Reversal of ophthalmic artery blood flow direction and severe ipsilateral carotid stenosis

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Abstract

Background: The assessment of ophthalmic artery flow direction by transcranial Doppler sonography has become part of the cerebrovascular routine examination in stroke patients. It provides helpful information for the investigation of collateral circulation and can evaluate the hemodynamic significance of high-grade internal carotid artery (ICA) stenosis. Our aim was to determine the value of assessing the direction of ophthalmic artery blood flow in the setting of routine color flow duplex ultrasonography examination of patients with ipsilateral carotid disease.

Methods: We reviewed 967 ultrasound carotid scans performed in our Neurosonology Unit from January 2003 to December 2011 with ICA stenosis ≥50%, and assessed ophthalmic artery flow direction.

Results: Ophthalmic artery flow reversal was seen in 73 cases, 62 (85%) of which were in cases of ICA stenosis ≥80%. Flow reversal in ophthalmic artery had a sensitivity of 43%, specificity of 99%, negative predictive value of 91% and positive predictive value of 85% for ICA stenosis ≥80%.

Conclusion: We found a significant association between reversal of ophthalmic artery flow and carotid stenosis ≥ 80% with an excellent specificity and negative predictive value. Assessing ophthalmic artery can be especially important in patients with difficult duplex scans or with stenosis in the pre-ophthalmic artery intracranial segment of internal carotid artery, where duplex scan may fail to detect the lesion. Evaluation of ophthalmic artery blood flow direction is therefore feasible and accurate with Doppler ultrasound, and it brings very useful information to better assess intracranial hemodynamic status that can influence treatment decisions.

Keywords: Carotid stenosis, Ophthalmic artery, Reversed ophthalmic artery flow, Cerebral collateral flow pathways, Transcranial Doppler, Carotid duplex ultrasonography.
Introduction

Doppler ultrasonography is now widely used for the diagnosis of internal carotid artery (ICA) stenosis. Its diagnostic accuracy, if performed by experienced sonographers, has shown to be $>90\%$ when compared with angiography [1, 2].

A significant number of previous studies have shown that transcranial Doppler examination can add important information to carotid duplex scanning [3-7]. Some have used a transcranial Doppler battery to assess the hemodynamic significance of ICA stenosis and reported that reversed ophthalmic artery flow (ROAF) has low sensitivity but a specificity of $100\%$ in $\geq70\%$ carotid stenosis on cerebral angiography or in lesions with a residual lumen diameter of less than 1.5 mm from “en bloc” endarterectomy [3, 4]. A more recent study specifically focused on the ophthalmic collateral pathway in patients with internal carotid artery disease has also established that the frequency of ROAF increases with worsening severity of stenosis. Moreover, the authors found that ROAF was strictly associated with high-grade ($\geq80\%$) ICA stenosis or occlusion, with excellent positive predictive value and decent negative predictive value [7].

The ROAF in the setting of significant ICA ($\geq70\%$) is not infrequent, with some reports estimating an incidence of approximately 25% [8, 9]. However, its role in cerebral collateralization is somewhat controversial [9-18]. The ophthalmic artery (OA) is traditionally regarded as an important source of cerebral blood supply in patients with ICA occlusion [10, 11]. Some authors have demonstrated that intracranial hemodynamic status is associated with overall collateral blood supply available to the brain not depending on specific patterns of collateralization, namely via anterior and posterior communicating arteries, or OA [12, 13]. Moreover, Vernieri and co-workers suggested that the prognosis of patients with carotid artery occlusion was significantly influenced by the number of collateral pathways and by vasomotor reactivity. Notably, in patients with only one or two intracranial collateral pathways, the functional aspect of cerebral hemodynamics appeared to overhang individual anatomic characteristics in influencing their outcome [13]. Conversely, other studies show conflicting results and are not clear about the specific role of OA as an important source of blood to the brain. Anzola and colleagues suggested that this pathway, although important for the intraorbital structures, was probably of limited functional significance to the hemispheric blood supply [14]. Accordingly, others proposed an hierarchy in cerebral collateralization, relegating the OA as a collateral of last resort [15, 16]. Hu and co-workers reported in a prospective 4-year follow-up study that asymptomatic patients with $\geq75\%$ carotid artery stenosis or occlusion and ROAF had an elevated risk of occurrence of ischemic event, in contrast to patients with forward OA flow [17]. Furthermore, Reinhard and colleagues found that dynamic cerebral autoregulation is substantially impaired when secondary collateral pathways (ophthalmic or leptomeningeal arteries) are activated [18]. In line with these findings, Tsi and co-workers observed that the presence of ROAF was associated with a shunt to an area of low-resistance intracranial circulation due to impaired intracranial hemodynamic status or insufficient collateral blood flow via the circle of Willis. Moreover, it was demonstrated that ROAF was highly associated to the combination of stenosis of the cervical and intracranial segments and less well correlated to high-grade cervical carotid stenosis/occlusion alone. Additionally, similarly to the presence of intracranial stenosis and previous stroke, ROAF was shown to be associated with a poorer functional outcome [9].

