# Validation of Ultrasound Parameters to Assess Collateral Flow via Ophthalmic Artery in Internal Carotid Artery Occlusion

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This study aimed to characterize the flow patterns using ultrasound (US) in the external carotid artery (ECA) in patients with total occlusion of internal carotid artery (ICA) and characterize collateral retrograde flow through the ophthalmic artery (OA, secondary collateral, internalization). This study was performed on 45 patients who were retrospectively selected with total occlusion of the ICA, who underwent digital subtraction angiography (DSA), magnetic resonance angiography (MRA), and US (43 men; mean age 68.1 ± 7.9 years). Collateral retrograde flow and collateral flow through the circle of Willis (primary collateral) were determined by DSA and MRA. We compared several US parameters such as ECA peak systolic velocity, mean velocity, end-diastolic (ED) velocity, pulsatility index (PI), and pulsatility transmission index (PTI). PTI was defined as the ratio of ipsilateral ECA PI to the ipsilateral common carotid artery (CCA). In this patient group, 27 patients showed retrograde flow through OA as assessed by DSA. The presence of primary collateral flow was significantly lower in patients with retrograde flow than without ($P < .05$). ECA ED velocity was significantly higher, and PI and PTI were significantly lower with retrograde flow through OA than without ($P < .05$). According to receiver operating characteristic analysis, PTI was the most highly correlated ultrasonologic parameter with internalization (cutoff value, .94; sensitivity, 92.6%; specificity, 94.5%). Using PTI was discriminative to determine internalization of ECA because a collateral pathway through OA in cases of ICA occlusion had less primary collateral pathways. **Key Words:** Carotid artery occlusion—collateral circulation—ophthalmic artery—carotid ultrasound—pulsatility transmission index.


## Introduction

Annual stroke rates in patients with carotid artery occlusion range from 0% to 5%[1,2] in asymptomatic patients to 27% in symptomatic patients.[3,4] In patients with occlusion of the internal carotid artery (ICA), collateral circulation plays a pivotal role in the pathophysiology of cerebral ischemia.[5] The major collateral is the circle of Willis, including the anterior communicating artery (ACoA) and posterior communicating artery (PCoA), which can compensate for diminished blood flow (primary collateral). On the other hand, collateral pathways through the ophthalmic artery (OA) and leptomeningeal vessels may be recruited as secondary collateral when collateral flow through the circle of Willis is inadequate.[6] Some studies have shown that the presence of collateral circulation through the ipsilateral external carotid artery (ECA) and OA is associated with hemodynamic impairment in the ICA.[7,8] Therefore, secondary collateral circulation may be an indicator of increased risk of future ischemic events.

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Received October 1, 2013; accepted October 12, 2013.

Grant support: None.

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1052-3057/$ - see front matter



http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2013.10.012

To assess secondary retrograde flow in the OA, a conventional arteriography is the most accurate examination. However, arteriography is not suitable as a screening test because of the ever-present risk of a disabling stroke and systemic complications and also because of its high cost. Schneider et al[9] used transorbital Doppler (TOD) ultrasonography to assess OA as a source of collateral cerebral blood supply. However, evaluation of OA requires the use of specialized techniques, knowledge, and specific tools. Moreover, although there have been no reports of thermal hazards from TOD when using the orbital window, there is the possibility of potential effects on the retina.

Diagnosis of complete occlusion can be complicated by the presence of large ECA collaterals via OA, which can be mistaken for the ICA.[10,11] The conversion to a low-resistance Doppler sonography waveform in the ECA has been termed "internalization" because the abnormal spectral tracings in the ECA mimic the spectral tracings in a normal ICA.[12] This change is often because of complete occlusion of the ICA with subsequent development of low-resistance collateral pathways between the ipsilateral external and internal circulation, typically through the ophthalmic vascular bed.[13] Although it is easier to assess the collateral pathway with occlusion of the ICA, there are no published criteria for internalization using carotid ultrasound (US) measurements. Therefore, we determined the criterion for judgment of internalization based on ultrasonography of the neck.

