

Determinants of the distribution and severity of hypoperfusion in patients with ischemic stroke



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ABSTRACT

Background: In acute cerebral ischemia, two variables characterize the extent of hypoperfusion: the volume of hypoperfused tissue and the intensity of hypoperfusion within these regions. We evaluated the determinants of the intensity of hypoperfusion within oligemic regions among patients who were eligible for recanalization therapy for acute ischemic stroke.

Methods: We analyzed data, including pretreatment diffusion-weighted imaging (DWI) and perfusion-weighted imaging, on 119 patients with acute middle cerebral artery infarctions. The intensity of hypoperfusion within oligemic regions was characterized by the hypoperfusion intensity ratio (HIR), defined as the volume of tissue with severe hypoperfusion ($T_{max} \geq 8$ seconds) divided by the volume of tissue with any hypoperfusion ($T_{max} \geq 2$ seconds). Based on the DWI data, we divided the patients into four stroke phenotypes: large cortical, small (<1 cm diameter) cortical, border-zone, and deep pattern.

Results: The mean (SD) volume of severe hypoperfusion was 54.6 (52.5) mL, and that of any hypoperfusion was 140.8 (81.3) mL. The HIR ranged widely, from 0.002 to 0.974, with a median of 0.35 (interquartile range 0.13–0.60). The volume of any hypoperfusion did not predict the intensity of hypoperfusion within the affected region ($r = 0.10$, $p = 0.284$). Angiographic collateral flow grade was associated with HIRs (p value for trend = 0.019) and differed among DWI lesion patterns. In multivariate analysis, diastolic pressure on admission (odds ratio 0.959, 95% CI 0.922–0.998) and DWI pattern of deep infarcts (odds ratio 18.004 compared with large cortical pattern, 95% CI 1.855–173.807) were independently associated with a low HIR.

Conclusions: The intensity of hypoperfusion within an oligemic field is largely independent of the size of the oligemia region. Predictors of lesser intensity of hypoperfusion are lower diastolic blood pressure and presence of a deep diffusion-weighted imaging lesion pattern. *Neurology*[®]

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GLOSSARY

AIF = arterial input function; **DWI** = diffusion-weighted imaging; **HDL** = high-density lipoprotein; **HIR** = hypoperfusion intensity ratio; **ICA** = internal carotid artery; **IQR** = interquartile range; **LDL** = low-density lipoprotein; **MCA** = middle cerebral artery; **MR** = magnetic resonance; **MRA** = magnetic resonance angiography; **NIHSS** = NIH Stroke Scale; **OR** = odds ratio; **PWI** = perfusion-weighted imaging.

Human cerebral tissue can endure complete loss of blood flow for seconds to minutes, moderate reduction in blood flow for minutes to hours, and mild reduction indefinitely.^{1,2} Multiparametric MRI including perfusion-weighted imaging (PWI) and diffusion-weighted imaging (DWI) have increasingly been used to identify the ischemic penumbra and select patients for recanalization therapy.^{3–10} Several studies have investigated candidate PWI indices and thresholds that best distinguish tissue truly at risk (penumbra) from regions experiencing mild but tolerable low blood flow (benign oligemia).^{3,8,11} However, the factors that determine the pro-

