Spontaneous and Endothelial-Independent Vasodilation Are Impaired in Patients With Spontaneous Carotid Dissection
A Case-Control Study

Ralf W. Baumgartner, MD; Barbara Lienhardt, MD; Maria Mosso, MD; Joubin Gandjour, MD; Nicolas Michael, MD; Dimitrios Georgiadis, MD

Background and Purpose—We undertook this case-control study in patients with unilateral spontaneous dissection of the cervical internal carotid artery to investigate spontaneous and endothelium-independent dilation of the nondissected, contralateral carotid arteries and the ipsilateral brachial artery using high-resolution ultrasound.

Methods—Spontaneous and endothelial-independent (nitroglycerin-mediated) absolute and relative dilation were assessed in the internal and common carotid and brachial arteries of 27 patients with unilateral spontaneous dissection of the cervical internal carotid artery and 27 age- and sex-matched healthy controls.

Results—Absolute and relative spontaneous and endothelial-independent dilation of the carotid, but not brachial arteries, were significantly lower in patients as compared with controls.

Conclusions—Vasodilation abnormalities may be a predisposing factor for spontaneous dissection of the cervical internal carotid artery. (Stroke. 2007;38:405-406.)

Key Words: arteries ■ nitroglycerin ■ ultrasonics

The etiology of spontaneous dissection of the cervical internal carotid artery (sICAD) is unknown. Patients with sICAD have a higher prevalence of fibromuscular dysplasia (5.5% to 12.5%) compared to subjects in large autopsy series (0.02%), may also have hereditary connective-tissue disorders and show abnormalities of collagen and elastic fibers in 55% to 68% of skin biopsy samples. These findings suggest the presence of vessel wall abnormality, which might impair vasomotion and predispose to dissection.

The goal of this case-control study performed in patients with unilateral sICAD was to investigate spontaneous and endothelium-independent dilation of the nondissected, contralateral extracranial carotid arteries and the ipsilateral brachial arteries using high-resolution ultrasound.

Methods

Patients and Controls
Between October 1992 and March 2000, 89 patients with unilateral sICAD were admitted in our department. Eighty-seven of these patients survived the acute phase of stroke. Diagnosis of sICAD was established by cervical MRI with T1 fat suppression technique (wall hematoma) and MR angiography. Angiographic criteria consisted of string sign, pseudoaneurysm, or intimal flap. At 6-month ultrasound follow-up, complete recanalization was diagnosed in 58 cases (67%).

Exclusion criteria were a history of neurological (except for sICAD), hypertension, diabetes mellitus, hypercholesterolemia, low-density lipoprotein cholesterol >1.0 mmol/L, ratio total/high-density lipoprotein cholesterol >5, hyperhomocystinemia, contraindication to the use of nitrates, caffeine or alcohol intake ≤12 hours before study onset, pregnant or breastfeeding woman, cerebrovascular atherosclerosis at color duplex sonography. These were met by 31 patients, 27 of whom (16 men; mean age, 48.5 ± 9.0 years) consented to participate in this study. Additionally, 27 age- and sex-matched healthy volunteers (15 men; mean age, 46.0 ± 14.0 years) were enrolled.

Data were analyzed without patient identification. The study was performed according to local ethical committee standards, and all participants gave written informed consent.

Ultrasound Investigations of the Cerebral Arteries and Vasodilation
The common carotid artery (CCA), internal carotid artery (ICA) (origin, cervical, siphon, and terminal segment), external carotid, anterior, middle, and posterior cerebral, subclavian, vertebral, and basilar arteries were insonated with color duplex sonography. Complete recanalization of a dissected artery was diagnosed when peak systolic velocity was ≤90 cm/s in women or ≤80 cm/s in men, and the peak systolic velocity quotient sICAD/contralateral cervical ICA was ≤1.12.

Vasodilation was studied in CCA (below carotid bifurcation), ICA (above bulb), and brachial artery (BRA) with a color duplex sonography scanner (Acuson XP128) using a 4 to 8 MHz linear probe ≥2 hours after breakfast, and after a supine rest of ≥15 minutes between 9:00 AM and 12:00 PM. In patients, CCA and ICA were investigated on the side opposite to sICAD, and BRA on the side of sICAD to avoid insonation of a vessel supplying a paretic arm. In controls, vessels were investigated on the same body side as in patients. M-mode imaging was used to assess arterial diameter (distance near to far walls at borderline between media and adventitia). Absolute (diameter change from end-diastole to peak-systole)

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Spontaneous and Endothelium-Independent Dilation of the Common Carotid, Internal Carotid, and Brachial Arteries in 27 Patients

