Clinical and Sonographic Patterns of Tandem Internal Carotid Artery/Middle Cerebral Artery Occlusion in Tissue Plasminogen Activator–Treated Patients

Ashraf El-Mitwalli, MD; Mohamed Saad, MD; Ioannis Christou, MD; Marc Malkoff, MD; Andrei V. Alexandrov, MD

Background and Purpose—The National Institutes of Health Stroke Scale (NIHSS) is predictive of thrombus presence but has limited ability to identify occlusion location in the anterior circulation. We describe clinical and sonographic patterns that are associated with tandem internal carotid artery (ICA) and middle cerebral artery (MCA) occlusions.

Methods—Consecutive acute ischemic stroke patients receiving intravenous tissue plasminogen activator (TPA) were studied. Pretreatment NIHSS scores and bedside transcranial Doppler (TCD) were obtained for all patients.

Results—A total of 95 patients treated with intravenous TPA at 132±60 minutes from stroke onset were studied. On TCD, 48 had isolated MCA occlusion (mean NIHSS 16.8±5.8, median 17, range 5 to 28); and 16 had tandem ICA/MCA occlusion (mean NIHSS 18.8±5.8, median 22, range 8 to 29; P=NS). In the MCA occlusion and tandem ICA/MCA occlusion groups, 19% and 11%, respectively, had NIHSS scores <12 points. Compared with the NIHSS scores in patients with hemiplegia, forced gaze deviation, and complete neglect, the lower NIHSS scores were attributable to partial arm and/or leg paresis, gaze preference, and partial neglect. In those patients, TCD showed ≥2 major collateral channels and low-resistance flow at the M1 origin, suggesting perfusion of perforating arteries. Although TCD cannot differentiate between high-grade ICA stenosis or occlusion, collateral flow patterns and stenotic signals at the terminal ICA differentiated tandem lesions from isolated MCA occlusion (P<0.01).

Conclusions—Tandem ICA/MCA occlusion was found on TCD in 17% of TPA-treated patients. NIHSS scores were similar in patients with isolated MCA and tandem occlusions. Lower NIHSS scores were seen in patients with a higher number of major collateral flow channels and higher Thrombolysis in Brain Ischemia (TIBI) flow grades at the MCA origin. (Stroke. 2002;33:99-102.)

Key Words: occlusion ■ stroke ■ tissue plasminogen activator ■ ultrasonography, Doppler, transcranial

The National Institutes of Health Stroke Scale (NIHSS) can reliably predict thrombus presence,1 with an odds ratio of 1.33 per 1-point increase in the total score. Higher NIHSS scores are also correlated with increasing thrombus burden (ie, thrombi located in the M1 middle cerebral artery [MCA] and internal carotid artery [ICA]).2 Different treatment strategies are advocated for patients with acute stroke who have proximal MCA and ICA thrombi. Intravenous tissue plasminogen activator (TPA) may lyse some of these thrombi; however, recanalization of the proximal ICA occlusion almost never occurs with this therapy.3,4 Intra-arterial thrombolysis had higher recanalization rates for M1 MCA occlusion in a recent study,5 yet even with an intra-arterial delivery of a lytic agent, ICA recanalization rates remain low. Newer thrombus-disrupting mechanical devices are undergoing pilot evaluations in patients with ICA and MCA occlusions.

Our comparative studies between transcranial Doppler (TCD) and angiography have shown that in the emergency room, TCD can reliably identify the presence and location of arterial occlusion,6,7 similar to results previously shown by others.8–15 TCD also has the ability to identify major collateral channels and residual flow signals in the MCA stem.8 These findings also have early prognostic significance for anterior circulation stroke, and clot localization can be helpful in selecting patients for therapeutic interventions.11,16 A few studies have attempted to correlate clinical findings with clot presence and location in acute ischemic stroke.1,2,11,17 Patients with ipsilateral motor/sensory deficit, homonymous hemianopia, and higher cortical dysfunction had MCA and/or ICA occlusion or a severe MCA stenosis, whereas pure motor or sensory symptoms without cortical signs were attributable to small perforating artery lesions without major vessel occlusion.18 Occasionally, we have observed that hyperacute stroke patients with MCA and/or ICA occlusions may present with mild stroke severity or mimic lacunar events.19

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in the present study, we sought to describe the clinical and sonographic patterns in patients who arrived at the emergency department with tandem ICA/MCA occlusion and were eligible for intravenous TPa therapy.

