Noninvasive Cerebrovascular Assessment of Takayasu Arteritis

Carlos Cantú, MD; Carlos Pineda, MD; Fernando Barinagarrenenteria, MD; Perla Salgado, MD; Alba Gurza, MD; Paola de Pablo, MD; Rolando Espinosa, MD; Manuel Martínez-Lavín, MD

Background and Purpose—Despite prominent neurological symptoms reported in Takayasu arteritis (TA), a complete evaluation of the cerebral circulation has not been consistently performed. The purpose of this study is to describe MR angiography (MRA), color Doppler flow imaging, and transcranial Doppler (TCD) findings in the extracranial and intracranial cerebral arteries in TA.

Methods—MRA, color Doppler flow imaging, and TCD were performed in 21 patients with TA. Intima-media thickness was measured in the common carotid artery. The correlation between noninvasive studies and panaorto-arteriography was examined for supraortic vessels. Cerebral angiography findings were compared with the noninvasive methods in 7 patients. Intracranial hemodynamic changes detected by TCD were compared with extracranial circulation lesions assessed by panaorto-arteriography.

Results—Noninvasive vascular techniques showed at least 1 abnormality in the extracranial and/or intracranial cerebral arteries in 20 of 21 patients (95%). Both MRA and color Doppler flow imaging showed a substantial correlation in the ability to detect obstructive lesions in supra-aortic vessels compared with panaorto-arteriography. High-resolution ultrasonography displayed common carotid artery wall thickening in 5 vessels that were considered normal by arteriography. In 24% of patients, MRA and TCD showed abnormalities consistent with stenosis of the basal cerebral arteries. In 10 patients with severe extracranial circulation involvement (detected by arteriography), TCD displayed intracranial hemodynamic changes consisting of dampened or blunted waveforms with low pulsatility.

Conclusions—The comprehensive assessment of cerebral circulation in TA patients by noninvasive methods allowed the detection of a high rate of diverse vascular abnormalities in both extracranial and intracranial circulation. (Stroke. 2000;31:2197-2202.)

Key Words: arteritis □ cerebrovascular circulation □ magnetic resonance angiography □ ultrasonography □ vasculitis

Takayasu arteritis (TA) is a chronic, inflammatory large-vessel arteriopathy that primarily affects the aorta, its main branches, and the pulmonary arteries. In TA, central nervous system disease is an important expression of vascular injury. More than half of patients may develop diverse neurological manifestations such as headache, visual disturbances, seizures, transient ischemic attack, cerebral infarction, intracerebral hemorrhage, and orthostatic syncopal attacks.1,2 Cerebral angiography is the best procedure to properly diagnose the extent and severity of neurovascular involvement.3 Nevertheless, this invasive neuroimaging method is associated with a 1.3% to 8.5% incidence of neurological and systemic complications.4,5

Recently, several case reports and series6–13 have highlighted the capacity of individual noninvasive imaging technologies to evaluate the presence, extent, and severity of vascular involvement in diverse vascular territories in TA. The purpose of this study is to describe MR angiography (MRA), color Doppler flow imaging (CDFI), and transcranial Doppler (TCD) findings in the extracranial and intracranial arteries in TA patients. We compare noninvasive studies with arteriography of the supraaortic vessels and correlate intracranial hemodynamic changes detected by TCD with extracranial circulation lesions assessed by panaorto-arteriography.

