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Colour Doppler Imaging of Superior Ophthalmic Vein in Thyroid-Associated Eye Disease

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Purpose: One of the possible etiologies of proptosis in patients with thyroid-associated eye disease is stated to be passive orbital venous congestion caused by the occlusive and constrictive changes of the superior ophthalmic vein (SOV). In an attempt to clarify the validity of this claim, quantitative information on the flow velocity of the SOV was obtained by colour Doppler imaging in 24 patients with thyroid-associated eye disease and compared with data from the control group.

Methods: On clinical examination, ocular motility, proptosis, soft tissue involvement, and the presence of optic neuropathy were evaluated. The interaction of these signs with the flow velocity of the SOV was investigated in conjunction with computed tomographic (CT) findings such as extraocular muscle enlargement, dilatation of the SOV, and apical crowding of the orbit.

Results: The mean blood flow velocity was significantly decreased in patients compared to the control group ($P < .05$). The CT measures that contributed to significant decreases in SOV blood flow velocity were apical crowding ($P < .05$) and the coexistence of horizontal and vertical extraocular muscle involvement ($P < .05$). Among the clinical measures, significant decreases could be attributed to soft tissue findings ($P < .01$) and to optic neuropathy ($P < .05$).

Conclusions: External compression of the SOV may contribute to the SOV blood flow decrease in orbits afflicted with thyroid eye disease, but proptosis is not relevant to the SOV blood flow decrease. **Jpn J Ophthalmol 2002;46:341–345** © 2002 Japanese Ophthalmological Society

Key Words: Colour Doppler imaging, superior ophthalmic vein, thyroid eye disease.

Introduction

The eye complications associated most typically with hyperthyroidism caused by Graves' disease range from discomfort and lid retraction to disfiguring proptosis, diplopia, and sight loss. Usually called Graves' ophthalmopathy, this condition is better termed thyroid-associated eye disease, emphasizing that a spectrum of thyroid disorders may occur in these patients.[1]

Venous obstruction is stated to be a contributing factor leading to proptosis, periorbital swelling, and chemosis in patients with the extraocular muscle changes of thyroid eye disease. The reduced outflow caused by external compression of the superior ophthalmic vein, or by the extension of the inflammatory process of the extraocular muscles along the septa to cause periphlebitis, could cause dilatation of vascular channels that traverse the orbital fat, thereby expanding the apparent orbital fat volume and pro-

Received: April 27, 1998
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Published by Elsevier Science Inc.

0021-5155/02/$–see front matter
PII S0021-5155(02)00485-9

Jpn J Ophthalmol
Vol 46: 341–345, 2002

ducing proptosis.[2] In an attempt to clarify the validity of this claim, quantitative information on the flow velocity within the superior ophthalmic vein (SOV) was obtained by colour Doppler imaging (CDI) in 24 patients with thyroid-associated eye disease and compared with data from the control group.

Colour Doppler sonography is widely used in the evaluation of orbital vessels.[3–7] This type of imaging makes it possible to gather Doppler information from a cross section of tissue simultaneously with the B-scan information. Thus, the colour blood flow image from the entire field can be accurately superimposed on the gray-scale real-time image. Because the sensitivity of detecting Doppler shift is not limited by the resolution of the gray-scale image, Doppler shifts even in very small vessels can be detected, depicting the course of the vessels. A value is assigned depending on the recorded direction of flow and the averaged flow velocity. This assigned flow velocity is a mean value because even in a small sample area a range of frequency shifts will be recorded.[3]

In this article we present measurements of superior ophthalmic vein flow velocity in normal eyes and in eyes affected by thyroid eye disease.

Materials and Methods

CDI was performed in 48 orbits of 24 patients with thyroid eye disease, including 6 optic neuropathy orbits, and in 20 orbits of 10 healthy volunteers. Informed consent in written form was obtained from all subjects. Of the patients with thyroid eye disease, there were 14 women and 10 men with a mean age of 39.6 years (range, 26–67 years). Among the 24 patients, 21 had Graves' hyperthyroidism, 2 had Hashimoto thyroiditis and were hypothyroid, and one was euthyroid. The mean interval from diagnosis was 2.6 years. Thyroid eye disease was considered to be present if eyelid retraction occurred together with objective evidence of thyroid dysfunction or exophthalmus or optic nerve dysfunction or extraocular muscle involvement. If eyelid retraction was absent, then thyroid eye disease was diagnosed when exophthalmos, optic nerve involvement, or restrictive extraocular myopathy coexisted with thyroid dysfunction and no other causes for the ophthalmic features were apparent.[8] The control group consisted of healthy volunteers (5 men and 5 women) with a mean age of 40.2 years (range, 24–58 years). The mean systemic blood pressure was 124.6 mm Hg systolic (range, 100–150 mm Hg) and 74 mm Hg diastolic (range, 50–85 mm Hg) among the patients with thyroid eye disease, and 135 mm Hg systolic (range, 95–155 mm Hg) and 74.5 mm Hg diastolic (range, 60–80 mm Hg) among the healthy volunteers.

