Colour Doppler Imaging of Ocular and Orbital Blood Vessels in Retinal Diseases

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Abstract

Colour Doppler imaging (CDI) is an established method for investigation of the ocular and orbital blood flow characteristics. It has been employed for assessment of blood flow parameters in a number of studies that investigated retinal diseases, including vascular pathology, degenerations, dystrophies, tumours, retinal detachment, etc. Decreased retrobulbar blood flow velocity in the central retinal and the short posterior ciliary artery has been reported in diabetic retinopathy. Reduced blood flow velocity in the central retinal artery and vein was also reported in patients with central retinal artery and vein occlusion. In exudative age-related macular degeneration there was an irregular blood flow in the retrobulbar short posterior ciliary arteries that was suggested to play a role in the pathogenesis of the disease. In addition to research, CDI has also been reported as a valuable tool for the clinical management of retinal diseases.

Keywords

Colour Doppler Imaging, retinal diseases, diabetic retinopathy, retinal vein occlusion, retinal artery occlusion, retinopathy of prematurity, age-related macular degeneration, myopia, retinitis pigmentosa, retinal detachment, retinal tumours

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Colour Doppler Imaging (CDI) is an established method for investigation of the ocular and orbital blood flow characteristics. It is an ultrasonographic method that has been employed for the evaluation of the circulatory status in much ocular pathology, but is most used for the investigation of the circulatory status in retinal vascular disorders and in glaucoma.[1–3]

Ultrasound imaging (sonography) is accomplished with a pulse-echo technique. Pulses of ultrasound (generated by a transducer) are sent into the patient where they produce echoes at organ boundaries and within tissues. These echoes then return to the transducer, they are being detected and then displayed. Colour-flow imaging extends the use of the pulse-echo imaging principle. Echoes returning from stationary tissues are detected and presented in greyscale in appropriate locations along the scan line. The depth is determined by the echo's arrival time and the brightness is determined by the echo's amplitude. If a returning echo has a different frequency than what is emitted a frequency change has occurred because the echo-generating object was moving. If the motion is towards or away from the transducer, the Doppler shift is positive or negative, respectively. Along with the transducer, the colour-flow instrument consists of a pulser, a beam-former, a receiver, a memory and a display (see *Figure 1*).

In ophthalmology, CDI is most often used to study the circulatory parameters in the retrobulbar blood vessels – the central retinal artery, central retinal vein, ophthalmic artery and the short and long posterior ciliary arteries. However, intraocular blood vessels have also been studied, such as vortex veins, blood vessels in the intraocular tumours, in detached retina, etc. The measurement is usually obtained through closed eyelids in a supine or in a seated position. Nagahara et al. patented a device for CDI measurement in seated subjects that increased the reproducibility of the measurement by 50% (see *Figure 2*).[4] The reflected ultrasound from the moving cells in the measured blood vessels is recorded by the CDI device and represented as a velocity wave. Two such velocity waves from the central retinal artery and the central retinal vein are presented in *Figure 3*.

Several blood flow parameters can be obtained from the velocity wave, such as peak systolic blood velocity (PSV), end-diastolic blood velocity (EDV), mean blood velocity (MV), resistivity index (RI) and pulsatility index (PI): RI is calculated as (PSV-EDV)/PSV; PI is calculated as (PSV-EDV)/MV.

Although the CDI device is equipped for measurement of blood vessel diameter, the dimension of the retrobulbar blood vessels is too small to obtain a reliable estimation of their diameter. Therefore, total blood flow cannot be evaluated in the retrobulbar blood vessels using CDI.

The recording of the blood flow parameters of the central retinal artery and vein is obtained inside the optic nerve, a few millimetres away from the lamina cribrosa (see *Figure 3*). A specific finding of the blood flow in the central retinal vein is its pulsatile character. As the velocity wave in the central retinal vein is not in direct relation to the cardiac systole and diastole, the blood flow parameters in this vessel are usually described as maximum (V max) and minimum blood velocity (V min).