Subjects and Methods
Consecutive patients receiving intravenous TPa for symptoms of acute ischemic stroke were studied. Pretreatment TCD was performed and interpreted at the bedside by a standard insonation protocol with the use of 2-MHz single-channel portable equipment (Multigon 500M, Multigon Industries; MultiDop-T, DWL-Neuroscan). We used the Thrombolysis in Brain Ischemia (TIBI) flow grading system and other prospectively validated diagnostic criteria for MCA occlusion.11,20 Our criteria for MCA occlusion have a sensitivity and specificity of >90%.6,20 For identification of a hemodynamically significant ICA obstruction, we expanded the battery of TCD findings described by Wilterdink et al21 and subsequently validated these criteria.6,22 Briefly, this broad battery included 3 major and 3 minor criteria.22 Major criteria were as follows: collateral flow signals (anterior and posterior communicating arteries and ophthalmic artery), abnormal ICA siphon or terminal ICA signals (absent, minimal, blunted, dampened, or stenotic waveforms), and delayed systolic flow acceleration in the MCA (arrival of maximum frequencies in late systole, ie, >0.2 second). Minor criteria were as follows: decreased pulsatility index (<0.6 or interhemispheric difference ≥30%), flow diversion signs (velocity: posterior cerebral artery>MCA, posterior cerebral artery>ICA, and contralateral anterior cerebral artery>MCA), and compensatory velocity increase (≥20% increase in the contralateral hemispheric vessels or vertebrobasilar arteries). In a study of 517 stroke patients, when this broad battery was used versus angiographic findings to detect a severe stenosis or occlusion of the extracranial or intracranial ICA, sensitivity was 79% and specificity was 86%.22 Tandem ICA/MCA occlusion was diagnosed when TCD detected abnormal TIBI MCA waveforms or an asonic MCA segment in the presence of 1 major or 2 minor findings according to the broad TCD battery for an ICA obstruction (Table 1). In other words, an abnormal TIBI waveform indicates the presence of an MCA occlusion, whereas an additional finding of at least 1 collateral channel indicates a proximal hemodynamically significant lesion in the feeding vessel.6,7,22 TCD was performed and interpreted at bedside by an experienced sonographer not involved in the clinical assessment of the patient. Pretreatment NIHSS scores were obtained for all patients by a neurologist not involved in TCD performance or interpretation.

Results
From November 1996 through July 2000, a total of 95 patients were treated with intravenous TPa at 132±60 minutes from stroke (median time 120 minutes). These were consecutive TPA-treated patients who also had pretreatment diagnostic TCD: 48 had isolated MCA occlusion (mean NIHSS 16.8±5.8, median 17, range 5 to 28), and 16 had tandem ICA/MCA occlusion (mean NIHSS 18.8±5.8, median 22, range 8 to 29; P=NS). During the study period, the Stroke Treatment Team also treated another 174 patients with TPa who did not have pretreatment TCD and for whom the location of the occlusion (if any) was unknown. These patients had a median NIHSS score of 14 (mean 14±6, range 4 to 33).

Sonographic findings in patients with tandem ICA/MCA occlusions versus isolated MCA occlusions were as follows: anterior communicating artery, 62% versus 0%; posterior communicating artery, 65% versus 0%; reversed ophthalmic artery, 86% versus 0%; flow diversion, 85% versus 0%; positive

TABLE 1. Sonographic Criteria for Tandem ICA/MCA Occlusions

<table>
<thead>
<tr>
<th>Lesion Location</th>
<th>Major Criteria</th>
<th>Minor Criteria</th>
</tr>
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<tbody>
<tr>
<td>MCA</td>
<td>Abnormal TIBI waveforms: absent (grade 0), minimal (1), blunted (2), dampened (3).</td>
<td>Flow diversion to ACA or PCA.</td>
</tr>
<tr>
<td>ICA</td>
<td>Major collaterals: anterior and posterior communicating arteries, reversed ophthalmic artery.</td>
<td>Decreased pulsatility of flow.</td>
</tr>
<tr>
<td></td>
<td>Abnormal ICA or TICA TIBI waveforms.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Delayed systolic flow acceleration in the MCA or TICA (with normal velocity range).</td>
<td></td>
</tr>
</tbody>
</table>

TICA indicates terminal ICA; ACA, anterior cerebral artery; and PCA posterior cerebral artery.

