Diagnosis of Right-to-Left Shunt With Transcranial Doppler and Vertebrobasilar Recording

Massimo Del Sette, MD; Lavinia Dinia, MD; Domenica Rizzi, MD; Annalisa Sugo, MD; Beatrice Albano, MD; Carlo Gandolfo, MD

Background and Purpose—Right-to-left shunt (RLS) due to patent foramen ovale is a well-established risk factor for cryptogenic stroke and is highly prevalent in cases of migraine, cluster headache, and obstructive apnea. It can be diagnosed by gaseous-contrast transcranial Doppler, yet in a small percentage of cases it cannot be done owing to an insufficient temporal window. The aim of the study was to compare transtemporal with transoccipital approaches for gaseous-contrast transcranial Doppler for RLS diagnosis.

Methods—We evaluated 183 subjects with a standard protocol for RLS diagnosis by simultaneously monitoring the right middle cerebral and vertebrobasilar circulations.

Results—Vertebrobasilar recording reached high specificity (100%) and good sensitivity (83.72%) for the diagnosis of RLS after the Valsalva maneuver. For only medium and large shunts, both sensitivity and specificity reached 100%. Time to bubble appearance after injection was higher in the vertebrobasilar circulation (4.36 ± 1.7 vs 6.77 ± 2.5 seconds; P < 0.001). There was a positive correlation between the number of bubbles in the right middle cerebral and vertebrobasilar circulation (r = 0.97).

Conclusions—Transcranial Doppler with vertebrobasilar monitoring is highly sensitive and specific in detecting RLS, particularly when medium or large. It can be proposed for subjects with an insufficient temporal bone window. (Stroke. 2007;38:000-000.)

Key Words: middle cerebral artery | patent foramen ovale | right-to-left shunt | stroke | temporal bone window | transcranial Doppler | vertebrobasilar circulation

The presence of right-to-left shunt (RLS), in most cases due to a patent foramen ovale, is a well-known risk factor for ischemic stroke.1–4 The prevalence of RLS is higher in stroke patients < 45 years of age and in cases of cryptogenic stroke of all age groups.5,6 Moreover, a high prevalence of RLS has been recently reported in other clinical condition, such as migraine, cluster headache, obstructive apnea, and diving, but the clinical relevance of RLS in these conditions is not yet clear.7–13 Gaseous-contrast transcranial Doppler (cTCD) is a highly sensitive and specific technique for the diagnosis of RLS due to patent foramen ovale.14–18 Recent evidence has been accumulated on the importance of the dimension of the shunt, evaluated by cTCD, in the stratification for risk of stroke, and a semiquantitative classification with 4 categories has been suggested. It takes into account the number of microbubbles (Mb) recorded within the spectrum of the middle cerebral artery (MCA) during gaseous contrast injection and considers the test negative when no Mb is detected on the Doppler spectrum. When the test is positive, it can be classified as a low-grade shunt (1 to 10 Mb), medium-grade shunt (> 10 Mb), and large-grade shunt (> 10 Mb plus a “curtain effect,” seen when the Mb are in so great a number that they are no longer distinguishable).14–19 The shunt is classified as permanent if already present under basal conditions and latent when it is detected only during the Valsalva maneuver.18

In ~10% of subjects, TCD cannot be performed because of an insufficient temporal bone window; thus, the only way to diagnose patent foramen ovale in this subgroup is by transesophageal echocardiography, which is a semi-invasive examination and is not feasible in uncooperative subjects. The aim of our study was to establish whether cTCD with vertebrobasilar circulation (VBC) monitoring can be proposed as a screening examination for RLS, especially for subjects with an insufficient temporal window.

Patients and Methods
We evaluated 195 consecutive subjects admitted to our Laboratory of Neurosonology for RLS diagnosis. There were 105 asymptomatic subjects, 57 patients with ischemic stroke or transient ischemic attack, 29 with migraine, and 4 divers. The project was approved by the local ethics committee, and asymptomatic subjects were relatives of patients with patent foramen ovale who were willing to know their diagnosis of Right-to-Left Shunt (RLS). The prevalence of RLS is higher in stroke patients.
TABLE 1. Comparison of VBC and MCA Recording at Rest

<table>
<thead>
<tr>
<th></th>
<th>MCA+</th>
<th>MCA-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>VBC+</td>
<td>16</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>VBC-</td>
<td>12</td>
<td>155</td>
<td>167</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>155</td>
<td>183</td>
</tr>
</tbody>
</table>

Sensitivity 57.14%; specificity 100%; positive predictive value 100%; negative predictive value 92.81%.