The diseases of the retina comprise a wide spectrum of conditions, most of which have an uncertain aetiology and pathogenesis. The involvement of local blood circulation in retinal pathology has been of interest to many ophthalmologists and a large number of studies have been published using various methods of blood flow measurement. In this review, we will discuss the findings of studies that employed CDI for the investigation of blood flow parameters in various retinal diseases including vascular, degenerative and dystrophic, tumours and retinal detachment.

Colour Doppler Imaging in Diabetic Retinopathy

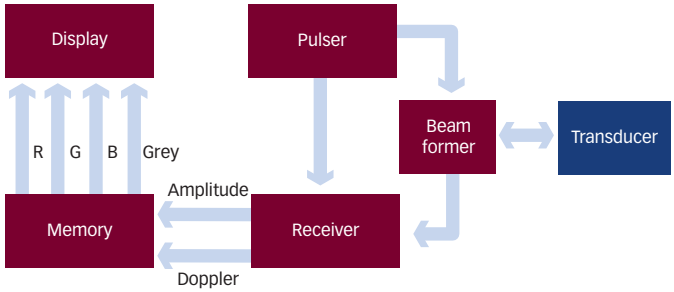
CDI has been applied in a large number of studies that investigated ocular blood flow parameters of retinal vascular diseases. Most of those studies concerned the ocular blood circulation in diabetes.[1,5–21] A number of studies reported that altered retrobulbar blood flow parameters are already present in patients without diabetic retinopathy.[5,8,15,19–21] The blood flow velocity in the central retinal artery in diabetic patients without diabetic retinopathy was significantly decreased than in control subjects.[5,8,19,20] In non-proliferative and in proliferative diabetic retinopathy the reduction of blood flow velocity and the increase of the indices of resistivity was most evident in the central retinal,[1,5,11,12,13,15,17] but also in the short posterior[8,17] and in the ophthalmic arteries.[8,14,17] Regarding the fact that histopathology studies reported luminal narrowing in the retrobulbar blood vessels of diabetic eyes,[22–25] the results from CDI studies suggest a decreased retrobulbar blood flow in diabetic retinopathy.

Conversely, the blood velocity in the central retinal vein was increased among patients with background diabetic retinopathy as compared to patients without diabetic retinopathy[8] and controls.[15] Furthermore, the blood velocity in the central retinal vein increased with the progression of diabetic retinopathy.[7] Because the retinal blood inflow must be equal to the retinal blood outflow, these results suggest that there may be a local circulatory disturbance in the central retinal vein. Local constriction to the central retinal vein imposed by a rigid artery or intraocular pressure variations was suggested as possible factors for these results.[7,26] Increased resistivity to retinal venous outflow is compatible with the clinical findings that suggest venous congestion in diabetic retinopathy: venous dilatation, beading, loops, reduplications, intraretinal microvascular irregularities and retinal oedema. The blood flow velocities in the central retinal, short posterior, ophthalmic arteries and in the central retinal vein decreased after panretinal photocoagulation of diabetic retinopathy.[16]

Colour Doppler Imaging in Retinal Vein Occlusions

Studies of retrobulbar blood flow parameters in patients with central retinal vein occlusion (CRVO) have demonstrated that the blood flow velocity in the central retinal vein is reduced in the affected versus the control[27–30] and fellow eyes.[31–34] It has also been suggested that a characteristic decrease in the blood flow velocity in the central retinal vein was highly predictive of iris neovascularisation.[30] Most of the studies in eyes with CRVO that investigated arterial blood flow reported impaired blood flow parameters in the retrobulbar arteries, suggesting that altered arterial blood flow is involved in the pathogenesis of CRVO.[30–33,35–38] In branch retinal vein occlusion (BRVO), there have been reports of non-significant differences[34] and of decreased blood flow velocities in the central retinal artery and vein in affected eyes versus fellow eyes.[32] CDI has been used in a number of studies that investigated the effect of treatment of retinal vein occlusion (haemodilution, intravitreal injections of anti-vascular endothelial growth factor [VEGF] agents and corticosteroids, radial optic neurotomy) to the retrobulbar blood flow parameters.[35,39–41]