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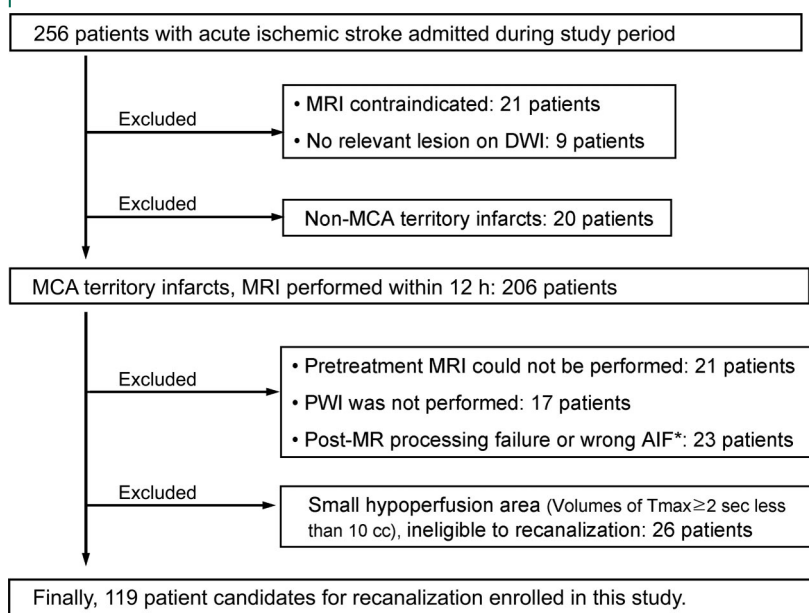
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Figure 1 Selection of patients



*Wrong location of measurement of arterial input function (AIF) on the volume of hypoperfusion. DWI = diffusion-weighted imaging; MCA = middle cerebral artery; MR = magnetic resonance.

portion of oligemic tissue that is severely rather than mildly hypoperfused have not been previously investigated.

Our hypothesis is that the intensity of hypoperfusion abnormality within the oligemic field may vary among acute cerebral ischemia patients and be at least somewhat independent of the size of the oligemic region. In the present study, we evaluated the determinants of the intensity of hypoperfusion within the oligemic field among patients who were eligible for recanalization therapy for acute ischemic stroke.

METHODS We analyzed demographic, clinical, laboratory, and radiographic data collected prospectively from consecutive patients admitted for acute cerebral ischemia to a University Medical Center from December 2002 through May 2007. Inclusion criteria for this study were 1) presentation within 6 hours of symptom onset, 2) acute ischemic lesions within the middle cerebral artery (MCA) distribution on DWI, and 3) at least modest volume (≥ 10 mL) of any hypoperfusion within the MCA field on pretreatment PWI (figure 1). The local institutional review board approved the study, and we received patient consent to perform the study.

All patients underwent MRI (1.5-tesla, Siemens Medical Systems, NJ). The MRI protocol included DWI, gradient-recalled echo, fluid-attenuated inversion recovery, and T2*-perfusion-weighted imaging, and magnetic resonance angiography (MRA) imaging of the cervical and intracranial vessels, using MRI methods previously described.^{12,13} The intensity of perfusion abnormality in each voxel was assessed with the perfusion parameter T_{max} , which is the time to peak magnetic

resonance signal intensity change after deconvolution; T_{max} perfusion lesion maps were generated by deconvolution of an arterial input function and tissue concentration curves based on previous methods.¹⁴

Image analysis was performed with software developed in-house using the Interactive Data Language produced by ITT Visual Systems (Boulder, CO). MRI lesion volume measurements were performed by a neuroradiologist (Y.S.R.) blinded to the clinical information. For each patient, DWI and PWI lesion volumes were outlined automatically with subsequent manual correction, and volumes were calculated with a computer-assisted volumetric analysis program (Medical Image Processing, Analysis and Visualization, version 2.1, Center for Information Technology, NIH). The hypoperfusion intensity ratio (HIR) of $T_{max} \geq 8$ seconds/ $T_{max} \geq 2$ seconds ($V_{T_{max} \geq 8}/V_{T_{max} \geq 2}$) was calculated to index hypoperfusion intensity, reflecting the proportion of tissue experiencing any hypoperfusion ($T_{max} \geq 2$ seconds) that was severe ($T_{max} \geq 8$ seconds). Patients whose $V_{T_{max} \geq 8}/V_{T_{max} \geq 2}$ ratio was in the lowest quartile were defined as having mild intensity of hypoperfusion.

