Diffusion- and Perfusion-Weighted MRI Patterns in Borderzone Infarcts

Claudia J. Chaves, MD; Brian Silver, MD; Gottfried Schlaug, MD; John Dashe, MD; Louis R. Caplan, MD; Steve Warach, MD, PhD

Background and Purpose—The pathophysiology of borderzone infarcts is not well understood. We investigated whether combined diffusion-weighted imaging (DWI) and perfusion-weighted imaging (PWI) could identify pathophysiologically meaningful categories of borderzone infarcts.

Methods—Seventeen patients with borderzone infarcts were identified from the Beth Israel Deaconess Medical Center Stroke Database. All patients had DWI and PWI, the majority of them within the first 24 hours of symptom onset.

Results—Three patterns of perfusion abnormalities were associated with the diffusion lesions: 1, normal perfusion (5 patients); 2, localized perfusion deficits matching the area of restricted diffusion (5 patients); and 3, extensive perfusion deficits involving 1 or more vascular territories (7 patients). All but 1 patient with pattern 1 had transient peri-infarct hypotension as the presumed stroke mechanism. Two patients with pattern 2 had cardiac or aortic embolic sources; none had large-artery disease or arterial hypotension. Reperfusion was detected in all patients with this pattern who submitted to a follow-up study. All patients with pattern 3 had severe stenosis or occlusion of a large artery: the internal carotid, anterior cerebral, or middle cerebral.

Conclusions—We postulate that the perfusion abnormality varies according to the mechanism of the borderzone infarction. Transient perfusion deficits occurring with hypotension in the absence of significant large-artery disease may not be revealed by PWI. Embolism may cause some cases of small borderzone perfusion deficits. Critical large-artery disease may cause large territorial perfusion deficits and predispose to borderzone infarction. (Stroke. 2000;31:1090-1096.)

Key Words: cerebral infarction ■ magnetic resonance imaging, diffusion-weighted ■ magnetic resonance imaging, perfusion-weighted

Borderzone infarcts are ischemic lesions that occur at junctions between 2 or 3 arterial territories. Approximately 10% of all brain infarcts are located in borderzone regions.1 Their pathogenesis is controversial and may involve various mechanisms, such as systemic hypotension, critical carotid stenosis, or occlusion and microemboli.2 Delineation of the stroke mechanisms is important in order to guide specific treatment.

Two new MR techniques, diffusion-weighted imaging (DWI) and perfusion-weighted imaging (PWI), are able to show areas of ischemic neuronal injury and hypoperfusion, respectively, within minutes of cerebral ischemia in animal models.3–7 DWI detects changes in the self-diffusion of water molecules associated with ischemic injury from the first minutes of critical ischemia. PWI can be used to calculate maps of the mean transit time and the relative cerebral blood flow and volume, thus identifying hypoperfused brain tissue.8 The superiority of these 2 techniques over conventional MRI in the detection of early abnormalities in patients with acute stroke9–11 and in prediction of stroke outcome12–16 have been well established.

We investigated the contributions of DWI and PWI to the pathophysiologival mechanisms underlying borderzone infarcts.

Subjects and Methods

Patients

We retrospectively identified 17 patients with borderzone infarcts selected from a total of 331 patients in the Beth Israel Deaconess Medical Center (BIDMC) Stroke Database, collected from 1995 to 1998. The patients selected met the following inclusion criteria: detailed clinical information, including vascular risk factors, complete neurological examination, hospital course, and outcome; documentation of the borderzone infarction by MRI, including DWI and PWI, according to the BIDMC stroke protocol; and investigation of the stroke mechanism by cardiac studies, carotid and vertebral artery ultrasound, MR angiography (MRA) of the extracranial and intracranial arteries, or cerebral angiogram. There were 17 patients, 11 men and 6 women, ranging in age from 56 to 91 years, average 73.8 years. Fourteen patients were Caucasian,
2 African American, and 1 Hispanic. MRAs of the intracranial arteries were obtained in 16 patients; the intracranial vessels of the other patient were studied with a cerebral angiogram. All patients’ extracranial carotid arteries were studied at least by 1 of the following tests: MRA of the neck in 9, duplex of the extracranial arteries in 8, and cerebral angiograms in 3. Cardiac investigations (ECG and transthoracic echocardiogram) were performed in all patients.

Borderzone regions can vary considerably in different patients because of collateral flow. In this study, the topography of the

Figure 1. MRI obtained 4 days after symptom onset. DWI showed a left anterior and posterior borderzone infarcts; the rMTT map was normal; MRA showed diffuse intracranial atherosclerotic disease but no area of significant stenosis.