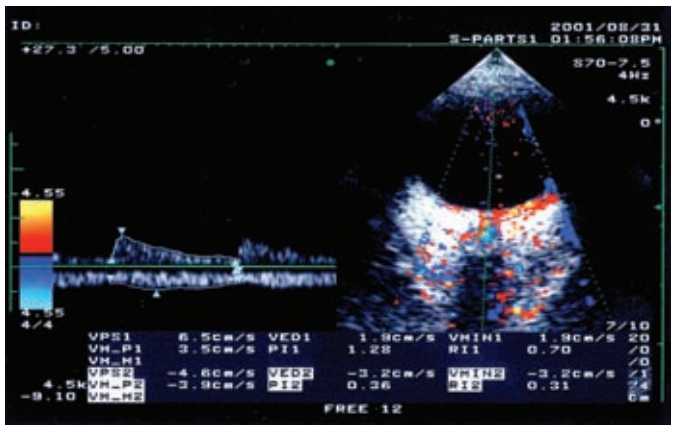
Figure 1: Diagram of a Colour Flow Instrument



B = blue; G = green; R = red.

Figure 2: Colour Doppler Imaging Measurement in a Sitting Position

Figure 3: Colour Doppler Imaging of the Central Retinal Artery and Vein



The ultrasound gate where the velocity measurement is taken is between the two yellow horizontal bars. The green vertical line represents the direction of the ultrasound beam. Velocity waves are represented on the left side of the photograph: the arterial velocity wave is shown above the green line; and the venous velocity wave is shown below. The values of the blood flow parameters that have been obtained are displayed at the bottom of the image.

Colour Doppler Imaging in Retinal Artery Occlusion and Ocular Ischaemic Syndromes

CDI has been reported as an important diagnostic tool in the assessment and differential diagnosis of central and branch retinal artery occlusion and ocular ischaemic syndrome.[42–45] In patients with central retinal artery occlusion (CRAO) a decreased or absent blood flow in the central retinal artery and vein was a typical finding, however, in patients with ocular ischaemic syndrome, this finding was accompanied by decreased blood velocity in the posterior ciliary arteries and in the ophthalmic artery.[42–44] Characteristic signs that have been detected in patients with ocular ischaemic syndromes are turbulent blood flow and 'aliasing' or reversed blood flow in the ophthalmic artery.[44] Furthermore, the possibility of CDI to identify hyper echoic retrobulbar plaques inside the central retinal artery was useful for the differential diagnosis of embolic CRAO.[45]

Colour Doppler Imaging in Retinopathy of Prematurity

The blood flow velocity in the central retinal and ophthalmic artery of premature infants with retinopathy of prematurity (ROP) in stages 2 and 3 was significantly increased than in control subjects.[46] The results of retrobulbar blood flow parameters of patients with ROP stage 1 and stage 3 with plus disease did not differ significantly from the control subjects.[46] In case-controlled and in longitudinal studies of the blood flow parameters in the retrobulbar blood vessels, CDI did not prove to be useful in the determination of the risk of progression to 'plus' disease in patients with ROP.[47–49]

Colour Doppler Imaging in Age-related Macular Degeneration

The characteristics of retrobulbar blood flow have been studied in non-exudative and in exudative age-related macular degeneration (ARMD). In non-exudative ARMD (including early, intermediate and advanced stages of ARMD) the blood velocity in the central retinal artery and short posterior ciliary arteries decreased and the RI in those arteries increased.[50] To the best of our knowledge, there have been no CDI reports of patients with only geographic atrophy. In exudative ARMD, the blood flow parameters were altered in the short posterior ciliary artery that suggests a compromised choroidal circulation.[51–53] The alteration typically consisted of increased RI in the short posterior ciliary artery.[51–53] The results of one of those studies suggested that irregular blood flow in the short posterior ciliary arteries may play a role in the pathogenesis of exudative ARMD.[51] There have been reports on the effect of various forms of treatment of exudative ARMD to the retrobulbar circulation.[54–58] After treatment with intravitreal anti-VEGF (bevacizumab), an initial decrease of the blood flow velocity in the central retinal[56] and short posterior ciliary arteries[56,57] had been detected in the early post-operative period, but returned to pre-operative values after one month.[56] On the other hand, combination therapy of exudative ARMD with intravitreal triamcinolone and photodynamic therapy had no significant effect on the retrobulbar blood flow parameters.[58] Photodynamic therapy alone had a temporary effect on the circulatory parameters in the short posterior ciliary artery that returned to the pre-treatment values four weeks later.[55]

