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原著

# 内頸動脈閉塞症における側副血行路としての眼動脈血流—血行力学的脳虚血との関係—

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## Ophthalmic Artery Flow as the Collateral Pathway in Patients with Internal Carotid Artery Occlusion

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We attempted to evaluate the function of ophthalmic artery (OA) flow as the collateral pathway in cases of internal carotid artery occlusion (ICAO).

**Methods.** We examined 18 patients having symptomatic ICAO who underwent OA color Doppler flow imaging (CDFI) and quantitative SPECT regional cerebral blood flow (rCBF) study.

**Results.** (1) The OA CDFI findings were reversed OA flow in 10 patients and antegrade flow in 8. (2) The mean resting rCBF was 25.2 ml/100 g/min in the patients with reversed OA flow, and 26.7 ml/100 g/min in the patients with antegrade OA flow. The mean cerebral blood flow reserve capacity with acetazolamide was 8.68% in the former and 28.3% in the latter. This difference was statistically significant ( $p < 0.05$ ). (3) In eight patients with severe hemodynamic compromise with a cerebral blood flow reserve capacity of less than 10% and a resting rCBF of less than 80%, the reversed OA flow was visualized significantly frequently ( $p < 0.05$ ).

**Conclusion.** In ICAO patients, OA CDFI findings are well correlated with the hemodynamic stage and development of other collateral pathways. Reversed OA flow indicates severe intracranial hemodynamic compromise.

**Key words:** color Doppler flow imaging, internal carotid artery occlusion, ophthalmic artery, SPECT

### はじめに

虚血性脳血管障害の症状発現には塞栓性と血行力学的因子があるが、内頸動脈閉塞症では血行力学的因子の評価が治療方針の選択に重要である<sup>2,3,20</sup>。血行力学的脳虚血では頭蓋内血行動態に影響する、ウイリス動脈輪を介した一次側副血行路、頭蓋外やleptomeningeal anastomosisによる二次側副血行路の発達が発現に関係する<sup>1)</sup>。従来、側副血行路の発達と頭蓋内血行動態の関係は、脳血管撮影や、magnetic resonance angiography (MRA)、経頭蓋超音波診断 (TCD)、single photon emission computed tomography (SPECT)、positron emission tomography (PET) により検討されてきた。

今回著者らは内頸動脈閉塞症の血行動態をSPECTで観察し、二次的側副血行路である眼動脈血流をドプラ血流検査で評価し、眼動脈血流の側副血行路としての役割を脳血行

動態の点から明らかにした。

### 対 象

脳血管撮影により診断された症候性一側内頸動脈閉塞症18例を対象とした。年齢は50歳から73歳平均年齢63歳で、男性14例女性4例であった。臨床症状は、一過性脳虚血発作10例、reversible ischemic neurological deficit (RIND) 4例、completed stroke 4例 (Modified Rankin Scale Score : 2以下)であった。対側内頸動脈に50%以上の狭窄を認めた症例はなかった。脳血管撮影上の側副血行路は、前交通動脈を介したものを認めた症例 (ACoA (+) 群) 15例、認めなかった症例 (ACoA (-) 群) 3例で、後交通動脈を介したものを認めた症例 (PCoA (+) 群) 6例、認めなかった症例 (PCoA (-) 群) 12例で、leptomeningeal anastomosisによる血流を認めた症例 (Lept (+) 群) 9例、認めなかった症例 (Lept (-) 群) 9例であった。

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## 方 法

眼動脈血流は Acuson 社製 Computed sonography 128XP により、眼動脈血流方向、収縮期最大血流速度を観察した。眼動脈ドプラ血流検査は、被検者を安静仰臥位で閉眼させ、眼瞼上にリニア型探触子をあて施行した。出力 50mW/cm<sup>2</sup>、周波数 7MHz で、一側眼動脈の検査時間は 5 分以内とした。眼動脈は眼窩内で可能な限り内頸動脈に近い部位で観察し、眼動脈血流方向は、頭蓋内内頸動脈から眼球方向を順流、眼球から頭蓋内内頸動脈方向を逆流とした<sup>15)</sup>。血流速度はパルスドプラ法により収縮期最大速度 (PSFV) を測定した。今回の検討では、血流方向による検討を中心に行ったため、角度補正は入射角 10° 以下の場合行なわなかった。

対照例 (36 例、平均年齢：62 歳、女性 17 例、男性 19 例) での平均 PSFV は 0.37m/sec で、血流方向は全例順流であった<sup>15)</sup>。

脳血流量は<sup>125</sup>I-IMP autoradiography (ARG 法) による SPECT で定量的に測定した<sup>9,10)</sup>。SPECT 検査は Multispect 3 (Siemens 社製) を用い、安静仰臥位閉眼状態で行った。ACZ 負荷 SPECT は、ACZ：17mg/Kg 静注 10 分後にトレーサーを投与し測定した。安静時と acetazolamide (ACZ) 負荷時に、JET study<sup>10)</sup> で設定された中大脳動脈領域の region of interest (ROI) で局所脳血流量を計測し、安静時血流と脳循環予備能を評価した。脳循環予備能は、{(ACZ 負荷後 CBF - 安静時 CBF)/安静時 CBF} X 100% で評価した。正常対照例の MCA 領域の安静時血流量は 40ml/100g/min であった。

眼動脈ドプラ血流検査及び脳血流検査は全例発症 4 週 - 6 週の症状が安定した時期に 1 週間以内に全て行なった。値は平均±標準偏差で表示し、統計学的解析は、student t-test, chi-square test により行い、p 値が 0.05 以下のとき有意と判定した。

## 結 果

### 1. 眼動脈ドプラ血流検査

眼動脈血流方向は、10 例で逆流 (R 群)、8 例で順流 (A 群) であった。PFV は、R 群：-0.29±0.25m/sec、A 群：0.12±0.06m/sec であった。ACoA, PCoA, leptomeningeal anastomosis を介する側副血行路の発達と眼動脈血流方向との関係では、PCoA (-) 群で有意に ( $p < 0.05$ ) 眼動脈血流が逆流している症例が多かったが、他の側副血行路と眼動脈血流の血流方向の検討では有意な関係はなかった。(Table)

### 2. 脳血流量

患側血流量は 25.9±4.00ml/100g/min で、患側脳循環予備能は 17.4±19.8% であった。健側の血流量 30.6±3.93ml/100g/min、脳循環予備能 35.3±17.1% で、脳血流量、脳循環予備能とも患側では健側に比し有意に ( $p < 0.05$ ) 低下していた。

Table Relationship between Collateral Pathway and Ophthalmic Artery Flow Direction

Collateral pathway	Ophthalmic Artery Flow Direction		
	Antegrade flow (cases)	Reversed flow (cases)	
Anterior communicating artery			NS
Positive	6	9	
Negative	2	1	
Posterior communicating artery			
Positive	5	1	$p < 0.05$
Negative	3	9	
Leptomeningeal anastomosis			
Positive	2	7	
Negative	6	3	NS

NS, not statistically significant; P, value revealed from the statistical analysis using chi-square analysis.

眼動脈の血流方向による患側安静時血流の比較では、R 群 25.2±4.08ml/100g/min、A 群 26.7±4.01ml/100g/min と差はなかったが、患側脳循環予備能は R 群 8.68±15.4%、A 群 28.3±20.2% と、R 群で有意に ( $p < 0.05$ ) 低値を示した。

患側血流量が正常対照値の 80% 未満で脳循環予備能が 10% 未満の症例 (S 群) は 8 例で、その以外の症例 (L 群) は 10 例であった。眼動脈血流方向は、S 群 8 症例中 7 例で逆流、順流は 1 例であった。一方、L 群 10 例中逆流していた症例は 3 例、他の 7 例は順流であった。血行力学的脳虚血の程度が強い S 群で有意に ( $p < 0.05$ ) 眼動脈血流の逆流症例が多かった。

## 考 察

内頸動脈閉塞症で、血行力学的脳虚血発作が着目されるのは、Powers ら<sup>20)</sup>の Stage 2 を示す症例では、その後の脳卒中中の危険性が高く、血流を増加させる脳血行再建術の適応となる症例が存在するためである<sup>5,17,19)</sup>。著者も、脳血行再建術が血行力学的脳虚血に対して有用であることを、局所脳血流の検討や運動負荷 SPECT 等により報告してきた<sup>11,19)</sup>。血行力学的脳虚血は、PET で脳血流量と酸素摂取率を計測するのが最も確実に診断可能だが施行可能な施設が限られている。従って、一般には装置が安価で、試薬の調整も容易な定量的 SPECT により脳血流量を脳循環予備能とともに計測し血行力学的脳虚血を診断されている。本報告では、定量的 SPECT とドプラ血流検査で脳循環動態を評価し、内頸動脈閉塞症で血行力学的脳虚血の病態を側副血行路としての眼動脈血流を中心に検討した。

今回の検討では、眼動脈の血流方向が逆流している症例で、脳循環予備能が有意に低く、血行力学的脳虚血の程度が強い症例が有意に多かった。これは、内頸動脈閉塞症で眼動脈血流が逆流し脳循環の側副血行路として機能しているにもかかわらず、脳血流量、脳循環予備能が不十分であることを意味する。従って、眼動脈ドプラ血流検査上の眼