Figure 2. First MRI (TP-1) obtained 8 hours after symptom onset: DWI showed right anterior and posterior borderzone infarcts (arrow) and a small right ACA cortical infarct (notched arrow); analysis of PWI showed prolonged rMTT matching the areas of restricted diffusion; MRA was normal. Follow-up MRI (TP-2) performed 88 days later showed a left anterior borderzone infarct on T2-weighted imaging and normalization of rMTT map.
Borderzone infarcts on DWI were assessed according to the mapping guidelines described by Damasio. Borderzone infarcts were classified as anterior borderzone, when the infarct occurred between the anterior cerebral artery (ACA) and middle cerebral artery (MCA) territories; posterior borderzone, between the MCA and posterior cerebral artery (PCA) and sometimes the ACA territories; and internal borderzone, between the deep and superficial perforators of the MCA.

Determination of the presumed stroke mechanism followed the Harvard Stroke Registry criteria. Large-artery disease was defined in the extracranial vessels (carotid artery) as stenosis $\geq 70\%$ and in the intracranial vessels as stenosis $\geq 50\%$.

**MRI Studies**

The MRI stroke protocol used in our institution include: DWI, Proton density, FLAIR, $T_2^*$-weighted, $T_1$-weighted, $T_2$-weighted imaging, PWI and MRA of the intracranial vessels; all of them performed on a 1.5-T MR whole-body system (Siemens AG) with echo planar imaging capability. MRAs of the extracranial vessels were performed using two-dimensional and three-dimensional time of flight (TOF) techniques.

**Diffusion-Weighted Imaging**

For DWI, 2 b values (0 and 1000 s/mm$^2$) were used. Other DWI parameters included the following: echo time of 118 ms, matrix size of $128 \times 128$, field of view of $260 \times 260$, and 7-mm slice thickness, with a set of 18 axial slices covering the whole brain. The MR diffusion sequence at $b=1000$ s/mm$^2$ was run 3 times, with diffusion gradients applied to each of the $x$, $y$, and $z$ directions. To minimize the effects of diffusion anisotropy, an average of the 3 diffusion directions was calculated to give the trace of the diffusion tensor.

**Perfusion-Weighted Imaging**

The PWI was performed through dynamic first-pass bolus tracking of gadolinium diethylenetriamine pentaacetic acid (0.1 mg/kg) with an echo-planar gradient-echo with an echo time of 60 ms and repetition time of 2 seconds. The dynamic perfusion series were processed on a pixel-by-pixel basis to produce maps reflecting the relative mean transit time (rMTT), which gave the most distinct boundary between regions of normal perfusion and those with abnormal perfusion. DWI and PWI acquired in the acute phase were analyzed without knowledge of patients’ clinical symptoms or the presumed stroke mechanism. Because acute ischemic lesions have slower diffusion, as measured by the apparent diffusion coefficient (ADC) of water, they were identified as areas of hyperintensity on DWI. Hypoperfusion on PWI was identified as an area of increased signal intensity in the rMTT map, and its size was visually assessed and classified as normal; localized perfusion deficit; and extensive perfusion deficit involving 1 or more vascular territories. Examples of these lesions are depicted in Figures 1, 2, and 3, respectively.

**Results**

The following 3 patterns of perfusion abnormality were identified: pattern 1, patients with normal perfusion; pattern 2, patients with localized perfusion deficits matching the area of restricted diffusion; and pattern 3, patients with extensive perfusion deficits involving 1 or more vascular territories. Perfusion defects were larger than DWI defects in this group of patients.

**Pattern 1: Normal Perfusion**

There were 5 patients with this pattern (Figure 1, Table 1). Two of these patients had bilateral borderzone infarcts. The other 3 patients had anterior, posterior, and anterior and posterior borderzone infarcts, respectively. Transient severe systemic arterial hypotension, with systolic blood pressure varying from cardiac arrest to 70 mm Hg, was documented in 4 patients at the time of the initial symptoms and was secondary to cardiac ischemic disease in 2 patients, aortic dissection in 1, and occurred during a...
carotid endarterectomy in another patient. Two of these patients also had large-artery disease, with generalized intracranial and extracranial atherosclerosis in one and unilateral 70% internal carotid artery (ICA) stenosis in the other. The 1 patient in this group who had no evidence of arterial hypotension, cardiac disease, or large-artery disease was admitted with thrombotic thrombocytopenic purpura and developed bilateral borderzone infarcts shortly after plasma exchange. MR studies, including DWI and PWI, were performed within 24 hours of symptom onset in 3 patients (in 2 of them within the first 8 hours). The other 2 patients had their first MRI 4 and 7 days, respectively, after the initial symptoms. Follow-up DWI and PWI obtained 2 days later in 1 patient did not show any new abnormality.