Subjects and Methods

Patients

During a period of 2 years, 21 consecutive patients seen at the rheumatology and/or the stroke clinics of 2 tertiary referral medical centers, who fulfilled the American College of Rheumatology criteria for the classification of TA,14 entered the study. In all cases, the diagnosis was corroborated by panaorto-arteriography. Patients were enrolled independently of their disease duration or activity status and the presence or absence of neurological complaints.2,15

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TABLE 1. Clinical Features of 21 Patients With TA

<table>
<thead>
<tr>
<th>Age, mean±SD, y</th>
<th>32.3±13.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, F/M</td>
<td>20/1</td>
</tr>
<tr>
<td>Age at disease onset, mean (range), y</td>
<td>21.2 (9–38)</td>
</tr>
<tr>
<td>Disease duration, mean (range), y</td>
<td>11.2 (1–38)</td>
</tr>
<tr>
<td>Takayasu type, No. (%)</td>
<td>I 1 (5) Il a 3 (14) Il b 2 (10) V 15 (71)</td>
</tr>
<tr>
<td>Vascular evaluation, No. (%)</td>
<td>Arterial hypertension 9 (43) Absence or weakness of peripheral pulses 19 (90) Absence or weakness of carotid pulses 17 (81) Carotid bruits 11 (52) Supraclavicular bruits 10 (48) Ischemic retinopathy 7 (33) Neurological features, No. (%)</td>
</tr>
</tbody>
</table>

Those individuals with other causes of large-vessel disease were excluded.

Methods
The institutions’ Human Research and Ethics committees approved the study protocol. Informed consent was obtained from all subjects. Angiographic abnormalities considered representative of TA included the confirmed presence of occlusion, stenosis, irregularity, and dilatation or aneurysm formation involving the aorta and its main tributaries. The topographic abnormalities found in panoaortoarteriography were classified according to the patterns established at the International Conference on TA. Cranial MRI, MRA, CDFI, and TCD were performed in all cases. In 7 patients with prominent neurological manifestations, the attending physician additionally indicated cerebral digital subtraction angiography (DSA).

Ultrasonographic Studies
Extracranial vessels were evaluated by real-time scale imaging and CDFI with a Toshiba 270 SA scanner with a linear array 7.5-MHz transducer. A complete duplex sonographic study was composed of insonation of supra-aortic vessels: brachiocephalic trunk, common carotid arteries (CCA), internal carotid arteries (ICA), external carotid arteries (ECA), and proximal vertebral arteries (VA) from C3 to C6. Patients with occlusion or severe stenosis of the CCA were observed for evidence of collateral supply to the ICA. The morphology of arterial walls, flow direction, recordings of peak systolic (PSV) and end-diastolic (EDV) blood flow velocities were ascertained in each examined artery. Measurement of intima-media thickness (IMT) was accomplished in the posterior wall of the CCA. Diagnostic criteria for extracranial carotid artery disease assessed by CDFI noted the parameters proposed by Steinke et al., such as color fading, PSV >120 cm/s, poststenotic turbulence for stenotic lesions, and vessel lumen without flow signal for occlusions. The diagnostic criteria for extracranial VA disease proposed by Bartels, which include increased flow velocities, poststenotic turbulence and aliasing phenomena for stenotic lesions, and absence of color flow signal with or without evidence of cervical collateral blood flow for occlusive lesions, were also used. Intracranial vessels were evaluated by TCD according to previously published criteria, with the use of a 2-MHz transducer (Transpect; Medasonics). Temporal windows were used to evaluate the middle (MCA), anterior (ACA), and posterior (PCA) cerebral arteries. The transorbital approach was used to evaluate the intracranial ICA (ICA siphon). The transcochlear approach was used for assessment of the basilar artery (BA) and distal VA. The PSV, EDV, and mean (MV) blood flow velocities were documented in all depths of successful insonation. Additionally, pulsatility index (PI) was calculated according to Gosling and King. PSV minus EDV divided by MV (reference value, 0.87±0.16). TCD diagnosis of intracranial artery disease included previously proposed criteria: PSV >140 cm/s and MV >80 cm/s for MCA and ACA stenotic lesions, and PSV >90 cm/s and MV >65 cm/s for ICA siphon stenosis. MCA occlusion was considered when ipsilateral MCA flow velocities were absent and all other ipsilateral arteries were detectable. The criteria of BA and PCA stenotic lesions included mean blood flow velocities >65 and >70 cm/s, respectively. Because of the anatomic variability of ACA and PCA, occlusion was not considered for these vessels. TCD indicators used to detect intracranial hemodynamic changes associated with significant extracranial obstructive lesions included dampened or blunted waveforms, slow acceleration, and decreased pulsatility, recorded in the MCA and BA.