動脈血流の逆流は、脳循環予備能の障害や血行力学的脳虚血の存在を示唆する重要な所見であることが明らかとなった。

内頸動脈閉塞症における二次的側副血行路である眼動脈血流は、ACoA、PCoAなどの一次側副血行路が十分な血流量を供給しない場合に機能するとされている<sup>12)</sup>。実際今回の検討でも、PCoAを介した側副血行路が描出されていない症例では有意に眼動脈が逆流し側副血行路として機能していた。これは、眼動脈血流とPCoAは、頭蓋内血流に対して相補的に作用し、PCoAの発達が良いであれば頭蓋内血流はPCoAにより維持され、眼動脈血流も順行性のままであるが、PCoAの発達が不良の場合頭蓋内血流を眼動脈血流でも維持しようとし眼動脈が逆流すると考えられた。(Fig.)しかしながら、ACoAを介した側副血行路と眼動脈の血流方向の関係には一定の傾向がなかった。今回の検討では、15例(83%)に前交通動脈を介した側副血行路が認められた。これらのうち9例(60%)の症例で眼動脈が逆流していた。ACoAを介した側副血行路の発達は血行力学的脳虚血の程度が比較的低い症例であるとの報告<sup>16)</sup>があるが、今回対象とした症例は、眼動脈が順流であった症例でもSPECT上安静時血流は低下しており血行力学的脳虚血の程度は比較的強い症例が多かった。従って、症例毎の血行力学的な脳虚血の程度に応じて、ACoAによる側副血行路だけでは不十分な場合、眼動脈血流による側副血行路も要し中大脳動脈領域の血流量を維持しようと機能していると考えられた。

今回の側副血行路と脳血流量の検討は、血行力学的脳虚血の程度は重篤でも、神経症状が軽微な症例を対象とした。更に発症1ヵ月後という亜急性期の検討であるので、発症前から側副血行路がある程度発達していた症例や今後様々な側副血行路が発達してくる可能性は否定できない。従って、病態の進行に応じて側副血行路の発達や血行力学的脳虚血の程度も時間の経過により変化し、側副血行路の発達や要求される脳血流量などが変化すると考えられる。

側副血行路としての眼動脈の評価は、脳血管撮影やMRA、TCDでなされることが多い。今回、側副血行路である眼動脈血流の観察は、眼動脈ドプラにより行なった。脳血管撮影で眼動脈の造影方向が同定できた症例では、眼動脈ドプラ血流検査所見と眼動脈造影所見がほぼ一致することを著者は既に報告している<sup>13)</sup>が、脳血管撮影では、眼動脈の造影方向が明らかでない症例や、造影されない症例も存在するが、そのような症例でも眼動脈ドプラ血流検査では眼動脈が同定可能である。また、MRAでは血流方向を同定することができないことや、側副血行路を過小評価する可能性がある。更に、TCDでは、眼動脈を観察していることの確証が困難でartifact混入の可能性を否定することは難しい。本報告では、眼動脈を生理的に直視下に観察可能な眼動脈ドプラ血流検査により、側副血行路としての眼動脈血流を観察した。

著者は、眼動脈血流波形と、定性的脳血流測定から、眼

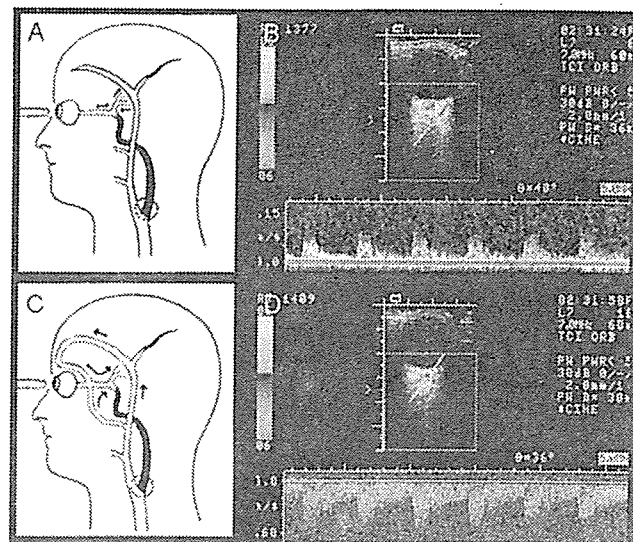


Fig. Relationship between hemodynamic pathways and ophthalmic artery color Doppler flow imaging in internal carotid artery occlusion. A, antegrade ophthalmic artery flow with a well developed collateral pathway via the posterior communicating artery. B, arched [DD1] stenotic ophthalmic artery color Doppler flow pattern. C, reversed ophthalmic artery flow with poor collateral blood flow via the posterior communicating artery. D, reversed ophthalmic artery color Doppler flow pattern.

動脈の波形異常を示した症例では、脳循環が障害されている可能性が存在することを既に報告している<sup>14)</sup>。今回の検討では、脳血流を脳循環予備能も含めて定量的に行い、客観的に評価した。局所脳血流量は、運動機能を反映する中大脳動脈領域で観察した。前頭葉や後頭葉など他の部位を評価することにより、高次脳機能や視機能など、他の脳機能を有する部位での血流を評価し、眼動脈血流をはじめとする側副血行路との関係を明らかにすることも興味深い。また、今回の対象症例は、症候性的内頸動脈閉塞症と非常に限定され、症例数も限られていた。今後、対象症例を増やし解析するとともに、無症候性的内頸動脈閉塞症の血行力学的脳虚血の程度と側副血行路の発達を時間的経過により観察し、一層内頸動脈閉塞症例での側副血行路の機能を明瞭とし、病態の進行を予防し、発症を未然に防ぐ可能性が考えられた。

眼動脈ドプラ血流検査の特徴は、非侵襲的に迅速かつ簡便に繰り返し、眼動脈血流の把握が可能な点である。眼動脈に対する超音波検査の注意点の一つは、眼窩内組織の熱の放散が不良なため、超音波の発熱効果による組織損傷である。著者は、出力50mW/cm<sup>2</sup>で5分以内に検査を終了した。出力50mW/cm<sup>2</sup>は米国のFood and Drug Administrationが推奨している17mW/cm<sup>2</sup>より高いが、American Institute of Ultrasound in Medicineが規定している安全限界100mW/cm<sup>2</sup>より低い<sup>15)</sup>。Huらは12年間にわたり25000例に50mW/cm<sup>2</sup>で眼動脈ドプラ血流検査を行い、合併症の生じた症例はなかったと報告している<sup>16)</sup>。今回対象とした症例でも検査後合併症を生じた症例はなかったが、眼動脈ドプラ血流検査の施行に当ってはパルスドプラ法の施行時間やカラード

プラの範囲を必要最小限とするなど、安全性には極力注意を払う必要がある。

## 結 語

症候性内頸動脈閉塞症でのドプラ血流検査における眼動脈血流の逆流所見は、脳血流量とともに脳循環予備能が低下し血行力学的脳虚血の程度が強いことをしめしており、病態の解析に際して注意を要する所見である。

内頸動脈閉塞性病変での眼動脈ドプラ血流検査は血行力学的脳虚血の指標として、病態の解析やスクリーニング検査、経過観察として非侵襲的で有用な検査法である。

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## Effect of Carotid Endarterectomy on Chronic Ocular Ischemic Syndrome Due to Internal Carotid Artery Stenosis

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**OBJECTIVE:** We evaluated the effect of carotid endarterectomy on chronic ocular ischemic syndrome due to internal carotid artery stenosis by use of data obtained from ophthalmic artery color Doppler flow imaging.

**METHODS:** We examined 11 patients with ocular ischemic syndrome due to internal carotid artery stenosis (>70% stenosis) who were being treated by carotid endarterectomy. Ophthalmic artery color Doppler flow imaging indicated ophthalmic artery flow direction and peak systolic flow velocity and was performed before and at 1 week, 1 month, and 3 months after surgery.

**RESULTS:** We assessed the ophthalmic arteries of 11 patients via color Doppler flow imaging. Before undergoing carotid endarterectomy, five patients showed reversed ophthalmic artery flow. In the other six patients who experienced antegrade ophthalmic artery flow, the average peak systolic flow velocity was  $0.09 \pm 0.05$  m/s (mean  $\pm$  standard deviation). Preoperative reversed flow resolved in each patient 1 week after undergoing surgery. All patients showed antegrade ophthalmic artery flow. The average peak systolic flow velocity in the patients who had preoperative antegrade flow rose significantly, to  $0.21 \pm 0.14$  m/s ( $P < 0.05$ ). There was no significant change as compared with findings at 1 week after surgery. During the follow-up period (mean, 32.4 mo), no patients complained of recurrent visual symptoms. At the end of the study period, visual acuity had improved in five patients and had not worsened in the other six patients.

