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
Ultrasonographic Investigations

Ultrasonographic investigation of the extracranial and intracranial cerebral arteries was performed by experienced neurologists with color duplex scanners (Acuson XP 10 or Sequoia). For extracranial insonation 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 insonation of the cervical ICA, transorbital and transcervical 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 insonated through the temporal window with the patient in a supine position. Intracranial VA and the basilar artery were insonated through the foramen magnum with the patient in a sitting position. Patients with insufficient ultrasonic windows were also investigated with the echocontrast agent Levovist at concentrations of 400 mg/mL, as reported previously.

SI CAD 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 prestenotic and poststenotic 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 ophthalmic artery; and (3) cross-flow through the anterior communicating artery. The criteria for >50% and >80% ICA stenoses have been published on peer-reviewed journals, developed in studies using CA as standard of reference, and elaborated with the same ultrasound equipment used in the present study.

Figure 1. Diagnostic work-up of 177 patients with carotid territory ischemia because of carotid dissection at ultrasound (n=77) or an undetermined etiology (n=100).

Cervical MRI, MRA, and CA Studies

MRI diagnosis of sICAD was based on detection of a mural hematoma in the cervical ICA. Angiographic diagnosis was based on detection of a flame-shaped occlusion, string sign, segmental stenosis beginning distal to the carotid bulb, or a dissecting aneurysm. In the presence of occlusion of the cervical ICA at angiography, MRI detection of a mural hematoma was needed for diagnosis of sICAD. Cervical MRI and angiograms were reviewed by 2 neurologists (D.H.B. and I.G.) at special reading sessions, blinded to the patient’s identities. In case the judgments of both neurologists differed on an imaging study, the case was discussed until a diagnosis was obtained by consensus.

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.
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>Amurolus fugax</td>
<td>Present (n=75) 11 (15) Absent (n=102) 11 (11)</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 Xl)*</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 &lt;=50%</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Stenosis 50–80%</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Stenosis &gt;80% or occlusion</td>
<td>62 (82)</td>
</tr>
</tbody>
</table>

*Local signs were located on the side of the suspected carotid dissection.

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 and sensitivities of 100% using extracranial Doppler sonography. 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≤50% stenosis, 3>80% stenoses, and 2 occlusions. Diagnosis of ≤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, which may also cause a focal raise of flow velocities.

Discussion

The results of ultrasound, cervical MRI, and angiographic assessment are shown in Figure 1. There were 6 falsely positive CDS findings, which included 1≤50% stenosis, 3>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%.

Figure 2. This patient (no. 4 in Table 2) with a false ultrasound diagnosis of >80% stenosis of the left ICA experienced a stroke in the territory of the left MCA. GA showed FMD with a 55% stenosis of the left cervical ICA (A, white arrow) and an embolic occlusion of the left MCA (B, white arrow) and FMD of the right ICA (C, white arrows) and left vertebral (D, white arrow) arteries.

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).
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 in the cases with intracranial FMD from the unusual length of the stenoses. It is well known that the flow direction of the OphA is not always reliable for distinguishing severe ICA stenosis or occlusion located before and after its origin, because antegrade OphA flow may also be observed in severe stenosis or occlusion of the extracranial carotid artery.20

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 palsies), 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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