Patients were evaluated in standardized fashion, including demographic data, medical history, vascular risk factors, and NIH Stroke Scale (NIHSS) score.¹⁵ All patients underwent routine blood tests, electrocardiography, cardiac telemetry for at least 24 hours, and echocardiography. Transthoracic echocardiography was performed in large artery territory stroke patients with history, physical examination, or electrocardiographic evidence of coronary artery disease and in all single penetrator artery territory stroke patients. Transesophageal echocardiography was performed up front in large artery infarct patients with no evidence of coronary artery disease and after transthoracic echocardiography in other large artery infarct patients when etiology was unexplained after initial diagnostic evaluation. Hemostatic markers of arterial prothrombotic tendency, including antiphospholipid antibodies (anticardiolipin antibody, dilute Russell viper venom time, β_2 -glycoprotein-1 antibody), were measured in patients younger than 50 years or with stroke cause undefined after initial workup. Venous hypercoagulable states were assessed in patients with right-to-left shunts. Cervical and intracranial MRA was performed in all patients, and selected patients additionally underwent additional vascular imaging, including digital subtraction angiography at attending physician discretion. Catheter angiograms were analyzed for site of occlusion and for degree of collateral flow using the American Society of Interventional and Therapeutic Neuroradiology scale.¹⁶ Angiographic collateral flow was graded without knowledge of MRI findings as follows: grade 0, no collaterals visible to the ischemic site; grade 1, slow collaterals to the peripheral of the ischemic site with persistence of some of the defect; grade 2, rapid collaterals to the periphery of ischemic site with persistence of some of the defect and to only a portion of the ischemic territory; grade 3, collaterals with slow but complete angiographic blood flow of the ischemic bed by the late venous phase; and grade 4, complete and rapid collateral blood flow to the vascular bed in the entire ischemic territory by retrograde perfusion.¹⁶ Stroke mechanism categories were classified by use of the modified Trial of Org 10172 in Acute Stroke Treatment classification.¹³

Based on the DWI data, we divided the patients into four ischemic stroke topographic phenotypes: large cortical, small (< 1 cm in diameter) cortical, border-zone, and predominantly deep pattern. Large cortical patterns included territorial infarcts involving two or three MCA subdivisions (superior, inferior, or deep)¹⁷ and cortical infarcts involving one superficial subdivision (lobar type). The small cortical pattern was infarcts with small

Table 1 Clinical and radiologic characteristics of patients according to the quartile of hypoperfusion intensity ratio (Tmax ≥8 seconds/Tmax ≥2 seconds)