MR Studies
In all patients, cranial MRI and MRA examinations were obtained with the use of a 1.5-T superconducting imaging system (Signa General Electric Medical Systems). Standard cranial MRI was performed with sagittal and axial T1-weighted sequences (repetition time, 500 to 600 milliseconds; echo time, 13 to 20 seconds; 2 excitations; 256×192 matrix) and transaxial T2-weighted sequences (repetition time, 2300 to 2500 milliseconds; echo time, 30 to 80 seconds; 1 excitation; 256×192 matrix). Vascular MRI was performed with Multisequence Vascular Package (GE Medical Systems) with 3-dimensional time of flight. In all studies, the echo time was automatically set to a minimum by the vascular imaging software. In all cases, the frequency-encoding direction was anteroposterior. Obstructive artery disease criteria evaluated by MRA were established as follows: a stenotic lesion was considered when there was a signal reduction or a signal loss limited to a segment with signal rarefaction or a normal distal signal. Grading stenosis was not attempted. Occlusion was considered when complete signal loss was present even in a poststenotic segment.

Image and Data Analysis
CDFI and TCD studies were interpreted by a neurosonologist. Two readers, a neuroradiologist and a vascular neurologist, blindly interpreted MRI and MRA studies. The ability of CDFI and MRA to identify abnormalities in the supra-aortic vessels (CCA, proximal VA, brachiocephalic trunk) was compared with panoaortoarteriography on each arterial segment. Sensitivity, specificity, and correlation tests were obtained. A comparison between CDFI and MRA for the extracranial ICA bifurcation segment was accomplished. TCD and MRA results at the main basal cerebral arteries (MCA, ACA, PC, ICA siphon, BA) were compared. A descriptive comparison was performed between noninvasive methods and cerebral DSA, when available. Finally, intracranial hemodynamic TCD changes associated with occlusive disease of the cervical carotid arteries and VA were correlated with panoaortoarteriography findings.

Results
Demographic and clinical features of the 21 patients are shown in Table 1. Noninvasive imaging techniques showed at least 1
abnormality within extracranial and/or intracranial circulation in 20 patients (95%). Both MRA and CDFI studies displayed diverse abnormalities (stenosis, occlusion, aneurysm formation) in supra-aortic vessels, corroborated by panaorto-arteriography, as shown in Table 2. \(\kappa\) values indicated a substantial correlation in their ability to detect those abnormalities. For both MRA and CDFI, sensitivity and specificity were 95%. Moreover, 5 patients showed a reversed vertebral flow direction in VA, accompanied by ipsilateral proximal stenosis of the subclavian artery, consistent with subclavian steal phenomenon. Both non-invasive techniques demonstrated the unique long-segment involvement of the arterial vessels. On MRA, long stenotic lesions were demonstrated as an even concentric narrowing with a long segmental lumen reduction; the main discrepancy with panaorto-arteriography was overestimation of stenosis by MRA. As shown in Figure 1A through 1J, CDFI longitudinal sections showed a homogeneous thickening with isoechochogenicity or hyperechogenicity of the intima-media complex. CDFI was able to detect residual blood flow in critically narrowed arteries considered totally occluded by panaorto-arteriography (Figure 1E). High-resolution ultrasound displayed CCA wall thickening (macaroni sign) in 5 vessels that were considered normal by arteriography (Figure 1G and 1H).

When comparing both MRA and CDFI findings in the extracranial ICA bifurcation segment (Table 3), we observed collateral blood flow through the VA (Figure 1J) and/or carotid bifurcation in severely stenotic CCA (Figure 2). MRA demonstrated recanalization in 7 patients (10 arteries), whereas CDFI showed it in 8 patients (11 arteries). MRA depicted more clearly the presence of recanalization by collateral vessels in those patients with severe and extensive involvement of cervical arteries (Figure 2).