Colour Doppler Imaging in Myopia

The studies of the retrobulbar blood flow parameters in degenerative myopia reported a decreased blood velocity in the central retinal artery and vein and in the short posterior ciliary artery in affected eyes versus control eyes.[59,60] The pathoanatomic aspects of degenerative myopia include thinning and atrophy of the choroid and retina, decrease of the calibre and straightening of the retinal blood vessels, scarce choroidal arteries and thinning and loss of choriocapillaris. All of these characteristics are consistent with the CDI findings that suggest a decreased blood flow in the retina and choroid in degenerative myopia. In patients with myopic choroidal neovascularisation, the RI in the short posterior ciliary arteries was increased, suggesting that compromised choroidal circulation may be involved in the pathogenesis of choroidal neovascularisation.[60]

Colour Doppler Imaging in Retinitis Pigmentosa

In patients with retinitis pigmentosa, the blood flow velocity and the RI in the central retinal artery was decreased in patients compared with those of control subjects.[61] Peak systolic blood velocity was also decreased in the short posterior and ophthalmic arteries of patients as compared to normal subjects.[62] In patients with early forms of retinitis pigmentosa there was an altered haemodynamic response to darkness in the retrobulbar central retinal artery.[63] Cellini et al. detected a correlation between the increase of plasma levels of endothelin-1 and the decrease of peak systolic velocity in the ophthalmic artery and in the posterior ciliary arteries of patients with retinitis pigmentosa.[64] The authors suggest that an increase of endothelin-1 and retinal oxygen levels could lead to vasoconstriction and a decrease of the retinal blood flow, which may exacerbate the abiotrophic process in retinitis pigmentosa.[64]

Colour Doppler Imaging in Retinal Detachment

The possibility of CDI to detect blood circulation in detached retina, in neovascular membranes and in choroidal detachment is especially useful in the differential diagnosis of retinal detachment. CDI can be used to differentiate rhegmatogenous retinal detachment from vitreous membranes in cases where ophthalmoscopy is not feasible.[65,66] Some authors suggest that contrast enhancement improves the accuracy of CDI in such cases.[67]

The blood flow velocity in the retrobulbar central retinal, short posterior and ophthalmic arteries was decreased in eyes with retinal detachment compared to those of control subjects.[68] Eyes with proliferative vitreoretinopathy had lower blood flow velocity and higher RI in the ophthalmic artery than eyes without proliferative vitreoretinopathy, indicating a possible role of altered circulation in the development of this condition.[69]

Colour Doppler Imaging in Retinal Tumours

In retinoblastoma, CDI could identify and monitor tumour viability – lesions were hypervascular at diagnosis and when active while under treatment their vascularity regressed.[70] CDI had also been used as an auxiliary diagnostic tool for rare conditions such as adenoma of the retinal pigment epithelium.[71]

The studies using CDI have made a valuable contribution to our understanding of the characteristics of ocular and retrobulbar circulation in different retinal pathology. CDI is a safe, non-invasive and reproducible method that is practical for research in ophthalmology. Its potential for clinical practice may be especially considered in the differentiation of retinal pathology when optic media opacities are present, but also for the determination of the risk of progression in diabetic retinopathy and CRVO. Additional clinical studies are required in order to establish CDI as a standard method for detecting the risk of progression of these conditions. ■

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