	Quartiles of ratio of VolTmax ≥8 seconds/VolTmax ≥2 seconds				p Value
	<0.125, n = 29	0.125-0.33, n = 31	0.34-0.60, n = 30	>0.60, n=29	
Age	61.8 ± 20.0	64.39 ± 18.54	68.0 ± 18.1	65.3 ± 18.9	0.657
Female	15 (51.7%)	16 (51.6%)	14 (46.7%)	11 (37.9%)	0.686
Risk factors					
Hypertension	17 (58.6%)	15 (48.4%)	21 (70.0%)	21 (72.4%)	0.192
Diabetes	5 (17.2%)	8 (25.8%)	3 (10.0%)	8 (27.6%)	0.298
Hyperlipidemia	10 (34.5%)	8 (25.8%)	7 (23.3%)	7 (24.1%)	0.759
Smoking habits					0.025
Nonsmoker	19 (65.5%)	21 (67.7%)	19 (63.3%)	14 (48.3%)	
Ex-smoker	8 (27.6%)	1 (3.2%)	8 (26.7%)	6 (20.7%)	
Current smoker	2 (6.9%)	9 (29.0%)	3 (10.0%)	9 (31.0%)	
Atrial fibrillation	8 (27.6%)	6 (19.4%)	16 (53.3%)	11 (37.9%)	0.035
Stroke/TIA history	4 (13.8%)	6 (19.4%)	6 (20.0%)	5 (17.2%)	0.924
Coronary heart disease	6 (20.7%)	8 (25.8%)	6 (20.0%)	7 (24.1%)	0.941
Laboratory findings					
Systolic blood pressure	145.0 ± 31.5	154.8 ± 29.9	152.8 ± 35.4	161.5 ± 28.7	0.262
Diastolic blood pressure	75.5 ± 16.9	81.7 ± 13.3	84.5 ± 19.8	84.6 ± 19.2	0.165
s-Glucose on admission	112.1 ± 24.9	127.7 ± 52.2	130.5 ± 26.0	138.3 ± 60.8	0.149
Total cholesterol	161.8 ± 26.5	167.3 ± 38.6	163.3 ± 45.0	166.6 ± 40.9	0.942
Triglyceride	128.7 ± 87.4	105.1 ± 59.0	86.1 ± 45.6	136.6 ± 87.0	0.051
HDL cholesterol	42.3 ± 11.8	46.8 ± 14.8	46.1 ± 14.2	42.0 ± 11.7	0.403
LDL cholesterol	96.8 ± 26.1	102.2 ± 30.1	103.2 ± 40.6	97.2 ± 35.2	0.851
NIHSS score on admission, median (interquartile range)	11 (8-13)	17 (10-22)	19 (11-23)	18 (14-21)	0.001
Stroke subtypes					
Cardioembolic	15 (51.7%)	12 (38.7%)	21 (70.0%)	20 (69.0%)	0.096
Atherosclerotic	10 (34.5%)	8 (25.8%)	6 (20.0%)	7 (24.1%)	
Others	3 (10.3%)	6 (19.4%)	1 (3.3%)	1 (3.4%)	
Unknown	1 (3.4%)	5 (16.1%)	2 (6.7%)	1 (3.4%)	
MRI findings					
Volumetric analysis					
DWI lesion, mL	8.8 ± 9.4	23.3 ± 27.7	50.6 ± 45.3	88.3 ± 61.5	<0.001
Tmax ≥2 seconds, mL	123.6 ± 60.8	145.0 ± 97.3	151.5 ± 82.8	142.4 ± 80.7	0.596
Tmax ≥4 seconds, mL	61.0 ± 38.2	100.3 ± 71.0	116.9 ± 67.1	126.7 ± 76.2	0.001
Tmax ≥8 seconds, mL	7.9 ± 7.9	36.1 ± 24.9	73.1 ± 47.1	107.8 ± 69.1	<0.001
Topographic analysis					
Large cortical	3 (10.7%)	12 (38.7%)	24 (80.0%)	24 (85.7%)	<0.001
Small cortical	6 (21.4%)	7 (22.6%)	2 (6.7%)	0 (0%)	
Border zone	3 (10.7%)	2 (6.5%)	2 (6.7%)	1 (3.6%)	
Predominantly deep	16 (57.1%)	10 (32.3%)	2 (6.7%)	3 (10.7%)	
Vascular study findings					
Site of occlusion					0.024
Extracranial ICA	4 (13.8%)	7 (23.3%)	1 (3.4%)	4 (13.8%)	
Intracranial ICA	3 (10.3%)	2 (6.7%)	7 (24.1%)	6 (20.7%)	

—Continued

Table 1 Continued

	Quartiles of ratio of VolTmax ≥8 seconds/VolTmax ≥2 seconds				p Value
	<0.125, n = 29	0.125–0.33, n = 31	0.34–0.60, n = 30	>0.60, n = 29	
Proximal M1	12 (41.4%)	11 (36.7%)	4 (13.8%)	7 (24.1%)	
Distal M1	6 (20.7%)	2 (6.7%)	11 (37.9%)	8 (27.6%)	
MCA branches	2 (6.9%)	6 (20.0%)	6 (20.7%)	2 (6.9%)	
No occlusion	2 (6.9%)	2 (6.7%)	0 (0%)	2 (6.9%)	
Collateral grading score					0.016
0 or 1	1 (5.9%)	8 (38.1%)	8 (40.0%)	7 (50.0%)	
2 or 3	8 (47.1%)	7 (33.3%)	11 (55.0%)	5 (35.7%)	
4	8 (47.1%)	6 (28.6%)	1 (5.0%)	2 (14.3%)	
Premorbid medications					
Statins	5 (17.2%)	5 (16.1%)	5 (16.7%)	6 (20.7%)	0.968
Antithrombotics					0.057
Antiplatelet	13 (44.8%)	7 (22.6%)	9 (30.0%)	9 (31.0%)	
Warfarin	0 (0%)	2 (6.5%)	4 (13.3%)	2 (6.9%)	