In 7 patients, cerebral DSA showed results similar to those obtained by noninvasive methods at 14 carotid bifurcation segments, of which 6 showed arterial abnormalities and 8 were normal. Both MRA and cerebral DSA showed 3 occlusions, whereas CDFI detected 2 occlusions and 1 residual flow. On the other hand, both CDFI and cerebral DSA displayed 3 recanalizations, of which MRA detected only 1 recanalization and showed occlusion in the remaining.

In 7 carotid artery systems, noninvasive methods demonstrated the extension of the occlusive process—from the CCA origin up to the ICA siphon (Figure 3)—confirmed by cerebral DSA in 3 cases (cerebral DSA was not performed in the remaining 4 carotid systems, preventing confirmation of such finding). Furthermore, intracranial vessel involvement was shown in 5 of 21 patients (24%); both TCD and MRA displayed stenosis of the basal cerebral vessels in 10 arteries (ICA siphon 4, MCA 3, ACA 2, and VA 1). In these stenotic arteries, TCD showed a high pulsatility, suggesting wall stiffness (Figure 4A). Intracranial artery involvement was observed in patients without extensive involvement of the extracranial cervical arteries. However, cerebral DSA was not performed, preventing confirmation of the intracranial lesions in these cases.

On the other hand, in 10 patients with severe involvement of extracranial circulation (previously detected by panaorto-arteriography), TCD displayed remarkable intracranial hemodynamic changes consisting of an abnormal dampened or blunted pattern with low flow pulsatility (Figure 4B). These changes were observed in both MCA and BA in 3 patients and were associated with bilateral involvement of carotid and
vertebral extracranial systems. In 6 patients these changes were observed in the MCA but not the BA and were associated with bilateral involvement of the extracranial carotids. There was a unilateral involvement of the VA in 3 cases and no involvement of the VA in the remaining 3. The same abnormal pattern was observed unilaterally in 1 patient with brachiocephalic trunk occlusion. Intracranial circulation showed no hemodynamic changes when a unilateral involvement of the carotid system was present (5 patients) as a result of adequate collateral pathways, including the circle of Willis.

**Discussion**

Despite prominent neurological symptoms reported in TA patients, a complete evaluation of their cerebral circulation has not been performed previously. Our series disclosed a high frequency of vascular abnormalities in the cerebral circulation, with at least 1 vascular lesion observed in 95% of patients. The combination of MRA, CDFI, and TCD depicted a wide spectrum of vascular abnormalities in the cerebral circulation of patients, including occlusions, stenoses, aneurysms, collateral blood flow, and arterial wall thickening. This high rate of abnormalities was probably due to the systematic neurovascular assessment but could be also due to selection bias, since patients were gathered from referral centers and most of them had long-standing disease.

Finally, for those 7 patients who underwent cerebral DSA, no abnormalities were observed at the intracranial arteries. MRA in these patients also showed normal intracranial vessels. Nevertheless, the dammed or blunted pattern with low pulsatility previously described was detected in 3 patients by TCD. This hemodynamic abnormality was due to severe cerebral extracranial artery involvement.

**TABLE 3.** Comparison of MRA and CDFI Findings in the ICA

<table>
<thead>
<tr>
<th></th>
<th>CDFI</th>
<th>Normal</th>
<th>Stenosis</th>
<th>Occlusion</th>
<th>Recanalization*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRA</td>
<td></td>
<td>21</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Stenosis</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Occlusion</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Recanalization*</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>21</td>
<td>5</td>
<td>6</td>
<td>10</td>
<td>42</td>
</tr>
</tbody>
</table>

*Recanalization through collateral flow in those arteries that were occluded or had severe stenosis at CCA level. k value was 0.81 (P<0.001).
Moreover, several studies suggest a peculiar topographic distribution of arterial involvement in TA in different geographic areas. Lupi-Herrera et al reported a predominant pattern of disease affecting the aortic arch and its branches in the Mexican Mestizo population.