Pattern 2: Localized Perfusion Deficits Matching the Area of Restricted Diffusion

There were 5 patients with this pattern (Figure 2, Table 2). Two patients had ipsilateral anterior and posterior borderzone infarcts. These 2 patients also had small strokes in other vascular territories, one in the ACA and the other the MCA territories. The other 3 patients had anterior, posterior, and internal borderzone infarcts. None of these 5 patients had intracranial or extracranial arterial disease. One patient had an intra-atrial thrombus and another had mitral regurgitation with dilated left atrium. Three other patients had normal cardiac studies; however, 1 of them had aortic atherosclerotic plaques detected during cardiac catheterization. Arterial hypotension was not detected in any of these patients on admission. The infarct mechanism was considered to be embolic in 2 patients, from cardiac sources in one and intra-arterial (related to cardiac catheterization) in the other. In the other 3 patients, the mechanism of the infarct was undetermined. All patients had their first scan within 24 hours of symptom onset, 3 of them within the first 8 hours. Follow-up MRI was obtained in 4 patients between days 3 and 88 (mean 46 days, median 45 days); all of them had complete reperfusion on PWI.

**TABLE 1. Pattern 1: Normal Perfusion**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Clinical Presentation</th>
<th>Interval Between Symptom Onset and DWI</th>
<th>DWI</th>
<th>Vascular Studies (MRA/Duplex,Angio)</th>
<th>Cardiac Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Arterial hypotension during R carotid endarterectomy followed by L hemiparesis</td>
<td>8 hs</td>
<td>R posterior borderzone infarct</td>
<td>70% stenosis RICA</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>Four episodes of L upper extremity weakness after lunch in the setting of arterial hypotension</td>
<td>2:30 hs</td>
<td>R anterior borderzone infarct</td>
<td>Normal</td>
<td>EF 20%, severe hypokinesis of L ventricle</td>
</tr>
<tr>
<td>3</td>
<td>Aphasia and R hemiparesis after plasma exchange for TTP</td>
<td>16:30 hs</td>
<td>R internal and bilateral posterior borderzone infarcts</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>Hypotensive arrest due to aortic dissection, followed by R hemiparesis</td>
<td>7 days</td>
<td>Bilateral posterior and internal borderzone infarcts, R internal borderzone infarct</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>5</td>
<td>R hemiparesis and fluent aphasia during an episode of tachycardia, diaphoresis, and arterial hypotension</td>
<td>4 days</td>
<td>L anterior and posterior borderzone infarcts</td>
<td>Generalized intracranial and extracranial atherosclerotic disease</td>
<td>EF 30–35%, akinesis of posterolateral wall</td>
</tr>
</tbody>
</table>

TTP indicates thrombotic thrombocytopenic purpura; Duplex, carotid duplex; Angio, cerebral angiography; and EF, ejection fraction.

**TABLE 2. Pattern 2: Localized Perfusion Deficit Matching the Area of Diffusion Abnormality**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Clinical Presentation</th>
<th>Interval Between Symptom Onset and DWI</th>
<th>DWI</th>
<th>Vascular Studies (MRA/Duplex,Angio)</th>
<th>Cardiac Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sudden onset L motor, sensory, and visual neglect while at work</td>
<td>7:34 h</td>
<td>R anterior and posterior borderzone infarcts, small R ACA cortical infarct</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>Sudden onset of mild L hemiparesis and L visual field defect while at work</td>
<td>10 h</td>
<td>R posterior borderzone infarct</td>
<td>Normal</td>
<td>Mitral regurgitation, L atrial enlargement, normal ejection fraction</td>
</tr>
<tr>
<td>3</td>
<td>L hemiparesis after cardiac catheterism</td>
<td>4 h</td>
<td>R internal borderzone infarct</td>
<td>Normal</td>
<td>Normal heart, aortic atherosclerotic plaques</td>
</tr>
<tr>
<td>4</td>
<td>L hemiparesis and slurred speech after waking up</td>
<td>15 h</td>
<td>R anterior borderzone infarct</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>5</td>
<td>Sudden onset of diaphoresis, aphasia, R hemiparesis</td>
<td>2 h</td>
<td>R anterior and posterior borderzone infarcts, L frontal cortical infarct</td>
<td>Normal</td>
<td>Intra-atrial thrombus</td>
</tr>
</tbody>
</table>