**CONCLUSION:** Carotid endarterectomy was effective for improving or preventing the progress of chronic ocular ischemia caused by internal carotid artery stenosis. (Neurosurgery 48:328-333, 2001)

**Key words:** Carotid endarterectomy, Color Doppler flow imaging, Ocular ischemic syndrome, Ophthalmic artery

Severe extracranial carotid artery stenosis causes ocular ischemia, including acute manifestations after retinal embolism (amaurosis fugax, central retinal artery occlusion, and branch retinal artery occlusion) and chronic progressive ocular ischemia (ocular ischemic syndrome) (7, 10, 15). The latter may lead to permanent blindness secondary to neovascular glaucoma (10). Carotid endarterectomy is the best treatment for direct removal of the internal carotid artery stenotic lesion. Numerous prospective, randomized, and multicenter studies have been designed to evaluate the efficacy and safety of carotid endarterectomy (1, 3, 9, 16, 18, 23). The effect of carotid endarterectomy on embolisms in the retinal circulation is well known. However, no clear evidence has been found regarding the efficacy of carotid endarterectomy for chronic ocular ischemic syndrome caused by severe internal carotid artery stenosis. In this study, we discuss and analyze the effect of carotid endarterectomy on chronic ocular ischemic syndrome due to internal carotid artery stenosis at

its origin on the basis of data obtained from ophthalmic artery color Doppler flow imaging (CDFI) scans.

### PATIENTS AND METHODS

#### Patients

We examined 11 patients with chronic ocular ischemia due to internal carotid artery stenosis who were about to undergo primary carotid endarterectomy. All of the patients were men. Their ages ranged from 58 to 73 years (mean, 67 yr). The ocular syndrome in the 11 patients involved chronic ocular ischemic syndrome, including a decline in visual acuity in 9 patients, frequent amaurosis fugax in 3, and blurred vision in 2. Exclusion criteria were acute ocular ischemic symptoms such as sudden loss of vision, a single episode of the amaurosis fugax, or ocular or orbital pain (17). Six patients had visual acuity of 20/40 or worse, three patients had visual

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acuity between 20/40 and 20/20, and the remaining two patients had no decrease in visual acuity. In each patient, the intraocular pressure was within the normal range (<25 mm Hg), with minimal or no iris rubeosis. Ischemic changes of the optic fundi in 11 patients resulted in neovascularization of the disc in 4 patients, whereas in the other 7 patients, the optic fundi appeared normal. According to the criteria of the North American Symptomatic Carotid Endarterectomy Trial (18), the grades of internal carotid artery stenosis as determined by angiography were more than 90% in eight patients and more than 70% in three patients.

A standard carotid endarterectomy was performed for each patient. There were no intraoperative or postoperative complications. Postoperatively, the patency of the carotid endarterectomy was confirmed by means of angiography within 1 week after surgery. After we performed the carotid endarterectomy, ophthalmological maneuvers such as panretinal photocoagulation were performed in selected patients. The clinical symptoms—including ophthalmological findings such as visual acuity and funduscopic findings—were followed for a period of 6 to 46 months (mean, 32.4 mo).

### Methods

All of the patients underwent ophthalmic artery CDFI on the eye ipsilateral to the carotid endarterectomy with a computed sonography system (128XP/10; Acuson Corp., Mountain View, CA). The ophthalmic artery CDFI studies provided information regarding the flow direction and peak systolic flow velocity. They were performed within 1 week before the patient underwent surgery and at 1 week, 1 month, and 3 months after the operation. The physiological data were compared by a two-tailed paired Student's *t* test and Welch's *t* test. The value of  $P < 0.05$  was taken as the threshold for statistical significance. All values are reported as means  $\pm$  standard deviations. Five patients were found, by means of ophthalmic artery CDFI before surgery, to have experienced reversed ophthalmic artery flow. It was recognized that these negative peak systolic flow velocity values would create erroneous data points in the calculation of mean values from the entire group, so these measurements were excluded from statistical analysis. Therefore, postoperative comparisons of

patients with reversed ophthalmic artery flow were made on the basis of the restoration of normal antegrade flow in the ophthalmic artery and the restoration of normal flow velocity. Of 36 normal, healthy volunteers, all showed normal flow direction—that is, a flow away from the orbital apex to the globe. The average peak systolic flow velocity was  $0.36 \pm 0.07$  m/s. The normal range of the peak systolic flow velocity was calculated by subtracting and adding two standard deviations from the mean value.

### RESULTS

#### Ophthalmic artery color Doppler flow imaging (Table 1)

##### Before carotid endarterectomy

Five patients exhibited reversed ophthalmic artery flow; the average peak systolic flow velocity was  $-0.37 \pm 0.19$  m/s. Six patients had antegrade flow; the average peak systolic flow velocity in these patients was  $0.09 \pm 0.05$  m/s, which was significantly lower than control values ( $P < 0.05$ ). The peak systolic flow velocity was lower than the lower limit of the normal control value in all 11 patients.

##### At 1 week after carotid endarterectomy

The preoperative reversed ophthalmic artery flow was resolved in each patient after surgery. Antegrade ophthalmic artery flow was observed in all 11 patients. The average peak systolic flow velocity in the patients with preoperative reversed ophthalmic artery flow was  $0.22 \pm 0.14$  m/s. The average peak systolic flow velocity in the patients with preoperative antegrade flow rose significantly, to  $0.25 \pm 0.12$  m/s ( $P < 0.05$ ). Among 11 patients, 5 patients (45%) had peak systolic flow velocity in the normal range.

##### At 1 and 3 months after carotid endarterectomy

All 11 patients showed antegrade ophthalmic artery flow at 1 and 3 months after surgery. The average peak systolic flow velocities in patients with preoperative reversed ophthalmic artery flow were  $0.23 \pm 0.11$  m/s at 1 month and  $0.22 \pm 0.12$  m/s at 3 months after carotid endarterectomy. These values did not show a significant change as compared with the

TABLE 1. Ophthalmic Artery Peak Systolic Flow Velocity<sup>a</sup>

Ophthalmic Artery Flow Direction before Surgery	Before Surgery	After Surgery		
		1 Week	1 Month	3 Months
Reversed flow (n = 5)	$-0.37 \pm 0.19$	$0.22 \pm 0.14$	$0.23 \pm 0.11$	$0.22 \pm 0.12$
Antegrade flow (n = 6)	$0.09 \pm 0.05$	$0.25 \pm 0.12^b$	$0.28 \pm 0.12$	$0.27 \pm 0.13$

<sup>a</sup> All values are expressed as mean  $\pm$  standard deviation in meters per second.

<sup>b</sup> Significant difference from value before surgery ( $P < 0.05$ ).



values measured 1 week after the operation. The average peak systolic flow velocities in patients with preoperative antegrade flow were  $0.28 \pm 0.12$  m/s at 1 month and  $0.27 \pm 0.13$  m/s at 3 months after surgery. These values did not change significantly from the values obtained 1 week after carotid endarterectomy.

### Visual symptoms

During the follow-up period, there were no patient complaints of amaurosis fugax or blurred vision. At the final follow-up examination, visual acuity had improved in five patients, and the remaining six patients showed no worsening of visual acuity. Among the nine patients who had experienced a decline in visual acuity before surgery, five showed improvement in visual acuity. Eight patients had a visual acuity between 20/40 and 20/20, and one patient had a visual acuity of less than 20/40. The two patients without decreased visual acuity before surgery tested better than 20/20 without worsening of visual acuity during the follow-up period. The ischemic change of the optic fundi observed during the pre-

operative stage was resolved during the follow-up period in each patient.

### Illustrative case

A 63-year-old man visited our hospital complaining of declining visual acuity in the right eye. The right carotid angiogram revealed 95% stenosis of the right internal carotid artery at its origin (Fig. 1A). The right ophthalmic artery CDFI scan showed reversed flow, and the peak systolic flow velocity was  $-0.24$  m/s (Fig. 1B). The right optic fundus showed ischemic changes such as neovascularization of the disc and a small peripheral hemorrhage (Fig. 1C). The patient's visual acuity in the right eye was 20/60. A right carotid endarterectomy was performed. The patency of the carotid endarterectomy was confirmed by postoperative angiography (Fig. 1D). At 1 week after surgery, the right ophthalmic artery CDFI scan showed marked improvement. The flow direction of the ophthalmic artery was antegrade, and the peak systolic flow velocity was  $0.25$  m/s (Fig. 1E). The right optic fundus showed a disappearance of the ischemic changes at 1 week after the patient underwent surgery (Fig. 1F). The patient was followed for 19 months after the operation, and the ocular ischemic syndrome did not worsen. The patient's visual acuity was 20/30 at the end of the follow-up period.