HDL = high-density lipoprotein; LDL = low-density lipoprotein; NIHSS = NIH Stroke Scale; DWI = diffusion-weighted imaging; ICA = internal carotid artery; MCA = middle cerebral artery.

single or multifocal ischemic lesions of <1 cm in diameter on DWI, suggesting distal embolism.¹⁸ Border-zone infarcts included multiple border-zone infarcts (either superficial or deep), suggesting hypoperfusion, distal embolism, or both, as previously reported.¹⁹ The predominantly deep pattern was defined as deep infarcts in the striatocapsular area with or without concomitant small (<1 cm) DWI lesions outside the striatocapsular area. Two readers blinded to the clinical data analyzed the DWI data; interobserver agreement was 97.3% for the interpretation of DWI lesion pattern (large cortical vs small cortical vs border zone vs predominantly deep). A third reader’s opinion was obtained in cases of disagreement.

We analyzed the differences between the groups using the χ^2 test, Student *t* test, or one-way analysis of variance for means of normally distributed variables or the Kruskal–Wallis test for medians. The relationship of Tmax ≥2 seconds volume or DWI lesion volume with HIR was evaluated using Spearman correlation analysis. Independent factors for mild intensity of hypoperfusion (lowest quartile of V_{T8s}/V_{T2s} ratio) were evaluated using logistic regression. Two multivariable logistic regression models were used with the lowest quartile of V_{T8s}/V_{T2s} as the dependent variable and potential factors as independent variables. First, we performed multivariable logistic regression analysis to determine the independent predictors (causative variables) for the lowest quartile of V_{T8s}/V_{T2s}. Potential predictors considered for inclusion in this model were blood pressure and s-glucose levels on admission, pretreatment collateral grade, and site of occlusion, because these factors are known to influence hypoperfusion status. Second, a multivariable logistic regression model was used to evaluate clinicoradiologic variables that may help to identify patients with lowest HIR, controlling for 1) clinical and MRI findings (model 1, preangiography setting) and 2) angiographic findings as well as clinical and MRI findings (model 2, interventional setting). All potential confounding factors were entered into a logistic regression model, and factors that were not significant were sequentially deleted from the full model. Excluded variables were reintroduced at various stages of model development until only significant predictors remained. Results are given as odds ratio (OR)