SOV blood flow velocity determined in the eyes with varied clinical signs and computed tomography (CT) findings was compared with the mean SOV blood flow velocity in healthy orbits. Differences between groups were analyzed by use of the nonparametric Mann-Whitney *U*-test and significant was defined as $P < .05$.

All examinations were done in masked fashion by one radiologist experienced in sonography. The eyes were imaged with the patient supine, eyes closed, and gaze directed toward the ceiling. Contact jelly was applied to the closed upper lid before the scan was performed. An attempt was made to minimize the pressure applied to the globe during examination by resting the examiner's hand on the orbital margin before placing the transducer on the closed lid to avoid artifacts.

Examinations were done with a colour Doppler sonographic unit (Toshiba SSA-270A, Tokyo) using a 7.5-MHz linear phased-array transducer. The system makes it possible to detect amplitude, phase, and frequency shift, resulting in a real-time gray scale/colour flow image. Colour assignment depends upon the direction of blood flow and is operator selectable. When the eye and orbit are examined through the eyelids, the ultrasound beam is almost parallel to the orbital vessels; thus because of the direction of flow, arterial flow is shown red. Excessive "colour noise" due to involuntary ocular motion precluded the use of maximum sensitivity Doppler receiver gain for real-time colour flow display. Colour and pulsed Doppler examinations were done with medium and low flow settings (high Doppler gain, low pulse repetition frequency; low wall filter and high sensitivity of signal fast Fourier transform). To obtain Doppler spectra, a fixed sample volume of approximately 0.2×0.2 mm within a vessel was chosen by examining the colour flow image. Spectral sampling throughout the vessels in different planes was done and the maximum Doppler shift was recorded. The scans were digitally recorded on videotape and later reviewed by the help of sine-loop and frame-by-frame analysis of selected segments.

All clinical assessments were performed within 1 month of the CDI and CT study. On clinical examination of the patients, ocular motility, proptosis, soft tissue involvement, such as edema of the eyelids, chemosis, conjuctival injection, and the presence of optic neuropathy were evaluated. Proptosis was investigated according to the Hertel exophthalmometer reading. Specific optic nerve function studies in-

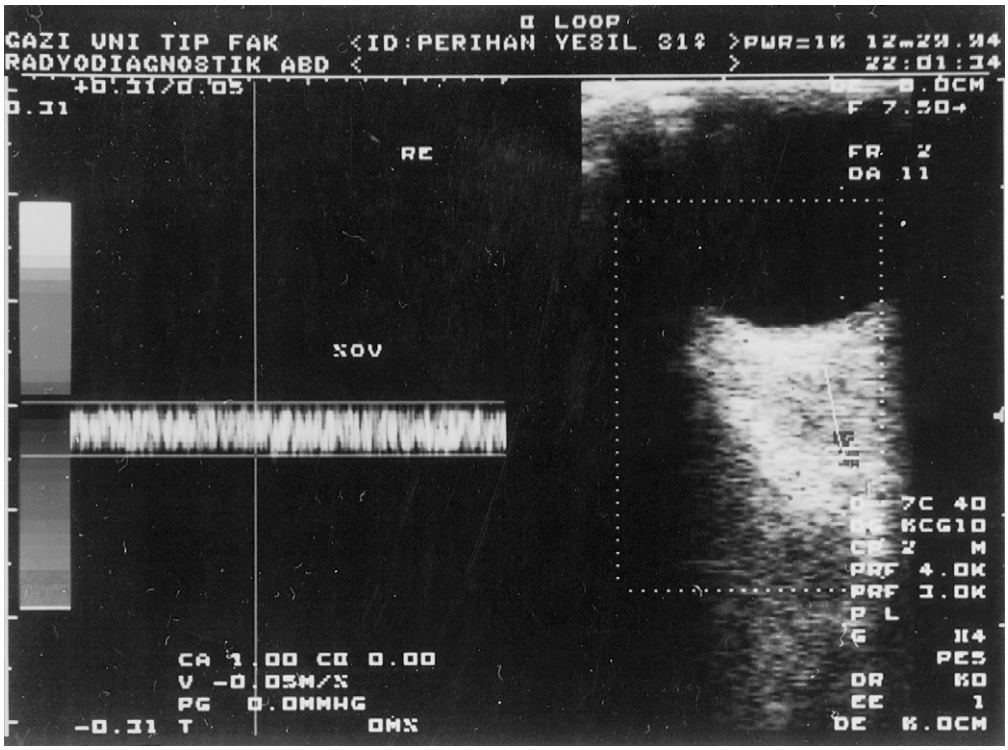

Figure 1. Colour Doppler imaging demonstrating the superior ophthalmic vein in the right orbit of a patient with thyroid associated eye disease. The nonpulsatile venous flow is directed away from the transducer and is therefore coded blue. Spectral analysis (on the left) confirms the characteristic venous flow pattern.

