Accuracy of Color Duplex Ultrasound Diagnosis of Spontaneous Carotid Dissection Causing Ischemia

David H. Benninger, MD; Dimitri Georgiadis, MD; Joubin Gandjour, MD; Ralf W. Baumgartner, MD

Background and Purpose—Spontaneous dissection of the cervical internal carotid artery (sICAD) is mainly assessed with MRI and magnetic resonance angiography (MRA), which are not always at hand. In contrast, color duplex sonography (CDS) is readily available. We undertook this prospective study to examine the accuracy of CDS to diagnose sICAD in patients with first carotid territory ischemia.

Methods—Consecutive patients with first carotid territory stroke or transient ischemic attack or retinal ischemia underwent clinical and laboratory examinations, ECG, CDS of the cerebral arteries, cranial computed tomography in case of stroke or transient ischemic attack, and echocardiography and 24-hour ECG in selected cases. Patients were included, if they were <65 years of age, CDS showed a probable sICAD (cervical internal carotid artery stenosed or occluded), or had no determined etiology of ischemia. All of the included patients underwent cervical MRI and MRA±cerebral catheter angiography. The sonographer was blinded to the results of MRI and angiography studies.

Results—We included 177 of 1652 screened patients. Excluded patients (n=1475) were ≥65 years old (n=818), had another determined cause of ischemia (n=1475), and had intracranial hemorrhage (n=58). CDS diagnosed sICAD in 77 of 177 patients, and the etiology of ischemia was undetermined in the remaining 100 patients. Cervical MRI and angiography showed 74 sICAD; there were 6 falsely positive and 3 falsely negative CDS findings. Thus, sensitivity, specificity, and positive and negative predictive values for CDS diagnosis of patients with sICAD causing carotid territory ischemia was 96%, 94%, 92%, and 97%, respectively.

Conclusions—Color duplex ultrasound allows the reliable exclusion of sICAD in patients with carotid territory ischemia, whereas diagnosis of CDS of sICAD must be confirmed with cervical MRI and MRA. (Stroke. 2006;37:377-381.)

Key Words: dissection ■ stroke ■ ultrasonography

Spontaneous dissection of the cervical internal carotid artery (sICAD) is an important cause of ischemic stroke in young adults.1–3 Nowadays, the diagnosis of sICAD is essentially established with cervical MRI and magnetic resonance angiography (MRA).4–7 However, MRI and MRA are often not available around the clock. Thus, many centers use ultrasonic to assess sICAD, although no study has examined the diagnostic reliability of this approach. The aim of this prospective study was to determine the accuracy of color duplex sonography (CDS) to diagnose patients with sICAD causing carotid territory ischemia.

Methods

In this prospective study, consecutive patients with suspicion of first-ever carotid territory stroke, transient ischemic attack (TIA), or retinal ischemia underwent the usual evaluation, which included the assessment of medical history, medical and neurological examination, routine blood sampling, 12-lead ECG, CDS of the cerebral arteries, and brain computed tomography in case of stroke or TIA. Transthoracic or transoesophageal echocardiography and 24-hour ECG were performed at the discretion of the treating physician. Patients with stroke or TIA were recruited in our stroke unit, and those with retinal ischemia were mainly referred from the Department of Ophthalmology. The recruitment period lasted from October 1997 until December 2004. The study was performed according to the guidelines of the local ethics committee.

Patients were included in the present study if they fulfilled the following criteria: (1) age ≥65 years, because most patients with sICAD are in this age group;6–10; and (2) suspicion of sICAD at CDS [cervical internal carotid artery (ICA) stenosed or occluded] or no determined etiology of ischemia according to the Trial of Org 10172 in Acute Treatment criteria. ICADs were classified as spontaneous when occurring spontaneously or secondary to a precipitating event (eg, coughing, abrupt head movements); patients with a history of blunt head or neck trauma were excluded. All of the included patients underwent cervical MRI and MRA. Patients without MRI and MRA signs of sICAD underwent, in addition, cerebral catheter angiography (CA), when the treating physician deemed this investigation to be necessary.