<table>
<thead>
<tr>
<th>Artery</th>
<th>Parameter</th>
<th>Patients</th>
<th>Controls</th>
<th>P*</th>
<th>Patients</th>
<th>Controls</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common carotid</td>
<td>Dilation (µm)</td>
<td>513 (593–698)</td>
<td>785 (679–885)</td>
<td>0.02</td>
<td>552 (469–660)</td>
<td>844 (732–943)</td>
<td>0.0004</td>
</tr>
<tr>
<td></td>
<td>% Dilation</td>
<td>7.8 (6.6–9.3)</td>
<td>10.2 (8.9–11.6)</td>
<td>0.02</td>
<td>6.3 (5.3–7.5)</td>
<td>9.9 (8.7–11.3)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Internal carotid</td>
<td>Dilation (µm)</td>
<td>334 (281–406)</td>
<td>432 (371–561)</td>
<td>0.03</td>
<td>257 (222–301)</td>
<td>447 (362–546)</td>
<td>0.0002</td>
</tr>
<tr>
<td></td>
<td>% Dilation</td>
<td>5.0 (4.4–5.9)</td>
<td>6.8 (5.9–8.4)</td>
<td>0.01</td>
<td>3.5 (2.9–4.2)</td>
<td>6.1 (4.9–8.2)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Brachial</td>
<td>Dilation (µm)</td>
<td>172 (128–235)</td>
<td>235 (187–284)</td>
<td>0.1</td>
<td>270 (212–340)</td>
<td>263 (201–337)</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>% Dilation</td>
<td>4.2 (3.3–5.6)</td>
<td>4.9 (3.7–5.9)</td>
<td>0.4</td>
<td>4.2 (3.2–5.3)</td>
<td>4.1 (3.5–2.2)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

All data (dissection and 27 age- and sex matched controls) are expressed as median (95% confidence intervals).

* Mann-Whitney U test.

and relative (end-diastolic plus peak systolic divided by end-diastolic diameter) dilation were calculated off-line, using a vascular distension recorder (Vadirec 101; Medical Systems Arnhem). Off-line analysis was performed in a blinded fashion. Endothelium-independent vasodilation was assessed 5 to 20 minutes after sublingual administration of 0.8 mg nitroglycerin because its effect starts within 2 to 3 minutes and is stable for 60 minutes.

Normally distributed data were compared using paired t test, and non-normally distributed data using Mann-Whitney U test. Significance was declared at P<0.05.

Results

Absolute as well as relative spontaneous dilation values were significantly lower in patients, as compared with controls, for both the CCA and ICA (Table). The same was true for nitroglycerin-mediated vasodilation, and difference between both groups was more prominent compared with spontaneous vasodilation. No significant differences in dilation values were observed between patients and controls in BRA measurements (Table).

The vessel diameters of the CCA, ICA, and BRA, and blood pressure values were similar in both groups (data not reported).

Discussion

Our main findings were the significantly lower spontaneous and endothelium-independent dilation values in the carotid arteries of patients with sICAD, as compared with healthy controls. No such differences were observed in the BRA, which is in accordance with a previous study.5

In line with the present study, Guillen et al6 reported similar diameters of the CCA and ICA in patients with sICAD and controls. On the contrary, these authors found a higher spontaneous relative change of the CCA diameter in patients with sICAD compared with controls, whereas spontaneous ICA and BRA as well as nitroglycerin-induced vasodilation were not investigated. This discrepancy is difficult to explain. Technical inaccuracies are unlikely; computer-assisted, off-line analysis of B-mode images registered on a videotape and commercially available and validated vascular distention recorder were used by Guillen et al6 and in the present study, respectively. Our results were unequivocal for the ICA and CCA and became highly significant after the administration of nitroglycerin.

Ultrasonic vasodilation studies investigate the distensibility of the main components of the vessel wall: the elastic, collagen, and smooth muscle fibers.7 The CCA and ICA are elastic arteries, whose wall movements are mainly determined by the relative amounts of elastin and collagen and their anatomic relationship.8 Ultrastructural abnormalities of the elastic and collagen fibers were reported in 55% to 68% of patients with cervical artery dissection, resembling in some cases the aberrations found in Ehlers-Danlos syndrome type II or III.9 It is thus plausible to suggest that such abnormalities might explain the observed abnormal vasodilation. It is unclear, however, whether the impaired vasodilation is an epiphenomenon of a suspected, but yet unproven, structural wall abnormality or increases the risk for vessel dissection.

A limitation of the present study is that endothelial dependent vasodilation was not examined. However, determination of endothelial-dependent vasodilation of the carotid arteries is an invasive procedure, requiring use of catheter angiography, which would hardly be justified in a research setting.

In conclusion, these findings suggest that patients with sICAD may have a functional abnormality of the carotid wall, which may predispose to dissection.

Disclosures

None.

References

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