TABLE 2. NIHSS Scores and Diastolic Flow at Proximal M1 MCA Segment in Patients With Tandem ICA/MCA Occlusions

<table>
<thead>
<tr>
<th>NIHSS Score</th>
<th>Absent</th>
<th>Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥20</td>
<td>n=7</td>
<td>n=0</td>
</tr>
<tr>
<td>&lt;20</td>
<td>n=0</td>
<td>n=9</td>
</tr>
</tbody>
</table>

Patients with tandem ICA/MCA occlusions and positive end-diastolic flow in the proximal M1 MCA had lower NIHSS scores (P<0.0001 by Fisher exact test). This difference is attributable to partial arm and/or leg paresis (NIHSS score reduction by 4–6 points compared with hemiplegia, gaze preference, and partial neglect (2-point reduction compared with forced gaze deviation and complete neglect).
diastolic flow at the MCA origin, 56% versus 30%; and contralateral flow velocity increase, 93% versus 10% (Figure 1). Patients with tandem occlusions had NIHSS scores similar to those with isolated MCA occlusions. In the tandem occlusion and isolated MCA occlusion groups, 19% and 11%, respectively, had NIHSS scores <12. Lower NIHSS scores were attributable to partial arm and/or leg paresis, gaze preference, and partial neglect compared with hemiplegia, forced gaze deviation, and complete neglect in patients with NIHSS scores ≥20. On TCD, patients with lower NIHSS scores (n=9) had positive diastolic flow at the MCA origin (Table 2) and ≥2 major collaterals. All patients with NIHSS scores ≥20 (n=7) with tandem ICA/MCA occlusion had no diastolic flow at the M1 MCA origin (Table 2, \( P<0.0001 \)) and 1 or no major collaterals, indicating occlusion of perforating arteries and overall greater thrombus burden. These clinical and sonographic findings are illustrated in Figure 2.

**Figure 2.** ACOA indicates anterior communicating artery; PcomA, posterior communicating artery; L, left; and R, right. Although both patients have tandem ICA/MCA occlusions, the presence of a low-resistance flow at the LMCA origin (A) explains lower NIHSS scores in that patient that are due to flow to the perforators. In the second patient (B), the absence of diastolic flow at the LMCA origin indicates no flow to the perforating arteries, explaining higher NIHSS scores.

**Discussion**

The present study shows no overall differences in stroke severity before thrombolysis between patients with an isolated MCA occlusion and those with a tandem ICA/MCA occlusion in terms of the NIHSS scores. The lower NIHSS scores in some patients with tandem occlusions were attributable to partial arm and/or leg paresis, partial gaze preference, and neglect. However, the overall NIHSS scores were not helpful in differentiating occlusion location because in both groups, 11% to 19% of patients...
had NIHSS scores <12. This is consistent with our previous observations that NIHSS is sensitive for thrombus presence but nonspecific for its location. The present study was underpowered to analyze predictive values of individual components of the NIHSS scores for thrombus location because most patients had severe neurological deficits.

In 56% of the patients with tandem ICA/MCA occlusions, the NIHSS score range was 8 to 19. In these patients, TCD showed low-resistance flow at the M1 origin as well as a higher number of collateral channels compared with patients with NIHSS scores ≥20. Other studies showed that with an ICA occlusion, the neurological deficit and infarction volume depend on the functional capacities of collateral circulation, and an ICA occlusion without collateral flow leads to the most devastating acute ischemia. van Everdingen et al.5,23,24 have found that in patients with an ICA occlusion, brain hemodynamics and metabolism are influenced by the presence of at least 1 collateral channel rather than a total number, i.e., communicating arteries or reversed ophthalmic artery. In the present study, all patients with NIHSS scores <20 had ≥2 major collateral channels. Also, these patients had positive diastolic flow at the M1 MCA origin, which may suggest flow to perforators.3 In this situation, patients have less severe deficits because of partial scores in the following NIHSS sections: motor arm/leg function, best gaze, and neglect.

The limitations of the present study were the difficulty to differentiate between high-grade proximal ICA stenosis and occlusion by use of TCD studies only. Although direct carotid examination with duplex ultrasonography or CT angiography can be performed in the emergency room, a sonographer should be familiar with the TCD patterns of tandem lesions. Also, rapid screening for a severe ICA stenosis or complete occlusion can be potentially helpful in selecting patients treated with intravenous TPA for subsequent emergent angiography and new experimental devices for disruption of large arterial thrombi. Another limitation is the inability of TCD to provide diagnostic information in the absence of temporal acoustic windows. The latter can be avoided with the use of ultrasound contrast agents. Finally, a relatively small number of patients may preclude generalizations regarding the utility of TCD and the accuracy of our observations. Also, the utility and accuracy of TCD were not the objectives of the present study. Finally, diagnostic TCD examinations were performed at ~2 hours after stroke onset. Our results may not be reproducible at later times after stroke onset because of spontaneous recanalization or progression of infarction.

In conclusion, we report sonographic patterns of tandem ICA/MCA occlusions in patients treated with intravenous TPA therapy. Neurological deficits expressed with the NIHSS scores are similar in patients with tandem ICA/MCA occlusion and those with isolated MCA occlusions. Less severe stroke symptoms are attributable to the presence of collateral flow channels and positive diastolic flow in the proximal MCA.

References
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