Ultrasound studies were performed on an emergency basis by a vascular technician or a resident, and supervised by R.W.B. The sonographer was blinded to the results of cervical MRI and angiography. Cervical MRI, MRA, and CA studies were always performed after the ultrasound investigation. For the purpose of this study, MRI and angiographic studies were reevaluated by D.H.B. and J.G. These examiners were not at all involved in the ultrasound studies.
Ultrascanographic Investigations

Ultrasoundographic investigation of the extracranial and intracranial cerebral arteries was performed by experienced radiologists with color duplex scanners (Acuson XP 10 or Sequoia). For extracranial sonon of the ICA, the common carotid (CCA), external carotid, subclavian, and the vertebral (VA) arteries, 4- to 8-MHz linear probes were used. For extracranial sonon of the cervical ICA, transorbital and transcranial CDS studies, 2- to 3.5-MHz sector probes were used. Transorbital CDS studies assessed the ophthalmic arteries and the carotid siphon. Transcranial CDS studies were performed as reported previously. In brief, the terminal (C1) segment of the ICA, the middle, anterior, precommunicating posterior (P1), and postcommunicating posterior (P2) cerebral arteries, and the anterior communicating arteries were sonated through the temporal window with the patient in a supine position. Intracranial VA and the basilar artery were sonated through the foramen magnum with the patient in a sitting position. Patients with insufficient ultrasound windows were also investigated with the echocontrast agent Levovist at concentrations of 400 mg/mL, as reported previously.

ICAD was suspected in patients presenting with stenosis or occlusion of the cervical ICA in CDS in the absence of significant atherosclerotic disease of the extracranial carotid arteries defined as >30% local stenosis or occlusion of the common carotid artery, external carotid artery, or ICA at the origin and aortic dissection extending into the carotid arteries or vasculitis.

Stenoses of the cervical ICA were quantified as reported before. A ≤50% stenosis was diagnosed when intrastenotic peak systolic velocity (PSV) was >90 cm/s in women and >80 cm/s in men, and the PSV quotient intrastenotic ICA/contralateral cervical ICA was >1.12 (each reference value was higher than the PSV mean +3SD of 78 unpublished own healthy volunteers). A >50% stenosis was diagnosed when intrastenotic PSV was >120 cm/s and the PSV quotient intrastenotic ICA/CCA on the side of ICAD (ipsilateral) was >1.5. Intrastenotic velocities are frequently decreased in ICAD causing high-grade stenosis. To avoid falsely negative findings, only >80% stenoses were diagnosed using presntenotic and posntenotic hemodynamic criteria, and ≥2 of the following 3 had to be present: (1) the quotient of the resistance index (PSV−peak end-diastolic velocity/PSV) ipsilateral CCA/resistance index contralateral CCA >0.15; (2) reversed flow in the ipsilateral opthalmic artery; and (3) cross-flow through the anterior communicating artery. The criteria for >50% and >80% ICA stenoses have been published in peer-reviewed journals, developed in studies using CA as standard of reference, and elaborated with the same ultrasound equipment used in the present study. The last criterion was used because different ultrasound machines have been shown to measure different flow velocities under identical conditions of examination in both flow phantoms and patients.

ICA occlusion was assessed as reported before. Using CA as the “gold standard,” we have shown that ultrasound may misdiagnose subtotal stenosis as occlusion in acute ICAD. Therefore, ICAD causing >80% stenosis and occlusion were grouped together. Stenosis and occlusion of the extracranial VA was diagnosed as described by von Büdingen and von Reutern, and stenoses of the carotid siphon as reported by Ley-Pozo et al. Intracranial arteries were investigated for the presence of stenoses, occlusions, and cross-flow through the circle of Willis according to previously published criteria.

Statistics

Statistical analysis was carried out with the Systat software package. Differences between unpaired groups were compared by nonparametric analysis of variance (Mann-Whitney U test). Two-sided P values <0.05 were considered significant.

Results

As shown in Figure 1, 1652 consecutive patients with first carotid territory stroke (n=1243), TIA (n=291), amaurosis fugax (n=70), or retinal infarct (n=48) were screened. We excluded 1475 of 1652 patients. They were ≥65 years of age in 818 cases, had another determined etiology of carotid territory ischemia in 1081 cases, and showed intracranial hemorrhage in 58 cases.