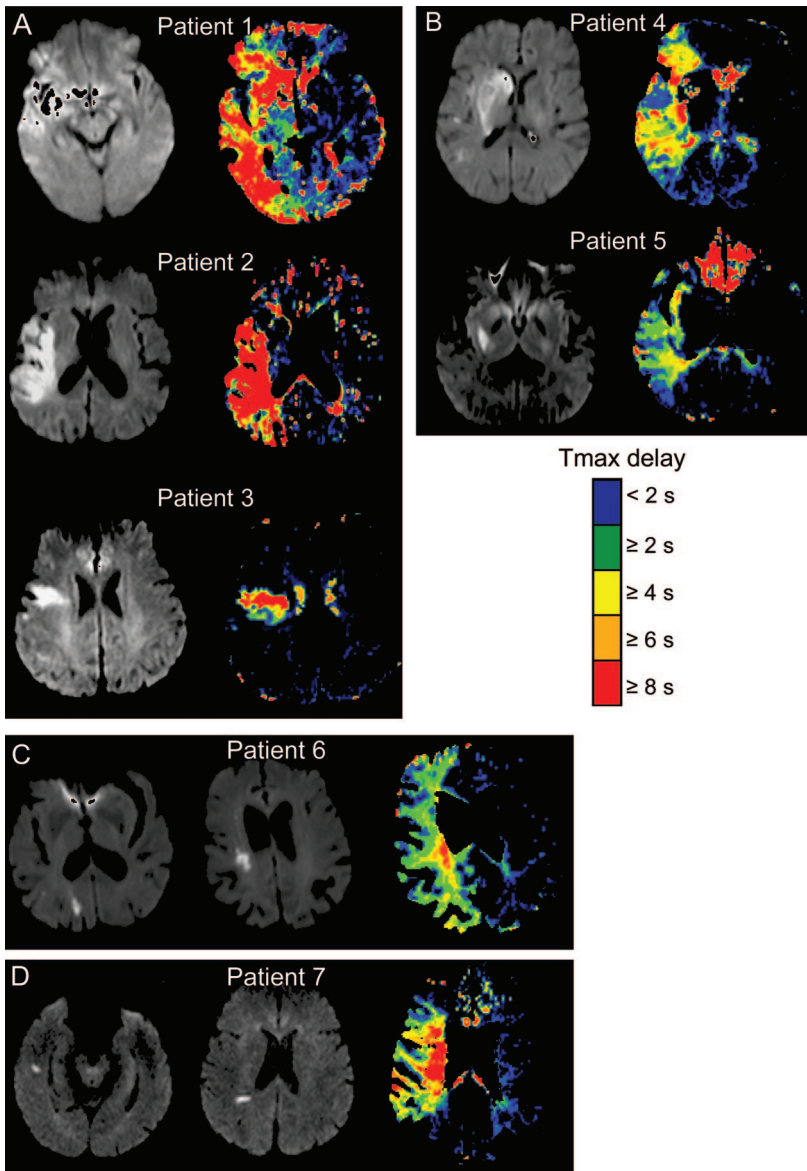
with 95% CI. Final significance was established at the *p* < 0.05 level.

RESULTS Of 256 patients admitted with ischemic stroke during the study period, 119 met the study criteria (figure 1). Among enrolled patients, 61% were female, and the average age was 65.9 ± 18.5 years (range 15–95 years). The racial classification of patients included 88 whites, 9 African-Americans, 15 Asian-Americans, and 7 of other or unknown race. In ethnicity, 22 were Hispanic and 97 were not Hispanic. Recanalization therapy was pursued in 82 of the 119 patients. MRI was performed before treatment in all patients (median 4.1 hours after onset of symptoms, interquartile range [IQR] 2.4–5.3 hours, full range 0.6–15.8 hours). The median DWI lesion volume was 12.7 mL (IQR 2.9–54.8 mL, full range 0.1–230 mL), and the median volume of any PWI oligemia (Tmax ≥2 seconds) was 115.0 mL (IQR 20.2–179.4 mL, full range 11.1–399 mL). The median HIR (V_{T8s}/V_{T2s}) was 0.35 (IQR 0.13–0.60, full range 0.02–0.97).

Patients’ characteristics depending on the quartile of HIR are shown in table 1. NIHSS on admission was lower and being a never-smoker was more prevalent in patients with low V_{T8s}/V_{T2s} ratios. Atrial fibrillation was more frequently observed in patients with high V_{T8s}/V_{T2s} ratios, and there was a trend that potential sources of cardioembolism were found more frequently in these patients.

The volume of any hypoperfusion and the HIR were not correlated. Correlation analysis between the

Figure 2 Perfusion-weighted imaging findings in different diffusion-weighted imaging lesion patterns



(A) Large cortical pattern, (B) predominantly deep, (C) border-zone, and (D) multiple small cortical pattern.