cluded visual acuity (fully refracted), pupillary reactions, visual fields (Goldmann perimetry), and colour vision testing using the Ishihara pseudochromatic plates. Optic neuropathy was diagnosed by the presence of a visual deficit (which consisted of any combination of decreased visual acuity, abnormal visual field and/or abnormal colour vision test results, and/or an afferent pupillary defect. Extraocular muscle involvement was evaluated clinically by the degree of clinical gaze restriction and radiographically by detecting the enlargement of extraocular muscles by CT scanning studies.

These CT scanning studies included the investigation of extraocular muscle diameters, apical crowding, optic nerve flattening at the orbital apex, proptosis, and superior ophthalmic vein dilatation. All patients were scanned in both axial and direct coronal planes. Maximum horizontal diameters of the medial and lateral rectus muscles were qualitatively observed from axial scans. Maximum vertical diameters of inferior rectus and superior muscle groups (superior rectus and levator palpebrae superioris) were assessed from direct coronal images. Superior ophthalmic vein dilatation was assessed in both axial and coronal planes. Apical crowding reflected circumferential effacement of fat planes about the optic nerve by enlarged extraocular muscles.

Results

The superior ophthalmic vein was detected in 30 orbits affected by thyroid eye disease and in 16 control orbits. It was identified at the anterosuperomedial orbit, before crossing laterally over the optic nerve to pass through the superior orbital fissure (Figure 1). The colour flow signal was encoded blue, indicating flow away from the transducer. On spectral analysis, the SOV demonstrated a characteristic continuous, low flow, nonpulsatile venous waveform.[4–6] In addition to flow from this large vessel, pulsatile arterial and venous flow inside the eye was seen, most likely representing venous flow in the vortex veins draining into the SOV. The mean blood flow velocity (cm/s) in the SOV was 6.87 $\pm$ 1.45 in healthy orbits. CDI study did not reveal a dilatation of the SOV in any of the orbits with thyroid eye disease. The superior ophthalmic vein blood flow velocity was evaluated in thyroid eye disease eyes in conjunction with various findings determined from the CT scans. The results are summarized in Table 1. The mean SOV

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Table 1. Evaluation of Superior Ophthalmic Vein (SOV) Blood Flow Velocity in Relation to Structural Abnormalities, as Determined by Computed Tomography

Structural Abnormality*	Number of Orbits	Mean SOV Blood Flow Velocity (cm/s)†
Apical crowding	7	5.14 ± 1.06
SOV enlargement	7	SOV not detected with CDI
Horizontal EOM enlargement	2	6.50 ± 3.53
Vertical EOM enlargement	5	6.20 ± 1.64
Horizontal + vertical EOM enlargement	10	5.60 ± 1.50

*EOM: extraocular muscle.
†Values are mean ± SD.

blood flow velocity was significantly lower in the presence of apical crowding ($P < .05$). A significant difference was also obtained when comparing the group with horizontal plus vertical extraocular muscle enlargement with the normal group ($P < .05$). Among the patients without swelling of the extraocular muscles, mean SOV blood flow velocity was 6.61 ± 1.44 cm/s. A significant impairment of the Doppler hemodynamics of the SOV was not noticed when comparing the results of these patients with the normal group ($P < .05$).

Isolated superior rectus muscle enlargement was not demonstrated in any of our patients. Of the 15 patients with an exophthalmometer reading >19 mm, CT scan confirmed the presence of an enlarged SOV in 7 patients. The SOV could not be identified in any of these patients in the CDI study.

Superior ophthalmic vein blood flow was also evaluated in thyroid disease eyes showing varied clinical signs. The results are summarized in Table 2. Although no significant difference was noticed in blood flow velocities between the two groups of patients, one group had exophthalmometer readings smaller than 19 mm (12–18 mm; mean = 15.4 mm), the other, >19 mm (19–26 mm; mean = 22.8 mm). A significant decrease in SOV blood flow velocity was obtained comparing either of the groups with the controls ($P < .05$). Likewise existence of soft tissue findings (such as conjunctival injection, chemosis, lid edema), vertical plus horizontal limitation of ocular motility and optic neuropathy were associated with significant impairment of the Doppler hemodynamics of the SOV ($P < .01$, $P < .05$, and $P < .05$, respectively). Among the 24 patients without optic neuropathy, mean SOV blood flow velocity was 6.37 ± 1.40 cm/s. A significant difference was not obtained when comparing the results of these patients and the normal group ($P > .05$).