We included 177 of 1652 patients (73 women and 104 men; mean age, 50±12 years) who underwent cervical MRI and MRA with or without CA. Before cervical MRI and angiography studies were performed, 77 of 177 included patients were assumed to have a sICAD, because CDS showed a stenosis or occlusion in the cervical ICA (Table 1). The remaining 100 patients were presumed to have no determined cause of ischemia.
according to the Trial of Org 10172 in Acute Treatment criteria, and the cervical ICA was normal at CDS. The cause of carotid territory ischemia were sICAD in 74 patients, fibromuscular dyplasia (FMD) in 3 patients, cardiac embolism related to patent foramen ovale with atrial septum aneurysm and vasospasm of the cervical ICA in 1 patient each, and remained undetermined in 99 patients (Figure 1).

The results of ultrasound, cervical MRI, and angiographic assessment are shown in Figure 1. There were 6 falsely positive CDS findings, which included 1\(^{\text{st}}\)50% stenosis, 3\(^{\text{rd}}\)80% stenoses (Figure 2), and 2 occlusions. These 6 patients are described in detail in Table 2. Furthermore, there were normal CDS findings in the cervical ICA of 3 patients with sICAD who showed no luminal narrowing at angiography and a cervical pseudoaneurysm in 1 case. Thus, the sensitivity for CDS diagnosis of patients with sICAD causing carotid territory ischemia was 96%, the specificity 94%, the positive predictive value (PPV) 92%, and the negative predictive value (NPV) 97%.

**Discussion**

The main finding of this study performed in patients with first carotid territory ischemia is that normal ultrasound findings in the cervical ICA allowed the reliable exclusion of an underlying sICAD reflected by sensitivity and NPV values of 96% to 97%. Consequently, the next diagnostic step would be the search for another determined etiology of ischemia, whereas MRI and MRA of the neck, as well as cerebral CA, could be avoided. This standard operating procedure is likely to reduce both the amount of diagnostic work-up and the associated costs.

Ultrasound showed a high sensitivity for diagnosing patients with sICAD in this series. Previous studies reported sensitivities of 95% to 96% for detecting sICAD using extracranial Doppler and duplex sonography combined with transcranial Doppler sonography\(^{19,24}\) and sensitivities of 100% using extracranial Doppler sonography.\(^{27}\) Still, a comparison of the present with these former ultrasound studies is difficult, because they were not performed in a context comparable to the present setting. Ultrasound missed 2 sICAD without stenosis at angiography and 1 sICAD causing a pseudoaneurysm but no stenosis. This is a predictable limitation of the present ultrasound assessment, which was based on hemodynamic criteria. The aforementioned cervical pseudoaneurysm was also missed by B-mode and color Doppler imaging, which is probably because of the location in the depth of the neck.

The lower specificity and PPV (92% to 94%) of ultrasound for diagnosing patients with sICAD is because of the fact that 6 patients without dissection showed false pathological ultrasound findings in the cervical ICA, that is, 1\(^{\text{st}}\)50% stenosis, 3\(^{\text{rd}}\)80% stenoses, and 2 occlusions. Diagnosis of \(\leq\)50% stenoses is based on the presence of a focal velocity increase, because the location in the depth of the neck prevents the detection by B-mode and color Doppler imaging in most cases. Carotid dissection is associated with an increased prevalence of redundancies, such as kinking,\(^{28}\) which may also cause a focal raise of flow velocities.

**TABLE 1. Clinical and Ultrasound Findings in 75 Patients With and 102 Patients Without Carotid Dissection Causing Carotid Territory Ischemia**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Carotid Dissection [n (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present (n=75)</td>
</tr>
<tr>
<td>Amaurosis fugax</td>
<td>11 (15)</td>
</tr>
<tr>
<td>Retinal infarct</td>
<td>0</td>
</tr>
<tr>
<td>TIA</td>
<td>24 (32)</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>60 (80)</td>
</tr>
<tr>
<td>Local signs (Horner syndrome, palsy of cranial nerves IX, X, or XII)*</td>
<td>25 (33)</td>
</tr>
<tr>
<td>Cervical carotid artery at ultrasound</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Stenosis (\leq)50%</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Stenosis 50–80%</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Stenosis (\geq)80% or occlusion</td>
<td>62 (82)</td>
</tr>
</tbody>
</table>

*Local signs were located on the side of the suspected carotid dissection.
In our patient, a ≤50% stenosis was misdiagnosed in a kinked cervical ICA, because it is impossible to differentiate whether increased flow velocity results from the redundancy itself or an additional stenosis.