Duplex indicates carotid duplex; Angio, cerebral angiography.
TABLE 3. Pattern 3: Extensive Perfusion Deficits Involving 1 or More Vascular Territories

<table>
<thead>
<tr>
<th>Patient</th>
<th>Clinical Presentation</th>
<th>Interval Between Symptom Onset and DWI</th>
<th>Vascular Studies (MRA/duplex,angio)</th>
<th>Cardiac Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R weakness and aphasia; worsening of symptoms after episode of arterial hypotension</td>
<td>3 d</td>
<td>L anterior borderzone infarct</td>
<td>L carotid siphon occlusion</td>
</tr>
<tr>
<td>2</td>
<td>L leg weakness, preceded by 2 similar TIAs</td>
<td>2 d</td>
<td>R anterior borderzone infarct</td>
<td>R carotid stenosis (siphon)</td>
</tr>
<tr>
<td>3</td>
<td>After standing up R hemiparesis and field cut in the setting of arterial hypotension</td>
<td>6:47 h</td>
<td>L anterior and posterior borderzone infarcts</td>
<td>L ICA stenosis (suprACL)</td>
</tr>
<tr>
<td>4</td>
<td>Acute onset of L gaze deviation, R hemiparesis, and hemineglect, preceded by 2 similar TIAs</td>
<td>4:17 h</td>
<td>L anterior borderzone infarct</td>
<td>Tight stenosis L ICA bifurcation</td>
</tr>
<tr>
<td>5</td>
<td>Acute onset of L hemiparesis while sitting; worsening of symptoms after episode of arterial hypotension</td>
<td>4:45 h</td>
<td>R anterior borderzone infarct</td>
<td>R ACA occlusion</td>
</tr>
<tr>
<td>6</td>
<td>Found by nurse with mild R hemiparesis and aphasia</td>
<td>16:23 h</td>
<td>L internal borderzone infarct</td>
<td>L MCA stenosis</td>
</tr>
<tr>
<td>7</td>
<td>Found with R hemiparesis and aphasia; worsening of symptoms after episode of arterial hypotension</td>
<td>8:00 h</td>
<td>L internal borderzone infarct</td>
<td>L ICA occlusion</td>
</tr>
</tbody>
</table>

TIA indicates transient ischemic attacks; AF, atrial fibrillation; Duplex, carotid duplex; Angio, cerebral angiography; and EF, ejection fraction.

Pattern 3: Patients With Extensive Perfusion Deficits Involving 1 or More Vascular Territories

There were 7 patients with this pattern (Figure 3, Table 3). Four patients had anterior borderzone infarcts, 2 had internal borderzone infarcts, and 1 had unilateral anterior and posterior borderzone infarcts. The mechanism of the stroke was considered to be large-artery disease with hemodynamic ischemia in all 7 patients. Ipsilateral ICA occlusion or tight stenosis was detected in 2 and 3 patients, respectively, and stenosis or occlusion of the ACA or MCA in 1 patient each. Cardiac evaluation was normal in 3 patients and showed moderate decrease in the ejection fraction in 2 patients. One patient had first-degree atrioventricular block, but no significant arrhythmia was observed during Holter monitoring; another patient had transient atrial fibrillation associated with arterial hypotension (90/60 mm Hg) relative to baseline at stroke onset. Transient arterial hypotension with subsequent worsening of the clinical symptoms occurred in 3 patients during the hospitalization. None of the patients had an abnormally high hematocrit. Five patients had their first MRI study within the first 24 hours of symptom onset, 4 of them within the first 8 hours. In the other 2 patients, the first imaging study was done 2 and 3 days after onset of the symptoms, respectively. Follow-up MRI was obtained in 6 patients, between days 3 and 85 (mean 36 days, median 21 days), and showed persistent hypoperfusion in 5 of them.

Discussion

Although autopsy results and CT studies have characterized borderzone infarcts, their pathogenesis is still not well understood. Systemic hypotension, microembolism, and critical carotid artery stenosis or occlusion with hypoperfusion are considered to be the probable mechanisms.

In our series, 3 different patterns of perfusion abnormalities were identified among the 17 patients studied: normal perfusion, localized perfusion deficit matching the area of diffusion abnormality, and extensive perfusion deficit involving 1 or more vascular territories exceeding the focal DWI defects.