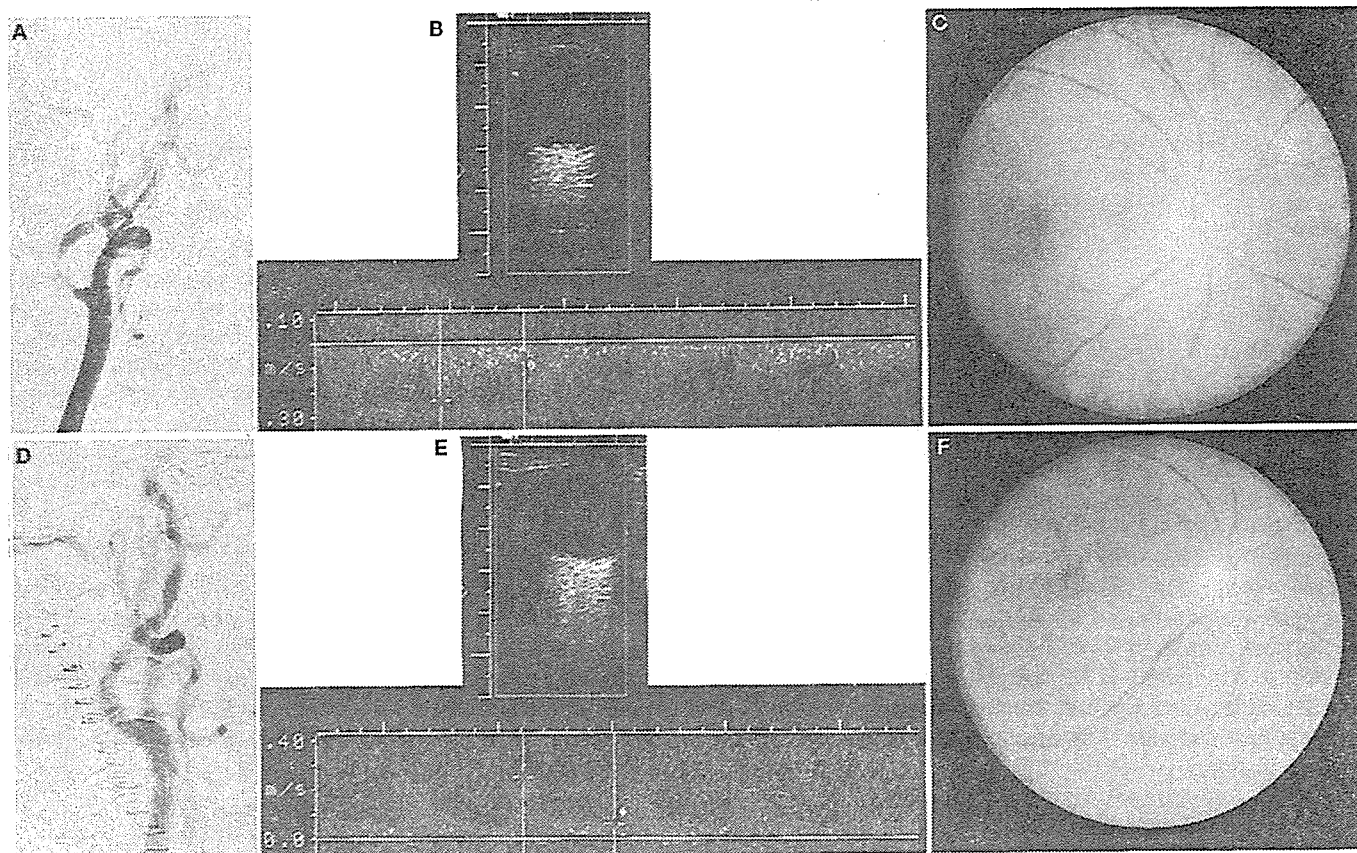


FIGURE 1. A, preoperative right carotid angiogram showing severe stenosis of the right internal carotid artery at its origin. B, preoperative right ophthalmic artery CDFI scan showing the reversed ophthalmic artery flow. C, preoperative right optic funduscopic scan showing neovascularization on the disc and a small peripheral hemorrhage. D, postoperative right carotid angiogram showing good patency achieved by the carotid endarterectomy. E, right ophthalmic artery CDFI scan obtained 1 week after carotid endarterectomy showing restoration of the normal ophthalmic artery flow. F, postoperative right optic funduscopic scan showing disappearance of the ischemic change.

## DISCUSSION

Hemodynamically significant carotid artery stenosis causes decreased or reversed ophthalmic artery flow and causes ocular complications such as transient monocular blindness, retinal artery occlusion, and ocular ischemic syndrome (13, 15, 24). Chronic ocular ischemic syndrome is the clinical manifestation of chronic ocular hypoperfusion (22). The prognosis for the visual symptoms affected by chronic ocular ischemia is generally poor (14). There is a highly significant correlation between internal carotid artery stenosis and ophthalmic artery peak systolic flow velocity (19). In this study, we examined the ophthalmic artery CDFI scans of patients with chronic ocular ischemic syndrome resulting from internal carotid artery stenosis before and after the patients underwent carotid endarterectomy. In the preoperative stage, the findings of the ophthalmic artery CDFI scans were abnormal in all patients. Five patients had reversed ophthalmic artery flow, and the other six patients had antegrade ophthalmic artery flow. Peak systolic flow velocity was low in all patients. The 11 patients exhibited a hemodynamically significant reduction in ophthalmic artery flow, which caused the ocular ischemic syndrome.

There have been reports that carotid endarterectomy resulted in significantly increased flow in the ophthalmic artery and that it also corrected reversed ophthalmic artery flow (4, 7, 10, 19). Reversed ophthalmic artery flow may contribute to the development of ocular ischemic syndrome characterized by a shunt to the low-resistance intracranial circuit and reduced blood flow to the eye (5, 6). Reversed ophthalmic artery flow was observed preoperatively in five patients in this study. For patients with chronic ocular ischemic syndrome due to reversed ophthalmic artery flow, normal ophthalmic artery flow must be established to prevent ocular ischemia (12). After undergoing carotid endarterectomy, all five patients in this series who had had reversed ophthalmic artery flow experienced resolution. Therefore, carotid endarterectomy is the appropriate treatment option for patients with ocular ischemic syndrome due to reversed ophthalmic artery flow caused by internal carotid artery stenosis. Preoperative studies in the other six patients in this series showed antegrade ophthalmic artery flow with reduction of peak systolic flow velocity. In these patients, peak systolic flow velocity significantly increased immediately after surgery. However, the peak systolic flow velocity in these six patients was still less than the value of the lower limit of the control patients after undergoing surgery. Riihelainen et al. (19) reported that individual responses to carotid endarterectomy varied and that such variations may be caused by local factors. In the present study, the success of the carotid endarterectomy was confirmed by angiography in each case. Therefore, the reason for the peak systolic flow velocities after surgery not reaching the normal control value in some patients might be attributable to the condition of the ophthalmic artery itself.

In the present study, 11 patients showed improvement in ocular ischemic syndrome, disappearance of the frequent amaurosis fugax and blurred vision, and no further progression in loss of visual acuity. We report clear evidence of the effect

of carotid endarterectomy on chronic ocular ischemia due to internal carotid artery stenosis on the basis of data obtained from ophthalmic artery CDFI scans. Carotid artery reconstruction is effective for the treatment of ocular ischemic syndrome and is most beneficial if performed early, before the onset of irreversible neovascular glaucoma or irreversible ischemia to the retina (20, 21). Chronic ocular hypoxia eventually leads to iris rubeosis. The presence of iris rubeosis most likely implies a greater degree of ischemia in the globe and increased total ocular damage (21). Furthermore, iris rubeosis occurs after neovascular glaucoma (2). At this point, the increased intraocular pressure exceeds the already compromised retinal arterial perfusion pressure, and central retinal artery obstruction develops secondarily (2). Therefore, the presence of iris rubeosis was considered an indicator of poor visual prognosis (21). In our series, each patient displayed a good visual outcome after carotid endarterectomy. We performed carotid endarterectomies on patients with little or no iris rubeosis and with normal intraocular pressure.

Ophthalmic artery CDFI is a relatively new examination method that has been used to evaluate vessel structures and blood flow velocity parameters in the ophthalmic artery (8, 19). Ocular hypoperfusion is the hallmark of the ocular ischemic syndrome, and the evaluation of vascular velocities and direction in the ophthalmic artery certainly aids in the diagnosis of this condition. In this study, we evaluated ischemic ocular syndrome on the basis of data obtained from ophthalmic artery CDFI scans. Ophthalmic artery CDFI displays both anatomic and velocity data on blood flow in a color-coded, real-time format. It is a simple, reproducible, and noninvasive method of detecting the flow profile in the ophthalmic artery for patients with severe occlusive carotid artery disease, especially those with ocular ischemic syndrome (11). It can be used to diagnose, monitor, and follow these patients (5, 12).

We showed the effect of carotid endarterectomy on chronic ocular ischemic syndrome due to internal carotid artery stenosis on the basis of the data obtained from ophthalmic artery CDFI scans. However, our study has several limitations: our series was very small, the study was nonrandomized, and the follow-up period was relatively short. In the future, we need a randomized trial combined with longer-term follow-up to further evaluate the effect of carotid endarterectomy on chronic ocular ischemic syndrome.