The 3 patients with false-positive >80% stenoses had no wall hematoma at MRI, and angiography delineated FMD causing moderate stenoses of the cervical ICA (Figure 2), C1 ICA extending in the middle cerebral artery (MCA), or ACA in 1 case each. Ultrasound showed pathologically slow velocities in the ipsilateral cervical ICA and ophthalmic artery (OphA) and the narrowed MCA and ACA. The slow ICA velocities probably resulted in the patient with extracranial FMD from the concomitant acute occlusion of the ipsilateral MCA and ipsilateral VA at the atlas loop at MRA and CA (Figure 2); normal echocardiography.

Interestingly, all of the patients with FMD experienced the sudden onset of yet-unknown and intense headache before the onset of stroke symptoms, suggesting the additional presence of an intracranial dissection. MRI detection of a dissection hematoma in extracranial FMD may be impaired31–33 and has not been reported in patients with intracranial FMD to our knowledge. Furthermore, FMD may modify the angiographic appearance of sICAD.31–33 Thus, all of the patients with FMD might have experienced sICAD, which was missed by MRI and angiography.

Two patients with a tapering ICA occlusion at ultrasound and angiography showed no wall hematoma. One ICA occlusion was most likely because of vasospasm, as repetitive ultrasound and MRA studies showed spontaneous changes of the ICA diameter during the subsequent 5-year follow-up.34 The other ICA occlusion was probably because of embolism related to a patent foramen ovale associated with an atrial septum aneurysm. Thus, angiographic findings were also false positive, which confirms their nonspecific character.19

Although no controlled study has evaluated antithrombotic therapy in patients with sICAD, many authors recommend the administration of heparin,32,33,35 which is also supported by the fact that arterial embolism is the main mechanism of ischemia.36–37 On the other side, heparin is associated with a greater bleeding risk than aspirin, which is the main reason that the International Stroke Trial found no beneficial effect of heparin in patients with acute ischemic stroke.38 Thus, patients who are treated with heparin because of a falsely positive ultrasound diagnosis of sICAD will undergo an unnecessary risk of bleeding. Furthermore, ultrasound missed intracranial cerebral artery stenoses because of FMD, suggesting that it may also fail to detect cerebral artery narrowing because of intracranial dissection. The wall of the ICA becomes smaller in its intracranial segment, suggesting a higher risk of rupture, which will be enhanced by anticoagulant agents.33 Therefore, we and other authors do not administer heparin in patients with intracranial dissection. Finally, patients with false-positive ultrasound diagnosis of sICAD will probably not undergo a search for another etiology of stroke and may receive an inappropriate stroke prevention therapy. These considerations suggest that ultrasound diagnosis of sICAD should be confirmed with cervical MRI and MRA and that the decision to administer anticoagulants should not be based on ultrasound findings.
A shortcoming of this study is that the sonographer was just blinded to the results of cervical MRI and MRA and CA. However, the aim of the present investigation was to examine the accuracy of ultrasound in a common clinical situation, when the sonographer is typically aware of the results of ancillary investigations.

We have shown in a previous study that sICAD, causing no ischemic events but either no or just local symptoms and signs on the side of dissection (eg, headache, neck pain, Horner syndrome, and cranial nerve palsy), showed just in 71% abnormal findings in the cervical ICA.8 The latter findings suggest that ultrasound is not useful for excluding sICAD, causing no ischemic symptoms and signs. Another study is necessary to evaluate the reliability of ultrasound assessment of patients with suspicion of sICAD causing no ischemic events, because inclusion and exclusion criteria would differ from the present study.

In conclusion, the present data suggest that ultrasound allows the reliable exclusion of an underlying sICAD in patients with carotid territory ischemia and reduces the diagnostic workup and the associated costs. However, the false-positive findings indicate that the diagnosis of sICAD should be confirmed by cervical MRI and MRA.

References

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Stroke. 2006;37:377-381; originally published online December 22, 2005;
doi: 10.1161/01.STR.0000198811.65068.16

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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