In regard to cervical circulation, we compared CDFI and MRA with panaorto-arteriography, observing a substantial correlation in their capability to depict both normal and abnormal arterial segments, as demonstrated by sensitivity, specificity, and $\kappa$ values. This could be explained by the presence of long and extensive arterial lesions that are easily detected by these noninvasive methods, in contrast to atherosclerosis, in which the involvement is usually focal. Most of the patients had recanalization at the carotid bifurcation level by collateral vessels; however, in some patients the involvement extended to the ICA siphon (Figure 3).

Ultrasonography allowed the detection of carotid artery wall involvement. Several studies have emphasized the usefulness of the arterial wall thickness measurement. Moreover, a regression of carotid wall thickening after corticosteroid therapy has been reported. Therefore, in addition to its diagnostic capabilities, carotid ultrasonography may provide a simple and accurate method for the evaluation of therapeutic effects of immunosuppressive drugs in TA. This method could be used for long-term follow-up.

The main advantage of CDFI over MRA relies on its ability to visualize residual blood flow, particularly when color flow imaging is used. Overestimation of moderate stenosis by MRA is well known because of a phenomenon related to intravoxel defacing resulting from flow turbulence at the narrowed seg-

Figure 3. MRA images. Left, An even concentric narrowing of the CCA (arrows), extending up to the ICA, with a high-grade stenosis at bifurcation (arrowhead). Right, Panoramic view of cerebral circulation, showing long-segment artery involvement (arrowheads) from the right CCA origin up to the ICA territory, leading to signal loss at the siphon portion. CDFI of this patient is shown in Figure 1F.

Figure 4. TCD findings in TA patients. A shows 3 arteries with high blood flow velocities in stenotic range associated with an abnormal high flow pulsatility (PI >1.2), suggesting wall stiffness; these findings were observed in patients without extensive involvement of the extracranial cervical arteries. Conversely, panel B displays 3 arteries with normal flow velocities and diverse degrees of abnormal waveforms consistent with a dampened or blunted signal associated with low pulsatility flow (PI <0.65); these patients showed severe obstructive involvement of the extracranial cerebral circulation. R indicates right; L, left.
ment. In severe stenosis, an absence of MRA distal signal is considered a sign of occlusion; however, a slight residual flow is often missed by this technique. Conversely, the main disadvantage of ultrasound studies is its dependence on operator skills. MRA is exempt from this dependence and is particularly useful in depicting the pathological process in the presence of abundant collateral circulation.

Traditionally it has been considered that the inflammatory process of TA spares intermediate-size arteries. However, the systematic noninvasive assessment of intracranial circulation performed in the present study demonstrates abnormalities consistent with a stenosis of the basal cerebral arteries in 24% of TA patients. In these stenotic arteries, TCD showed high flow pulsatility, suggesting wall stiffness. Several studies have shown that MRA and TCD are capable of detecting intracranial stenosis associated with other etiologies. Nevertheless, angiographic confirmation would be desirable given the relevance of this finding in our TA patients.

Finally, several changes in intracranial hemodynamics characterized by a dampened or blunted spectra with low flow pulsatility observed by TCD were found in 10 patients. This pattern, which occurred mainly when both carotid arteries were affected, was also more prominent when the vertebral arteries were involved. A similar hemodynamic finding was described in 1 TA patient during a cerebrovascular reactivity assessment with the acetazolamide stress test.

In conclusion, the comprehensive assessment of cerebral circulation in TA patients by noninvasive methods allowed the detection of diverse vascular abnormalities in both extracranial and intracranial circulation. This battery of tests could be considered in those patients presenting neurological complaints or extensive involvement of cervical circulation.

References

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