The objective of our study was to determine the value of assessing the direction of ophthalmic artery blood flow in the setting of color flow duplex ultrasonography examination of symptomatic or asymptomatic patients, in order to better characterize the hemodynamics related to ipsilateral carotid stenosis.

Methods

All records from patients referred to the Neurosonology Unit at São João Hospital Centre between January 2003 and December 2011 were reviewed. Duplex scanning was performed using Philips HDI 5000 ultrasound device, with a 4-7 MHz linear array transducer for cervical carotid evaluation and a pulsed 2-4 MHz transducer via transorbital approach for OA exam, with adapted power. The grade of ICA stenosis was assessed using the European Carotid Surgery Trial (ECST) method and combined with velocimetric criteria [19, 20]. We selected duplex scans with $\geq50\%$ ICA stenosis in which orbital color flow duplex ultrasonography examination was available. Cases with carotid occlusions, previous endarterectomy or stenting, isolated parietal carotid thrombus, arterial dissection or incomplete data were excluded. The range of carotid stenosis was correlated with OA flow direction using the one-way analysis of variance (ANOVA) followed by Bonferroni’s post-hoc comparisons tests. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were then calculated. Microsoft Excel (MS Office 2010) was used to collect all data and perform descriptive statistics. SPSS Statistics version 20 (IBM, Armonk, NY, USA) was used to perform the remaining analysis.

Results

We have selected duplex scans of 967 ICA stenosis: 346 with 50-59%, 316 with 60-69%, 162 with 70-79%, 119 with 80-89%, and 24 with 90-99% stenosis (Figure 1). Seventy-three of these stenotic cases had ipsilateral ROAF. We did not find collateralization from this artery in any of the cases with 50-59% stenosis. However, with worsening severity of stenosis, the frequency of ROAF increased, as can
be seen in Figure 2, being 43% (62 cases) when carotid stenosis was ≥80%. There was a significant increase in collateralization from this artery for stenosis 80-89% comparing to 70-79% and in the 90-99% group comparing to 80-89%. Overall, when ROAF was detected, there was a sensitivity of 43%, a specificity of 99%, a negative predictive value of 91%, a positive predictive value of 85%, and an accuracy of 91% for a high-grade stenosis of ≥80% (Table 1).

**Discussion**

Our study has shown an increase of the frequency of ROAF with the worsening severity of cervical ICA stenosis. Detection of ROAF had a sensitivity of 43%, a specificity of 99%, a negative predictive value of 91%, a positive predictive value of 85%, and an accuracy of 91% for a high-grade stenosis of ≥80% (Table 1).

To our knowledge, this study is one of the largest series correlating the flow direction of the OA and ipsilateral ICA stenosis, and according to the data previously reported by Reynolds and colleagues [7], we confirm that ROAF has a high specificity for severe ipsilateral ICA stenosis.

One possible limitation of the study is the lack of comparison with digital angiography. Despite duplex scan acknowledged as having a high diagnostic accuracy, we accept that the presence of ROAF associated with <80% stenosis could be related to distal ICA stenosis/occlusions not detected by this technique. Another issue that should be referred is that in this study the presence of other intracranial collateralization systems was not analyzed, which could interfere with the existence of ROAF in each patient.

The present study shows that the analysis of the OA flow as common practice in any Neurosonology laboratory constitutes a powerful tool. It can be especially im-

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**Figure 1.** Number of ICA stenosis measured by the ECST method.

ICA = Internal carotid artery; ECST = European Carotid Surgery Trial

**Number of ICA stenosis measures by ECST method**

![Graph showing number of ICA stenosis measures by ECST method.]

**Figure 2.** Percentage of cases presenting ROAF according to the grade of ipsilateral ICA stenosis.

OA = ophthalmic artery; ICA = Internal carotid artery; ECST = European Carotid Surgery Trial; ROAF = Reversed ophthalmic artery flow
important in patients with difficult duplex scans that may limit the effectiveness of the exam, bringing advantage in better characterizing the hemodynamic significance of ipsilateral ICA stenosis. Additionally, ROAF might be the only ultrasound exam clue in the case of a severe stenosis in the pre-ophthalmic artery intracranial segment of internal carotid artery, where duplex scan may miss the lesion. More importantly, ROAF may indicate inadequate collaterals through the circle of Willis and poor cerebral hemodynamic status [9].

In conclusion, evaluation of ophthalmic artery blood flow direction is feasible and accurate with Doppler ultrasound, and it brings very useful information to better assess intracranial hemodynamic status that can influence treatment decisions.

Abbreviations

ANOVA: Analysis of variance; ECST: European Carotid Surgery Trial; ICA: Internal carotid artery; OA: Ophthalmic artery; ROAF: Reversed ophthalmic artery flow

Competing interests

The authors declare no conflict of interest.

References


Table 1. Statistical measures for the presence of ROAF.

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<tr>
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<th>Accuracy</th>
<th>Specificity</th>
<th>Negative predictive value</th>
<th>Positive predictive value</th>
<th>Sensitivity</th>
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<tr>
<td>High-grade stenosis (≥80)</td>
<td>91%</td>
<td>99%</td>
<td>91%</td>
<td>85%</td>
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ROAF = Reversed ophthalmic artery flow.