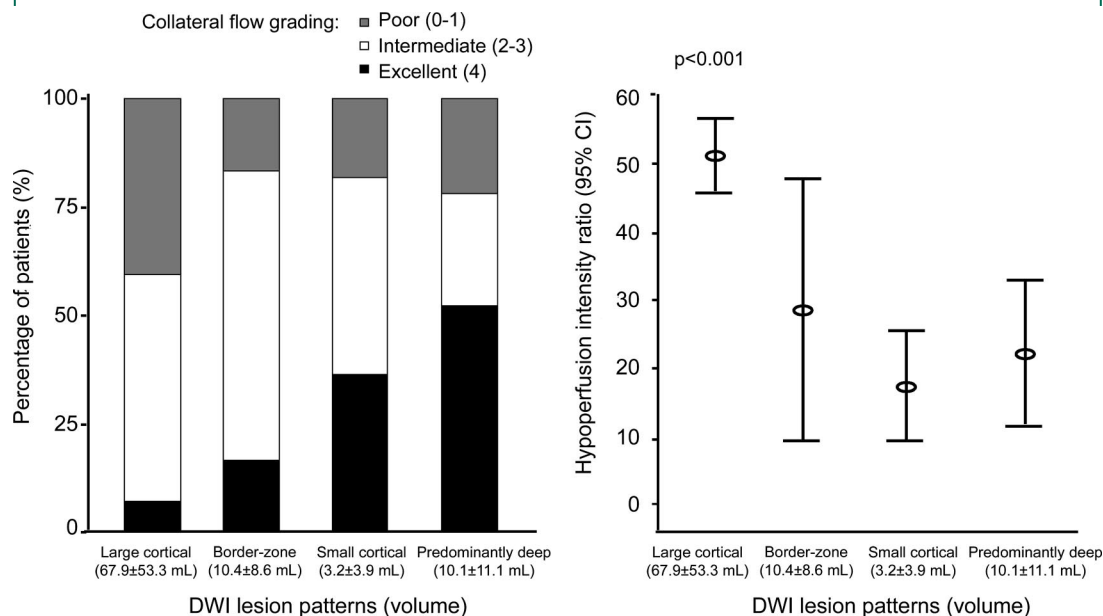
volume of $T_{\max} \geq 2$ seconds area and the $V_{T_{8s}}/V_{T_{2s}}$ ratio was $r = 0.10$, $p = 0.284$. The extent of any hypoperfusion did not differ among the quartiles of HIR (table 1 and figure e-1 on the *Neurology*[®] Web site at www.neurology.org). In contrast, both DWI lesion topography and DWI lesion volumes were associated with the HIR (figure 2 and figure e-1). The proportion of affected tissue experiencing severe hypoperfusion (high HIR) was greatest in patients with large cortical patterns, whereas patients with other DWI patterns showed less intense perfusion defects (figures 2 and 3).

Digital subtraction angiography was performed in 94 patients. Patients with high $V_{T_{8s}}/V_{T_{2s}}$ ratios had poor collateral flow compared with those with low

ratios. Compared with patients with large cortical pattern, patients with other patterns more often had excellent collaterals (grade 4 in 42.5% vs 7.1%) and were less like to have poor collaterals (grade 0 or 1 in 20.0% vs 40.5%) ($p < 0.001$; figure 3). Diastolic blood pressure was not different depending on the collateral grading (83.3 ± 14.2 mm Hg in grade 0 or 1 vs 79.0 ± 22.1 mm Hg in grade 2 or 3 vs 78.5 ± 13.2 mm Hg in grade 4; $p = 0.603$). Multiple regression analysis was performed to further evaluate the independent predictors for relatively small proportions of affected tissue severely hypoperfused (lowest quartile of $V_{T_{8s}}/V_{T_{2s}}$). After adjusting for covariates, excellent (grade 4 vs grade 0 or 1; OR 20.444, 95% CI 2.227–187.692; $p = 0.008$) and intermediate collateral grades (grade 2 or 3 vs grade 0 or 1; OR 6.708, 95% CI 0.764–58.868; $p = 0.086$) were independently associated with low HIRs (p value for trend = 0.019). Systolic (OR 1.006, 95% CI 0.973–1.040) and diastolic blood pressure (OR 0.965, 95% CI 0.907–1.027), s-glucose levels on admission (OR 0.978, 95% CI 0.950–1.007), and T-zone occlusion (OR 2.571, 95% CI 0.309–21.413) were not associated with low HIRs in this model.