## Methods

### *Subjects*

We retrospectively analyzed patients admitted to our institute with unilateral ICA occlusion who underwent digital subtraction angiography (DSA), magnetic resonance angiography (MRA), and carotid US between April 1999 and March 2009. In our study, the data were obtained using a standard of care clinical protocol. According to the standard ethical guidelines for clinical research in Japan, the requirement of informed consent was waived. We excluded patients with bilateral ICA occlusion and OA stenosis or occlusion in which the lesions affected the collateral circulation. We evaluated clinical features, carotid US parameters, MRA, and DSA data. The following underlying clinical features were examined: age, sex, ICA occlusion side, hypertension (blood pressure ≥ 140/90 mm Hg or history of antihypertensive medication), hypercholesterolemia (serum total cholesterol ≥ 5.7 mmol/L or history of antihypercholesterolemic medication), diabetes mellitus (fasting blood glucose 7.0 mmol/L, a positive 75-g oral glucose tolerance test, or history of antidiabetic medication), current smoking habit, and contralateral ICA stenosis (≥70% stenosis confirmed by carotid US, MRA, or DSA).

### *Digital Subtraction Angiography*

Informed consent for DSA was obtained from both the patients and their family. Selective DSA was performed using a biplane, high-resolution angiography system (Angio Rex Super-G and DFP-2000A; Toshiba, Tokyo, Japan) with a matrix of 1024 × 1024 pixels. A catheter was inserted into the right brachial artery or femoral artery according to the Seldinger method and guided to the cerebral arteries. After a selective common carotid artery (CCA) injection on the side of the ICA occlusion, ECA collaterals were detected on the angiogram by the contrast filling of ECA, OA, carotid siphon, middle cerebral artery, or anterior cerebral artery. The degree of collateral flow via the OA observed in DSA was graded on a 3-point scale according to a previous report[14]: grade 0, slight collateral distribution (eg, no filling of OA); grade 1, small but definite collateral supply (eg, retrograde flow in OA with filling of carotid siphon); and grade 3, full collateral filling (eg, to the middle cerebral artery and/or anterior cerebral artery; Fig 1).

### *Magnetic Resonance Angiography*

MRA was performed using a 1.5-T MR unit (Magnetom Sonata; Siemens, Erlangen, Germany). Previous studies have indicated that MRA provides a reliable method to assess the direction of flow in the circle of Willis[15,16]; therefore, we determined the collateral flow via the ACoA and PCoA using MRA. Stenosis of the A1 segment of the ACoA and PCoA of 70% or more was assessed as being incapable of fulfilling the collateral role.

### *Carotid Ultrasound*

A carotid US examination was performed using a 7.5-MHz, linear-array transducer (SSA-270 A; Toshiba) within approximately 7 days before or after DSA (4.3 ± 3.6 days). One investigator with no previous knowledge of the patients' clinical information, including angiographic findings, measured several parameters of the carotid US (the flow velocities of ECA and CCA). The sample volume was set within two thirds of the diameter of the CCA or ECA, and care was taken to maintain an adequate angle of 60° or less between the beam and the wall of the CCA or ECA. The CCA flow was measured at 1-2 cm proximal to the bulb, and the ECA flow was measured before the bifurcation of the superior thyroid artery. The pulse repetition frequency was 3.0 or 3.5 Hz, and the low-pass filter was set at 70 Hz. We aimed to measure two thirds of the diameter in the center of the artery and actually measured mostly centerline velocity. We obtained the peak systolic flow velocity (PSV), the end-diastolic flow velocity (EDV), and the time-averaged peak mean flow velocity of the ipsilateral CCA and ECA. The pulsatility index (PI) was automatically calculated by the instrument as PSV – EDV/mean flow velocity (MV). The pulsatility transmission index (PTI)[17] was defined as a ratio of the PI of the ipsilateral ECA to a reference artery (CCA).