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**COMMENTS**

Kawaguchi et al. describe an interesting series of 11 patients with high-grade cervical carotid stenosis and documented chronic ocular ischemia. Some of these patients had reversal of ophthalmic flow, and others simply had reduced antegrade ophthalmic artery flow. All were measured by ophthalmic artery color Doppler flow imaging. All of these patients had high-grade stenosis by North American Symptomatic Carotid Endarterectomy Trial criteria, and all were revascularized successfully. Patency was proved by postoperative angiography. Slightly fewer than 50% of patients had restoration of visual function, and the remainder of patients had no further progression. The study is documented beautifully and sheds further light on the syndrome of chronic ocular ischemia, which is rarely discussed. I wonder whether this syndrome often is overlooked when we regard high-grade stenosis patients as asymptomatic. I am not certain that I could document 11 cases of chronic ocular ischemia that my institution has treated with carotid artery surgery. These authors' recommendations are interesting, and their work is scientifically valid, but it is unlikely to change any of the indications for carotid endarterectomy. All of the patients studied in the series had high-grade stenosis that would qualify for carotid reconstruction by either North American Symptomatic Carotid Endarterectomy Trial criteria or Asymptomatic Carotid Atherosclerosis Study criteria. I do think, however, that this report is worthwhile in instructing readers to look for chronic ocular ischemia in patients who might otherwise be dismissed as having non-carotid artery-related problems. I only wish that the authors had been successful in restoring visual function in a higher percentage of their patients. To their credit, they discuss this issue. I hope that after surgeons become aware of this phenomenon, patients with these conditions will be screened and identified by this mechanism so that carotid artery reconstruction will be undertaken somewhat sooner during the treatment process.

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The authors have documented, in a small series of patients, resolution of symptoms and signs of chronic ocular ischemia after carotid endarterectomy for high-grade internal carotid artery stenosis. Improved hemodynamics have been confirmed with periorbital Doppler flow studies. Senior colleagues in the Mayo Clinic's neuro-ophthalmological, neurology, and neurosurgery services—namely, Kearns (3, 4), Whisnant (1, 2), and Sundt (5), respectively—have played a key role over the past 4 decades in documenting the clinical symptomatology of this syndrome as well as its resolution after carotid endarterectomy and bypass surgery. We have witnessed improvement in many such cases, as reported in

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this series. Our experience leads us to believe that there is little question of the indications for and the efficacy of appropriate surgical treatment in these patients with high-grade extracranial carotid stenosis. I disagree with the authors that a randomized trial is necessary and wonder whether such a trial would even be ethical.

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Kawaguchi et al. describe 11 patients with various forms of ocular ischemic syndrome due to stenosis of the internal carotid artery. They used ophthalmic artery color Doppler flow imaging as well as signs and symptoms to make the diagnosis and to establish the patients' improvement after carotid endarterectomy. Unfortunately, ocular ischemic syndrome is a complex collection of signs and symptoms that result from chronic ocular hypoperfusion usually secondary to stenosis of the carotid artery. Kearns and Hollenhorst (2) first presented this syndrome in 1963 and called it *venous stasis retinopathy*, which is an unfortunate term because in these ischemic states the problem is neither on the venous side nor one of stasis. Others have called this ischemic syndrome *hypoperfusion retinopathy* or *ischemic oculopathy*.

Ocular ischemic syndrome probably is not common. It has been estimated to occur at a rate of seven cases per million and to affect at most 5% of patients who have significant

carotid artery disease (5). Reversal of ophthalmic artery flow by color Doppler imaging was demonstrated by Ho et al. (1) in 12 of 16 eyes studied. The infrequency with which this syndrome manifests, even in the context of carotid artery insufficiency, may be explained by the work of McFadzean et al. (3), who demonstrated that in ocular ischemic syndrome, hypoperfusion of the posterior ciliary arteries also needs to be present.

The only means of treating patients with ocular ischemic syndrome is carotid endarterectomy. Stabilization or improvement in vision probably occurs in only a small percentage of such patients, however. Indeed, even though patients' vision has been shown to improve in as many as 20% of eyes after endarterectomy, it usually deteriorates further within 1 year of surgery (4). In view of this, the authors have achieved remarkable success. They demonstrated an antegrade ophthalmic artery flow in all patients. Although they did report significant improvements in systolic flow velocity, as well as further improvements in visual acuity in 5 of their 11 patients and no worsening in the remaining 6 patients, I would have been impressed even more if a more comprehensive and rigorous means of evaluating patients' vision (e.g., mean decibel change on automated perimetry) had been performed.

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## Effect of Carotid Endarterectomy on the Ophthalmic Artery

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### Summary

**Background.** To evaluate the effect of carotid endarterectomy on ophthalmic artery flow direction and peak systolic flow velocity, the authors examined the ophthalmic artery on 32 patients who had undergone carotid endarterectomy.

**Methods.** The 32 patients had more than 70% stenosis of the internal carotid artery at its origin on angiography. The ophthalmic artery ipsilateral to the carotid endarterectomy was evaluated by the ophthalmic artery color Doppler flow imaging before surgery and then at one week, one month, and three months after surgery.

**Findings.** (1) Before carotid endarterectomy: eight patients showed reversed ophthalmic artery direction. In the other 24 patients with antegrade ophthalmic artery flow direction, the average peak systolic flow velocity was  $0.17 \pm 0.10$  m/sec. (2) At one week after carotid endarterectomy: The reversed ophthalmic artery flow direction was resolved in each patient. The average peak systolic flow velocity in the patients with preoperative antegrade flow rose significantly to  $0.28 \pm 0.10$  m/sec ( $p < 0.05$ ). (3) At one month and three months after carotid endarterectomy: All patients showed the antegrade ophthalmic artery flow direction. The average peak systolic flow velocities showed no significant change compared to the value at one week after carotid endarterectomy. (4) During the followed up period, there was no patient showing worsening or recurrence of clinical symptoms including the visual symptoms.

**Interpretation.** Carotid endarterectomy brought about the correction of the reversed flow and an increase in the peak systolic flow velocity of the ipsilateral ophthalmic artery immediately after surgery.

**Keywords:** Carotid endarterectomy; color Doppler imaging; ophthalmic artery.

### Introduction

The various prospective, randomized, and multi-centered studies already published were designed to evaluate the efficacy and safety of carotid endarterectomy [1, 2, 5, 16, 17, 21]. There are two possible favorable effects of carotid endarterectomy [8, 13, 14]. First, carotid endarterectomy removes atheromatous plaque, which is a possible source of cerebral emboli. Another, more hypothetical, explanation of the bene-

ficial effect is the restoration of cerebral perfusion pressure and improvement in the hemodynamic status of the brain. The internal carotid artery stenosis at its origin can influence the flow dynamics of the ophthalmic artery. The disturbed ophthalmic artery flow revealed the ocular ischaemic syndrome such as amaurosis fugax or decline of the visual acuity. Therefore, it is important to understand the flow pattern and condition of the ophthalmic artery in patients with internal carotid artery stenosis before and after carotid endarterectomy. To examine the ophthalmic artery, the authors performed ophthalmic artery color Doppler flow imaging (CDFI) on these patients with internal carotid artery stenosis treated by carotid endarterectomy. In this study, the authors discuss and analyze the effect of the carotid endarterectomy on the ophthalmic artery flow direction and peak systolic flow velocity based on the data of the serial ophthalmic artery CDFI.

### Patients and Methods

The ophthalmic artery CDFI was performed on thirty-two consecutive patients who had undergone primary carotid endarterectomy. Twenty-eight patients were male and four patients were female. The age range in the 32 patients was 58 to 73 years, with a mean of 66 years. The clinical symptoms and signs of the 32 patients were transient ischaemic attacks in 20, reversible ischaemic neurological deficit in 6, minor completed stroke in 2, and asymptomatic in 4 patients. Among 32 patients, 14 patients complained of chronic ocular ischaemic syndrome on the side ipsilateral to the affected internal carotid artery. According to the criteria of the ECST study [5], the grades of the angiographic internal carotid artery stenosis on the ipsilateral side were more than 90% stenosis in 14 patients and more than 70% stenosis in 18 patients. The range of carotid artery stenosis was within normal limits in all 32 patients. Standard carotid endarterectomy was performed at least 4 weeks after the last attack. There were no intra-operative or postoperative complications. Postoperatively, the patency of the carotid endarterectomy was confirmed by angiography in each patient within 2 weeks after surgery. All pa-

tients had follow-up visits after surgery, with the range of the follow-up period being 0.5 to 6 years (mean: 3.1 years). During this period, there were no patients presenting with a recurrent ischaemic attack or a worsening of the syndrome including the ocular signs.

#### Methods

The ophthalmic artery was estimated by CDFI using a Computed Sonography 128XP/10 (Acuson Corp., Mountain View, CA, USA). With 5 MHz probe, the power was less than 50 mW/cm<sup>2</sup>, and the examination was completed within 5 minutes. The ophthalmic artery CDFI findings from the eye ipsilateral to the carotid endarterectomy were analyzed. The ophthalmic artery CDFI was performed within one week before surgery, at one week after carotid endarterectomy, and at both one month and three months after surgery in each patient. These CDFI studies provided information regarding the flow direction and peak systolic flow velocity of the ophthalmic artery.

The physiological data were compared using a two-tailed paired or unpaired Student's *t* test. The value  $p < 0.05$  was taken as the threshold for statistical significance. All values are reported as means  $\pm$  standard deviation (SD). By means of CDFI before surgery, eight patients were found to have a reversed flow in the ophthalmic artery. It was recognized that these negative peak systolic flow velocity values would create erroneous data points in the calculation of mean values from the entire group, so these measurements were excluded from statistical analysis. The postoperative comparison in patients with reversed ophthalmic artery flow direction was done on the basis of the restoration of normal, antegrade flow in the ophthalmic artery and the restoration of normal flow velocities.