Normal perfusion studies were found in 5 patients. In 4 patients, severe transitory systemic hypotension was well documented at the time of the symptom onset and posited as the probable mechanism of these strokes. The transient nature of the arterial hypotension most likely led to temporary decrease in the cerebral blood flow, which was no longer present by the time the scan was performed in these patients. In the other patient, a hypercoagulable state secondary to thrombotic thrombocytopenic purpura probably associated with decreased intravascular volume related to plasma exchange was the inferred mechanism.

The role of severe arterial hypotension causing borderzone strokes has been described and confirmed by experimental studies with primates. Adams et al identified borderzone infarcts in brains of patients who died shortly after cardiac surgery and ascribed it to 1 or more episodes of abrupt arterial hypotension. Similar findings were reported by Howard et al in patients with borderzone infarcts detected by CT scan; in most of his patients the strokes were clearly associated with episodes of severe arterial hypotension, some of them during cardiac surgery. In the majority of these patients, bilateral symmetrical borderzone infarcts were the rule. In our series, transitory arterial hypotension was also associated with unilateral strokes in 3 patients; however, 2 of these patients had large-artery disease: ipsilateral 70% carotid artery stenosis in one and generalized diffuse atherosclerosis in the other. Only 1 patient had unilateral stroke and completely normal intracranial and extracranial arteries.
The second pattern we observed was localized perfusion deficit that matched the areas of restricted diffusion. None of these patients had intracranial or extracranial arterial occlusive disease or a history of systemic hypotension. In 2 patients, embolism from cardiac source or associated with cardiac catheterism was the presumed mechanism of the stroke. In the other 3 patients, the mechanism was undetermined despite the investigation. The possibility of intra-arterial embolism from an aortic source cannot be excluded in these patients, because this artery was not systematically studied in all of them. Also, the presence of reperfusion in all patients with this pattern, who were submitted to follow-up PWI studies, favors the embolic mechanism.

Tumor emboli and showers of cholesterol crystals have been described as causes of borderzone infarcts.21,22 However, the association between platelet emboli and borderzone strokes has been more controversial. Thrombotic occlusions of the pial vessels over conventional watershed infarcts29–31 were initially thought to be secondary to “stagnation thrombi” due to hypotensive episodes.29,30 More recently, the documentation of occlusion of the leptomeningeal arteries by platelet emboli23 and the detection of intra-arterial emboli by transcranial Doppler monitoring in patients with watershed infarcts32 have provided some evidence for the role of embolism in the pathophysiology of borderzone infarcts. Extensive perfusion deficits involving 1 or more vascular territories was the third pattern observed. All of these patients had severe large-artery disease with hemodynamic ischemia as defined by the Harvard Stroke Registry.19 Several authors23,24,33–35 have postulated the role of hyperperfusion in the pathophysiology of strokes in patients with critical carotid artery stenosis or occlusion. Bogousslavsky and Regli23 studied 51 patients with symptomatic unilateral borderzone infarcts detected by CT and found that the great majority of these patients had an ipsilateral ICA occlusion or tight stenosis associated with a hemodynamically significant cardiopathy, increased hematocrit, or acute hypotension. Weiller et al13 studied 37 stroke patients with single-photon emission CT scan and transcranial Doppler with CO2 stimulation and observed that the perfusion reserve and vasomotor reactivity were significantly reduced in patients with stroke secondary to carotid artery occlusion. Two different patterns were seen: changes were restricted to the area of the infarct in patients with a territorial stroke and involved a considerably larger area than the infarct in patients with borderzone infarcts, a finding similar to ours. Decreased cerebral blood flow in the anterior and posterior borderzone regions in patients with ICA and MCA occlusions has also been documented by positron emission tomography scan.34,35

Caplan and Hennerci26 have recently postulated the coexistence of hyperperfusion and intra-arterial embolism in patients with borderzone infarcts and carotid artery disease. These authors posited that the reduced perfusion limits the ability of the blood stream to clear (washout) emboli and that the brain borderzones are a favored destination for microemboli that are not cleared. Future investigation with both PWI and transcranial Doppler monitoring for emboli detection will be necessary to clarify this issue.

In summary, we propose that the perfusion abnormality detected by PWI varies according to the mechanism of the borderzone infarction. Transient perfusion deficits occurring with hypotension in the absence of a critical large-artery disease is usually accompanied by a normal PWI. Embolism may cause small perfusion deficits in the borderzone territory matching the area of diffusion abnormality. Critical large-artery occlusive disease is usually associated with large territorial perfusion deficits and predisposes to borderzone infarction. Prospective observations are needed to confirm the etiologic significance of these patterns, which may lead to a more rational approach to the management of patients with borderzone infarcts.

References


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