There were some common findings among 12 of the 18 orbits in which the SOV could not be detected with CDI study: (1) There was an exophthalmometer reading ≥21 mm. (2) CT scan confirmed the presence of an enlarged SOV in 6 orbits. (3) All but two of these orbits demonstrated apical crowding on CT scan. (4) Ten of these orbits had soft tissue involvement such as conjunctival injection, chemosis and lid edema. (5) Enlargement of vertical and horizontal extraocular muscles were identified both clinically and radiographically.

Discussion

The principal aim of this study was to evaluate the SOV blood flow velocity in relation to various clinical and CT manifestations of thyroid eye disease. Al-

Table 2. Evaluation of Superior Ophthalmic Vein (SOV) Blood Flow Velocity in Relation to Specific Clinical Signs

	Number of Orbits	Mean SOV Blood Flow Velocity (cm/s)*
Exophthalmometry < 19 mm	15	5.60 ± 1.54
≥ 19 mm	15	5.66 ± 1.63
Horizontal dysfunction	4	5.60 ± 1.50
Vertical dysfunction	3	4.66 ± 1.15
Horizontal + vertical dysfunction	17	5.82 ± 1.42
Soft tissue findings	16	5.37 ± 1.40
Optic neuropathy	6	5.33 ± 1.36

*Values are mean ± SD.

though the patients showed varied clinical and CT measures of thyroid eye disease, they demonstrated a significant decrease in SOV blood flow velocity ($P < .05$) compared to the control group, confirming a prior study.[7]

The CT measures, which seemed to contribute to significant decreases in SOV blood flow velocity, were apical crowding and horizontal plus vertical extraocular muscle enlargement. Among the clinical measures, significant decreases in SOV blood flow were obtained for soft tissue findings, for the coexistence of vertical and horizontal limitation, and for optic neuropathy. Exophthalmometry, a frequently used but highly variable method for quantitation of thyroid eye disease,[9,10] showed poor correlation with SOV blood flow velocity. Although a significant decrease in SOV blood flow velocity was obtained using either of the groups, with an exophthalmometer reading of <19 mm or >19 mm, no significant difference was obtained comparing these two groups with each other ($P = .90$). The decrease in SOV blood flow velocity in these two groups may contribute to other coexisting clinical and CT measures.

It should be taken into consideration that our results reflect only the assessment of the findings among the orbits in which SOV could be detected in CDI study. Among these orbits, the minimal blood flow velocity measured in the SOV was 3 cm/s. There were 18 orbits with thyroid eye disease in which SOV could not be detected with CDI. When an ultrasound beam is at an angle of 90° to a vascular structure or if a vessel contains only stagnant blood, no Doppler flow information is obtained,[3,4] The common findings among 12 of these 18 orbits suggest that the coexistence of an exophthalmometer reading of 21 mm, horizontal with vertical extraocular muscle involvement, soft tissue involvement, and apical crowding may contribute to a venous obstruction. External compression of the SOV might have caused SOV blood flow velocity to decrease to a level that only stagnant blood was found in the vessel; thus no Doppler information could be obtained.

Nakase et al demonstrated the existence of reversed, arterialized flow in SOV in thyroid eye disease. Reversed flow, ie, flow in the posteroanterior direction, was associated with optic neuropathy and apical crowding observed on CT. Nakase speculated that the reversed flow in the SOV strongly supported the existence of venous stasis in the orbit, which may be related to the development of optic neuropathy.[11] Arterialized flow was not seen in any of our patients. The presence of arterialized flow would be indicated by a retrograde flow pattern in the direction of the transducer and would therefore be coded red. Special attention was paid to the spectrum analysis. Spectrum analysis would reveal high velocity arterialized flow through a low resistance blood vessel like the SOV if there were retrograde flow. This pattern was not detected in any of the patients.

The clinical and CT signs associated with a significant decrease in SOV blood flow velocity and the common findings among the orbits in which the SOV could not be detected with CDI study suggest that external compression of the SOV may contribute to a decrease in SOV blood flow in orbits affected by thyroid eye disease. It was also determined that proptosis is not relevant to the SOV blood flow decrease. Further studies with larger numbers of patients could identify the specific clinical and CT signs that may be quantitatively related to the decrease in SOV blood flow velocity in eyes affected by thyroid eye disease.

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