## Results

### Before Carotid Endarterectomy

The ophthalmic artery flow directions were reversed in 8 patients and antegrade in 24 patients. The average peak systolic flow velocity in patients with reversed flow was  $-0.30 \pm 0.18$  m/sec. The average peak systolic flow velocity in the ophthalmic arteries of patients with antegrade flow was  $0.17 \pm 0.10$  m/sec.

### At One Week after Carotid Endarterectomy (Fig. 1)

The patients with preoperative reversed ophthalmic artery flow direction were all observed to have a return to normal antegrade ophthalmic artery flow direction. This reversal of the reversed ophthalmic artery flow direction was significant. In these eight patients, the peak systolic flow velocity was  $0.26 \pm 0.14$  m/sec. The average peak systolic flow velocity in the patients with preoperative antegrade flow rose to  $0.28 \pm 0.10$  m/sec, which showed a significant increase as compared with the preoperative level ( $p < 0.05$ ). There was no significant difference in the mean peak systolic flow velocities between the patients with preoperative reversed ophthalmic artery flow direction and the patients with

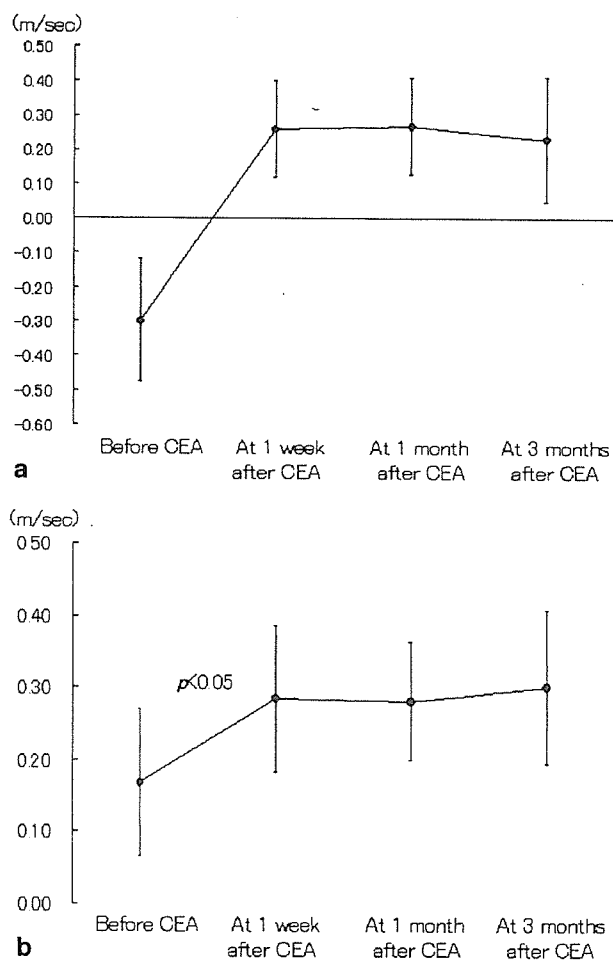


Fig. 1. (a) Course of the peak systolic flow velocity of the ophthalmic artery in patients with preoperative reversed ophthalmic artery flow direction. (b) Course of the peak systolic flow velocity of the ophthalmic artery in patients with preoperative antegrade ophthalmic artery flow direction

preoperative antegrade ophthalmic artery flow direction.

### At One Month after Carotid Endarterectomy (Fig. 1)

All patients showed the antegrade ophthalmic artery flow direction. The average peak systolic flow velocity of the patients with preoperative reversed ophthalmic artery flow direction was  $0.27 \pm 0.14$  m/sec. This value did not show significant change compared to the value at one week after surgery. The average peak systolic flow velocity in the patients with preoperative antegrade ophthalmic artery flow direction was  $0.28 \pm 0.08$  m/sec, which was not a significant change as compared with the value at one week after carotid endarterectomy.



### *At Three Months after Carotid Endarterectomy (Fig. 1)*

The flow direction of ophthalmic artery was antegrade in all patients. The average peak systolic flow velocities were  $0.23 \pm 0.18$  m/sec in the patients with preoperative reversed flow and  $0.30 \pm 0.11$  m/sec in the patients with preoperative antegrade flow. There was no significant change in the peak systolic flow velocity in either of the patients with preoperative antegrade flow or in the patients with preoperative reversed flow compared to the value at one month after carotid endarterectomy.

### *Ocular Symptoms*

Before carotid endarterectomy, 14 patients complained of chronic ocular ischaemic syndrome. Among these 14 patients, 6 patients showed the reversed ophthalmic artery flow direction, while only 2 patients without the chronic ocular ischaemic syndrome showed the reversed ophthalmic artery flow direction. This relationship between chronic ocular ischemic syndrome and reversed ophthalmic artery flow direction was significant ( $p < 0.05$ ). During the follow-up period, in 18 patients without preoperative chronic ocular ischaemic syndrome, postoperative chronic ocular ischaemic syndrome was prevented. Among 14 patients with preoperative chronic ocular ischaemic syndrome, 6 patients showed improved ocular symptoms, and in the remaining 8 patients, there was no worsening of the ocular ischaemic syndrome.

### *Illustrative Case*

A 70-year-old male visited the authors' hospital complaining of transient left hemiparesis, and right sided amaurosis fugax. Right carotid angiography showed 95% stenosis of the right internal carotid artery at its origin (Fig. 2A). Right ophthalmic artery CDFI showed reversed flow, and peak systolic flow velocity was  $-0.54$  m/sec (Fig. 2B). Right carotid endarterectomy was performed. At one week after surgery, the patency of the carotid endarterectomy was confirmed on right carotid angiography (Fig. 2C). At one week after carotid endarterectomy, the right ophthalmic artery CDFI showed a resolution of the reversed flow, and the peak flow velocity was  $0.44$  m/sec (Fig. 2D). The peak systolic flow velocity of the ophthalmic artery was  $0.42$  m/sec at one month after surgery, and it

was  $0.43$  m/sec at three months after surgery. The patient had follow-up visits for 2.5 years after surgery, and there was no ischaemic event including visual symptoms.

### **Discussion**

It is well known that carotid endarterectomy for severe stenosis of the internal carotid artery has proven to be highly beneficial in the secondary prevention of stroke in symptomatic patients [5, 16, 17]. The recent report from NASCET also demonstrated that in experienced surgical hands carotid endarterectomy is safe and effective in the near term and remarkably effective in the longer term in preventing recurrence of ipsilateral carotid ischaemia and in preventing disabling ipsilateral stroke [17]. Occlusive internal carotid artery diseases reveal ophthalmic artery flow disturbances [20]. The hemodynamic reduction of the ocular circulation due to severe internal carotid artery stenosis reveals ocular ischaemic syndrome. A small subgroup of patients who would benefit from carotid endarterectomy may experience ocular ischaemic syndrome [12]. Therefore, it is important to evaluate the ophthalmic artery in the patients treated by carotid endarterectomy (for the internal carotid artery stenosis.) However, there have been few reports about the effect of the carotid endarterectomy on the ophthalmic artery [3, 12]. To evaluate the effect of carotid endarterectomy on the ophthalmic artery, the authors examined the ophthalmic artery CDFI before and after surgery, including the follow-up period. According to the present study, the authors have demonstrated correction of the abnormal flow direction and improvement of the ophthalmic artery flow velocity after carotid endarterectomy.

In the present series, eight patients showed reversed ophthalmic artery flow direction before carotid endarterectomy. In these eight patients, the ophthalmic artery might function as a collateral circulation from the external to the intracranial circulation [4, 9, 10, 15]. The patients presenting the reversed ophthalmic artery flow direction have severe disturbed ocular hemodynamics. These patients should be at high risk of presenting an ocular ischaemic syndrome. The authors have demonstrated the resolution of the abnormal flow direction immediately after surgery. The normalization of the reversed ophthalmic artery flow direction immediately after surgery could prevent the presence of or worsening of the ocular ischaemic syndrome.