TABLE 2. Comparison of VBC and MCA Recording After the Valsalva Maneuver

<table>
<thead>
<tr>
<th></th>
<th>MCA+</th>
<th>MCA-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>VBC+</td>
<td>36</td>
<td>0</td>
<td>36</td>
</tr>
<tr>
<td>VBC-</td>
<td>7</td>
<td>140</td>
<td>147</td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
<td>140</td>
<td>183</td>
</tr>
</tbody>
</table>

Sensitivity 83.72%; specificity 100%; positive predictive value 100%; negative predictive value 95.24%.

Results

There were 183 subjects with a mean age of 44.47±15.15 years. We found RLS in 43 of 183 subjects (23.5%) after the Valsalva maneuver and in 28 (15.3%) at rest; all of the subjects with a positive test at rest had RLS after the Valsalva maneuver. We compared the results of the test at rest and after the Valsalva maneuver. At rest RLS was present in 28 subjects in the MCA and in 16 in the VBC; after the Valsalva maneuver, in 22 in the MCA and in 16 in the VBC. A simultaneous manual positioning of both MCAs was not possible, so we selected the same side for all patients. A sample volume of 8 mm in length and a low gain provided the optimal settings for the background spectrum; the sample volume allowed detection of gaseous emboli through the MCA and the VBC.21 The depth of recording was 45 to 55 and 75 to 85 mm, respectively. After informed consent was obtained, the test was performed with the patient lying down, at rest, and after the Valsalva maneuver, with injection of a mixture of 9 mL saline and 1 mL air, according to standard methods.17,18 The Valsalva maneuver started 5 seconds after beginning the injection of contrast medium for 10 seconds.

Intraobserver reliability was high (κ=0.94). In a subset of 35 subjects with RLS on the MCA recording, contrast transesophageal echocardiography was performed and the results were compared with those of cTCD and MCA monitoring: sensitivity and specificity of 94% were achieved. RLS was classified as small, medium, and large, according to the literature.20,21 and as described earlier in this Methods section.

Discussion

We showed that in subjects with RLS, cTCD with VBC recording reaches high levels of predictive value when compared with MCA recording, in particular for medium and large shunts. TCD is a sensitive and specific test for RLS diagnosis, and so far no serious complication has been reported. Transesophageal echocardiography is a more invasive test that is useful to clarify the cardiac or pulmonary source of the shunt and to identify the eventual presence of atrial septal aneurysm.22 TCD is not only a screening test but also an important tool to quantify shunts; in fact, there is evidence that larger shunts are associated with a higher risk of cerebrovascular events in patients with cryptogenic stroke and in subjects with migraine with aura.19,23 In our subjects, the diagnosis of large shunts, the most clinically important, was possible with a sensitivity and specificity of 100% with VBC monitoring.

In conclusion, TCD with VBC monitoring is a sensitive and specific test for RLS, in particular for medium and large shunts. Our data suggest a possible use for VBC recording in subjects with an insufficient temporal bone window.

TABLE 3. Comparison of VBC and MCA Recording for Medium and Large Shunts (>10 Mb)

<table>
<thead>
<tr>
<th></th>
<th>MCA+</th>
<th>MCA-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>VBC+</td>
<td>22</td>
<td>0</td>
<td>22</td>
</tr>
<tr>
<td>VBC-</td>
<td>0</td>
<td>161</td>
<td>161</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>161</td>
<td>183</td>
</tr>
</tbody>
</table>

Sensitivity 100%; specificity 100%; positive predictive value 100%; negative predictive value 100%.
Disclosures
None.

References
Diagnosis of Right-to-Left Shunt With Transcranial Doppler and Vertebrobasilar Recording
Massimo Del Sette, Lavinia Dinia, Domenica Rizzi, Annalisa Sugo, Beatrice Albano and Carlo Gandolfo

*Stroke*. published online June 28, 2007;
*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2007 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/early/2007/06/28/STROKEAHA.106.479485.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org//subscriptions/