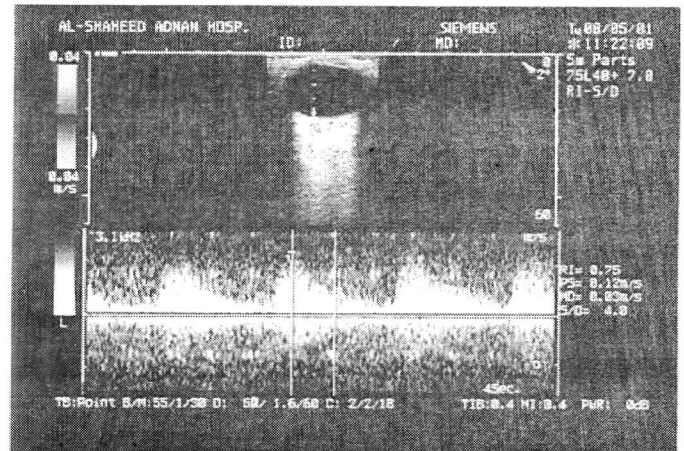


Figure 2: Central retinal artery (Abnormal Pulsated Doppler waveform).

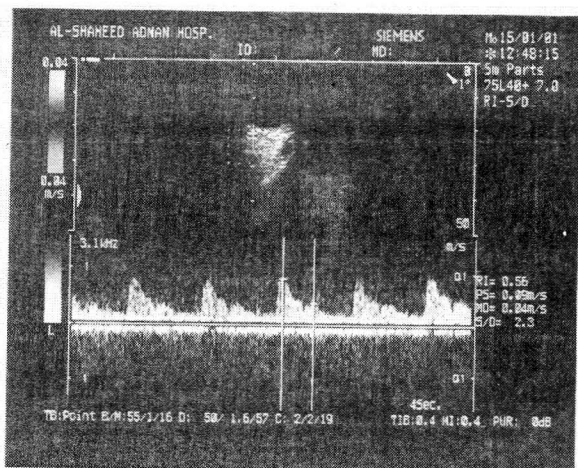


Figure 3: Posterior ciliary artery (Normal pulsated Doppler waveform).

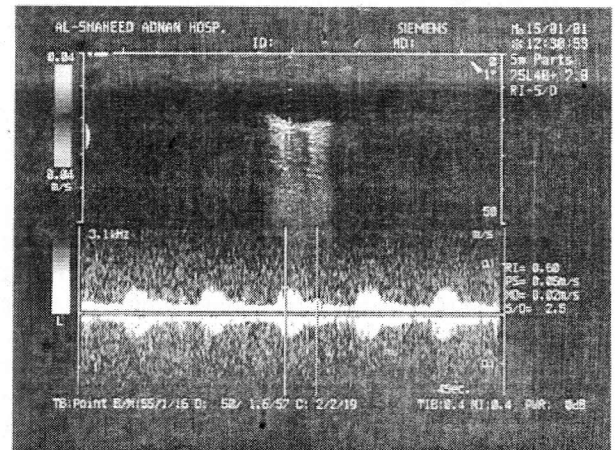


Figure 4: Posterior ciliary artery (Abnormal pulsated Doppler waveform)