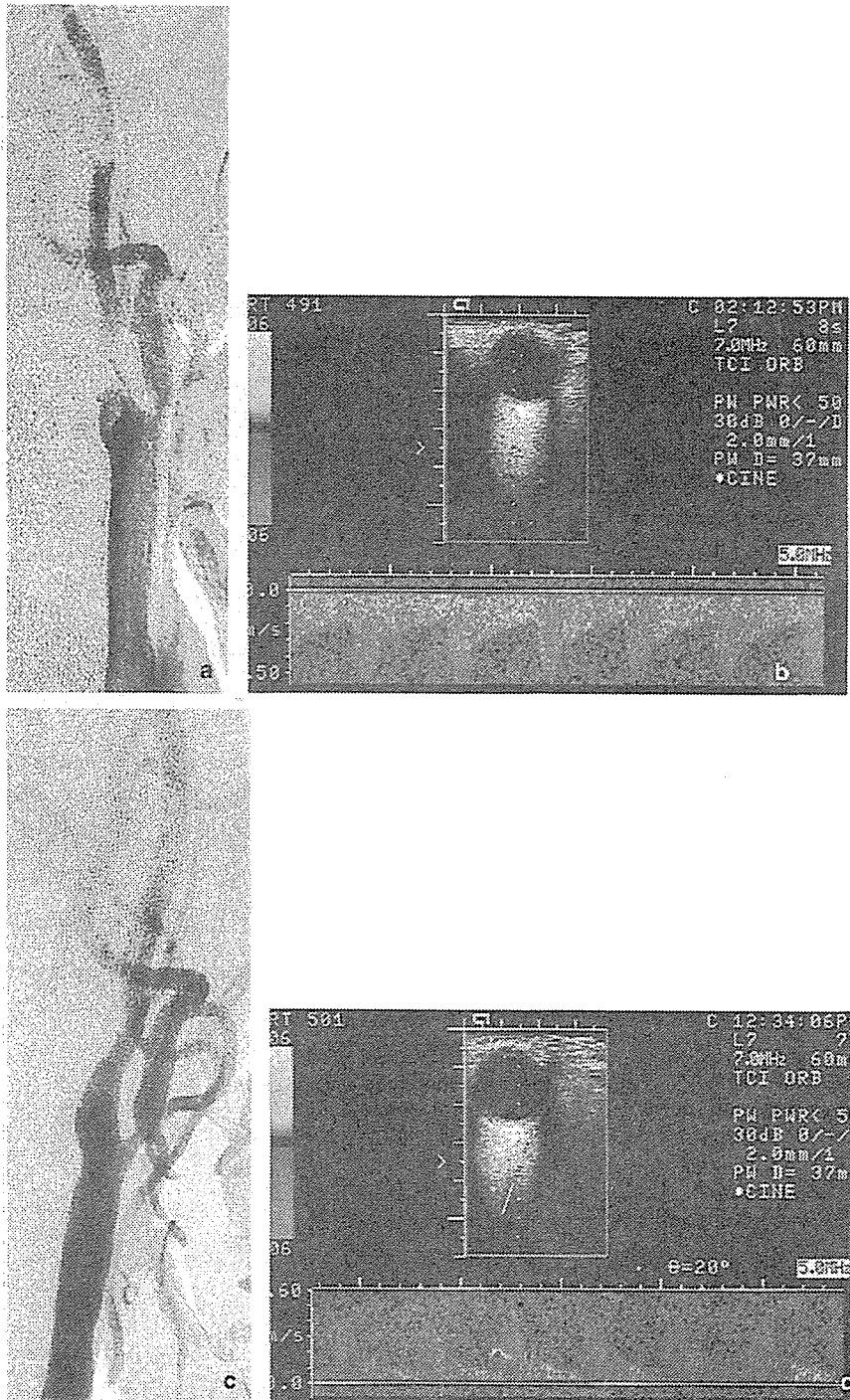


Fig. 2. (a) Preoperative right carotid angiography showing the severe stenosis of the right internal carotid artery at its origin. (b) Preoperative right ophthalmic artery color Doppler flow imaging (CDFI) showed the reversed ophthalmic artery flow direction. (c) Postoperative right carotid angiography show good patency after carotid endarterectomy. (d) Right ophthalmic artery CDFI at one week after carotid endarterectomy showing the restoration of the normal ophthalmic artery flow direction

Twenty-four patients demonstrated the antegrade ophthalmic artery flow direction with the low peak systolic flow velocity before surgery. Immediately after surgery, the significant increase in ophthalmic artery flow velocity was seen. This significant improvement of the ophthalmic artery flow velocity has also explained the correction of the ocular hemodynamic

compromise. In this series, the increase of the flow velocity and correction of the flow direction were seen in each case. Clinically, all 32 patients showed no new, worsening or recurrent ocular ischaemic syndrome during the follow up period. In patients with preoperative chronic ocular ischaemic syndrome, improvement or prevention of the worsening of chronic ocular



ischaemic syndrome could be achieved. Moreover, in patients without preoperative chronic ocular ischemic syndrome, chronic ocular ischaemic syndrome could be prevented during the follow-up period. Therefore, there is a good correlation during the postoperative stage between the course of the ocular ischaemic syndrome and improvement of the ophthalmic artery CDFI findings [12].

According to this study, the improvement of the peak flow velocity and normalization of the reversed ophthalmic artery flow direction was seen within one week after surgery. After this period, there was no significant improvement of the ophthalmic artery peak flow velocity. This effect of carotid endarterectomy was quite natural according to the surgical manoeuvre. Previous reports showed the hemodynamic improvement after carotid endarterectomy according to the serial single photon emission computed tomography imaging or transcranial Doppler flow studies [3, 7, 11, 18, 19]. In this report, the authors clarify the course over time of correction of the disturbed ophthalmic artery flow direction and peak systolic flow velocity after carotid endarterectomy based on the ophthalmic artery CDFI findings.

In the present study, the authors have demonstrated disturbed ophthalmic artery flow direction and peak systolic flow velocity before carotid endarterectomy in patients with severe internal carotid artery stenosis using the ophthalmic artery CDFI. The ophthalmic artery CDFI can be used as the screening test for patients with ocular ischaemic syndrome due to the occlusive internal carotid artery lesions. After carotid endarterectomy, the disturbed ophthalmic artery flow direction and peak systolic flow velocity improved remarkably based on the data of ophthalmic artery CDFI. The ophthalmic artery CDFI was used to evaluate the effect of carotid endarterectomy on the ophthalmic artery flow direction and peak systolic flow velocity. However, safety and the potential risk of ophthalmic artery CDFI are important problems. The most important thing in this examination was the tissue damage due to the heating effect of the ultrasound. In this study, patients were instructed to turn their eyes away from the probe during the examination. Authors used the low power setting ( $<50 \text{ mW/cm}^2$ ), and completed the examination within 10 minutes in each eye. The American Institute of Ultrasound in Medicine sets the safety power limit of the ophthalmic artery CDFI at less than  $100 \text{ mW/cm}^2$  [1, 2]. Hu *et al.* reported that continuous-wave ultrasound with a  $50 \text{ mW/cm}^2$

power setting for studying the ophthalmic artery has been used in their laboratory for 12 years on at least 25,000 patients without complications or known adverse effects [9]. Therefore, the transorbital ultrasound examination is safe for the eyes [1, 7–9].

## Conclusion

Carotid endarterectomy brought about the correction of the reversed flow and an increase in the peak systolic flow velocity of the ophthalmic artery in patients with more than 70% internal carotid artery stenosis. These improvements of the ophthalmic artery CDFI findings were seen immediately after carotid endarterectomy correlating well with the clinical ischaemic syndrome. The ophthalmic artery CDFI also could be used as the monitor for the evaluation of the carotid endarterectomy including the ocular hemodynamics.

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## Comments

Kawaguchi *et al.* present the effect of carotid endarterectomy on ophthalmic artery flow in patients with more than 70% stenosis in the ipsilateral internal carotid artery.

Based on ophthalmic artery color doppler flow imaging (CDFI), the authors evaluated the artery flow before and after carotid endarterectomy as a measure of restoration of cerebral perfusion pressure and improvement in the hemodynamic status of the brain. CDFI was performed on 32 patients who had undergone carotid endarterectomy.

Fourteen patients complained of the ocular ischaemic syndrome on the affected internal carotid artery side (amaurosis fugax or decline of the visual acuity). The effect of endarterectomy was evident in the first week after surgery and remained stable during the follow up period.

The authors demonstrated correction of the reversal flow direction and improvement of the ophthalmic artery flow velocity after carotid endarterectomy. The reversal flow direction on the ophthalmic artery functions as a collateral circulation from the external to the internal circulation. The patients who showed this abnormal flow direction should be at high risk of ocular ischaemic syndrome. The normalization of flow after surgery could prevent the presence or worsening of the ocular ischaemic syndrome.

This study showed a good correlation between the measured ophthalmic artery CDFI improvement and the clinical course of the ocular ischaemic syndrome, and could be used for the evaluation of carotid endarterectomy hemodynamic results.

*J. Mura – E. de Oliveira*

This clinical prospective study is aimed to demonstrate the haemodynamic effect of carotid endarterectomy on the ophthalmic arterial circulation. The authors utilized color Doppler flow imaging to measure direction of blood flow and blood flow velocity in the ophthalmic artery of the affected side. Their findings indicate that carotid endarterectomy corrected the reversed flow and increased the peak systolic flow velocity of the ipsilateral ophthalmic artery in all of the patients. The authors are to be congratulated for their excellent clinical results.

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## Effects of Bypass on CO<sub>2</sub> Cerebrovascular Reactivity in Ischaemic Cerebrovascular Diseases – Based on the Intra-Operative LCBF and CO<sub>2</sub> Cerebrovascular Reactivity Studies

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### Summary

The authors evaluated the effects of superficial temporal to middle cerebral artery (STA-MCA) bypass on CO<sub>2</sub> cerebrovascular reactivity (CVR) in ischaemic cerebrovascular diseases (CVDs).

Local cerebral blood flow (LCBF) and CO<sub>2</sub> CVR in 19 patients with ischaemic CVD subjected to standard STA-MCA bypasses were examined during surgery. Single photon emission computed tomography (SPECT) with acetazolamide (ACZ) activation was also performed before and at 1 month after surgery.

The results are as follows. 1) Before bypass, the average CO<sub>2</sub> CVR value was  $-1.50 \pm 2.30\%/mmHg$  (mean  $\pm$  SD). SPECT showed disturbed response to ACZ in all cases. Fifteen cases showed the steal phenomenon. After bypass, the mean CO<sub>2</sub> CVR value significantly ( $p < 0.05$ ) increased, and four cases resolved their steal phenomenon. 2) Before bypass, the mean LCBF was significantly ( $p < 0.05$ ) lower than the control level. After bypass, the mean LCBF significantly ( $p < 0.05$ ) increased. 3) In the postoperative SPECT findings, 13 cases showed a disturbed response to ACZ. The CO<sub>2</sub> CVR value in these 13 cases was  $-1.21 \pm 1.19\%/mmHg$ , which was significantly ( $p < 0.05$ ) low compared to the values for the 6 cases showing normal postoperative ACZ responses.

In ischaemic CVDs before bypass, the CO<sub>2</sub> CVR values were extremely low. After bypass, however, CO<sub>2</sub> CVR and LCBF values significantly improved. SPECT findings, including ACZ challenge, correlated well to the LCBF and CO<sub>2</sub> CVR values. STA-MCA bypass exerted a favourable effect on the CO<sub>2</sub> CVR and LCBF values immediately after bypass in the cases showing a reduced pre-operative response to CO<sub>2</sub>.

**Keywords:** CO<sub>2</sub> reactivity; cerebral ischaemia; STA-MCA bypass; steal phenomenon.

### Introduction

Even after the report of the International Co-operative Study of Extracranial/Intracranial Arterial Bypass [9], there have been many reports of the usefulness of bypass surgery for ischaemic cerebrovascular diseases (CVDs). The major problem in this study, however, was the lack of data and information

regarding cerebral blood flow (CBF). It has recently been shown that patients with occlusive carotid artery disease showing a marked reduction in their cerebral perfusion reserve belong to a subgroup who could benefit from bypass surgery [4, 7, 13, 18, 19, 24].

The CBF response to the inhalation of PaCO<sub>2</sub>, a common procedure to evaluate the haemodynamic significance of stenosis in extra- and intracranial arteries [8], may prove useful in the selection of symptomatic patients with carotid occlusions or inaccessible internal carotid artery (ICA) stenosis for revascularization by EC/IC bypass [5, 24]. However, there are still many unresolved issues surrounding local cerebral blood flow (LCBF) and CO<sub>2</sub> cerebrovascular reactivity (CO<sub>2</sub> CVR) in ischaemic CVDs.

The aim of this study was to evaluate the effects of bypass surgery on CO<sub>2</sub> CVR in ischaemic CVDs, and to identify the most appropriate candidates for bypass. For this purpose, we analysed the LCBF and CO<sub>2</sub> CVR data measured during surgery both before and after anastomosis, and we also examined the single photon emission computed tomography (SPECT) data obtained in the standard resting stage and the acetazolamide (ACZ) activation stage before and after bypass.

### Patients and Methods

#### Patient Population

LCBF and CO<sub>2</sub> CVR studies were carried out on cases with STA-MCA bypass performed for symptomatic ischaemic CVDs. A total of 19 cases (15 males and 4 females; ages 41–72 years, mean age: 61 years) were studied. The clinical symptoms were transient ischaemic attack (TIA) in 8 cases, reversible ischaemic neurological deficit

(RIND) in 8, and minor completed stroke (MiCS) in 3. CT scans showed the absence of a low density area (LDA) in 6 cases, spotty LDA in the basal ganglia in 6 cases, and LDA in a watershed zone in 6 cases and in the lobal cortex in 1 case. The angiographic findings showed internal carotid artery (ICA) occlusion in 12 cases, ICA stenosis ( $\geq 50\%$ ) in 4 cases, and middle cerebral artery (MCA) occlusion in 3 cases.

In this study, the STA-MCA bypass was performed on the clinically symptomatic cases showing a disturbed response to ACZ with or without a reduction in the resting CBF on SPECT. The clinical symptoms correlated to the site of the obstructive findings as indicated by angiography.

The standard STA-MCA bypass was performed more than 4 weeks after the onset, when the neurological symptoms were stable. During the surgery, the posterior temporal or temporo-occipital artery was chosen as the recipient artery. Postoperatively, the patency of the bypass was checked by angiography within 2 weeks of the operation in all cases. Postoperative angiography performed within two weeks of the operation, showed good patency of the bypass and a retrograde filling of the middle cerebral artery through the bypass in each case.

#### Follow-up Study of Clinical Symptoms

The follow-up period for the 19 cases ranged from 9 months to 3.7 years (mean follow-up period: 2.1 years). During the follow-up period, none of the patients complained of recurrent clinical ischaemic attack.

#### LCBF Measurement

The LCBF was measured during surgery by the thermal diffusion technique using a flow probe with a Peltier stack [6, 22] on the precentral gyri during surgery. After opening the dura, before anastomosis, the LCBF was first measured at normocapnia ( $\text{PaCO}_2$ ;  $37.6 \pm 2.4$  mmHg). Next, to investigate the  $\text{CO}_2$  CVR, the LCBF was measured at hypocapnia ( $\text{PaCO}_2$ ;  $29.8 \pm 4.4$  mmHg) induced by hyperventilation and the LCBF was measured continuously. After completing the anastomosis, the LCBF and  $\text{CO}_2$  CVR measurements were carried out in the same manner.

$\text{CO}_2$  CVR was calculated as a percentage of the change in LCBF per millimeter of mercury decrease in  $\text{PaCO}_2$ , expressed as a percentage in the change per millimeter of mercury (relative  $\text{CO}_2$  reactivity) [26]. The mean arterial blood pressure (MABP) was maintained at 90–112 mmHg with no significant change before and after bypass at any  $\text{PaCO}_2$ .

#### SPECT Studies

SPECT studies were performed in all cases with  $^{123}\text{I}$  N-isopropyl-p-iodoamphetamine (IMP) not only at the resting stage, but also at the ACZ activation stage before surgery and at 1 month after surgery. The resting images were analysed in comparison to the primary occipital visual cortex. The ACZ activation images were estimated using subtracted SPECT images, which were obtained by subtracting the resting SPECT images from the ACZ activation SPECT images. The response to ACZ on SPECT was divided into two groups. The one with a normal response to ACZ, and the other with a disturbed response to ACZ compared to the response of the healthy side.

#### LCBF and $\text{CO}_2$ CVR of Normal Controls

For the control study, we used the same technique and protocol to examine LCBF and  $\text{CO}_2$  CVR values at the inferior frontal gyri in

five patients with non-ruptured aneurysms. The mean age in these cases was 59.7 years; two patients were male and three were female. There were no remarkably abnormal findings on the CT scan in these five cases. From these control cases, the average LCBF (mean  $\pm$  SD) was determined to be  $65.0 \pm 15.3$  ml/100 g/min (MABP; 102.0 mmHg,  $\text{PaCO}_2$ ; 37.4 mmHg) and the average  $\text{CO}_2$  CVR (mean  $\pm$  SD) was  $3.26 \pm 0.58\%$ /mmHg.

#### Statistical Analysis

The physiological data were compared by a two-tailed paired or non-paired Student's *t* test. The value of  $p < 0.05$  was taken as the threshold for statistical significance. All values are reported as means  $\pm$  standard deviation.

## Results

#### LCBF Alteration Before and After Bypass

At normocapnia ( $\text{PaCO}_2$ ; 37.6 mmHg), the average LCBF was  $45.7 \pm 11.2$  ml/100 g/min before surgery, which was significantly reduced in comparison to the control cases ( $p < 0.05$ ). After bypass, the mean LCBF increased significantly ( $p < 0.05$ ) to  $59.3 \pm 13.0$  ml/100 g/min (Fig. 1). At hypocapnia (mean  $\text{PaCO}_2$ ; 29.9 mmHg), the average LCBF was  $49.1 \pm 14.1$  ml/100 g/min before surgery, which then significantly ( $p < 0.05$ ) increased to  $61.0 \pm 17.4$  ml/100 g/min after bypass.

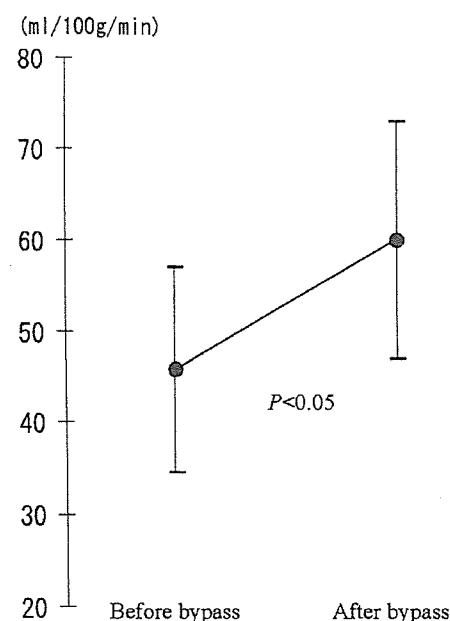


Fig. 1. Comparison of local cerebral blood flow before and after bypass