We then evaluated the clinicoradiologic variables (either preangiographic or postangiographic state) which may help in identifying patients with the lowest quartile of HIR (table 2). After adjusting for covariates, diastolic pressure on admission (OR 0.959 per 1-mm Hg increase, 95% CI 0.922–0.998) and DWI pattern of predominantly deep infarcts (OR 18.004 compared with large cortical pattern, 95% CI 1.855–173.807) were independently associated with low HIRs. Similar results were observed when angiographic results, including collateral grade and site of occlusion, were considered (table 2). Although collateral grading differed among the quartiles of HIR (table 1), neither excellent (grade 4 vs grade 0 or 1; OR 4.263, 95% CI 0.265–68.631; $p = 0.309$) nor intermediate collateral grades (grade 2 or 3 vs grade 0 or 1; OR 2.774, 95% CI 0.139–55.318; $p = 0.504$) were associated with low HIRs in this model. In contrast, DWI lesion volumes were the only significant independent predictor for having a large proportion of affected tissue severely hypoperfused (highest quartile of $V_{T_{8s}}/V_{T_{2s}}$; OR 1.030 per 1-mL increase, 95% CI 1.017–1.044). Receiver operating characteristic curves identified an optimal threshold of DWI lesion volumes of 14 mL for forecasting a high probability of the lowest quartile of $V_{T_{8s}}/V_{T_{2s}}$, yielding a sensitivity of 89% (95% CI 72%–98%) and a specificity of 65% (95% CI 54%–75%), whereas a DWI lesion volume of 69 mL forecast a high probability of the highest quartile of $V_{T_{8s}}/V_{T_{2s}}$, yielding a sensitiv-

Figure 3 Relationship between diffusion-weighted imaging (DWI) lesion patterns, collateral flow, and hypoperfusion intensity ratios



ity of 66% (95% CI 46%–82%) and a specificity of 92% (95% CI 85%–97%).

DISCUSSION This study found that the intensity of hypoperfusion within the affected field varied widely among acute cerebral ischemia patients with similar volumes of tissue exhibiting any degree of oligemia. No correlation was noted between the volume of mild perfusion defects and the proportion of the affected field experiencing intense hypoperfusion. This finding suggests that estimating the volume of penumbral tissue by simple visual inspection of the border between tissue experiencing normal vs any abnormal blood flow is not the most reliable guide to selecting patients for recanalization therapy (results of the Desmoteplase in Acute Ischemic Stroke Trial 2, presented at the 16th European Stroke Conference, Glasgow, UK). The intensity of hypoperfusion, as well as the extent of the hypoperfused area (mismatch volume), determines tissue fate. In contrast, the extent and pattern of advanced tissue bioenergetic failure, reflected in the volume and topography of DWI abnormality, were independently associated with the intensity of hypoperfusion. In a prior study using both voxel-by-voxel and volume analyses of serial MRI studies, it was found that PWI measures of ischemia intensity can differentiate irreversibly injured core from penumbral, salvageable tissue, with the best threshold for identifying core infarcted tissue adjusted T_{max} of ≥ 6 or ≥ 8 seconds.¹² The findings of the present study are consistent with this observation, showing that the proportion of the affected field experiencing

severe oligemia with $T_{max} \geq 8$ seconds correlated with DWI lesion volume.

Our study also found that DWI lesion patterns were an independent correlate of the HIR. We investigated DWI lesion patterns in the present study because several studies have suggested that infarct topography correlates with the underlying stroke pathogenic mechanism²⁰ and characteristics (type and nature) of clots^{21,22} and are associated with stroke outcome.²³ DWI lesion has advantages as a guide to acute treatment decision making, as a complement to assessments of perfusion and diffusion lesion volume, because it is simpler and less time-consuming to assess than volumetric analysis.

Pretreatment collateral grade on angiography predicted infarct volume after recanalization therapy.^{24,25} We have recently reported the relationship between diffusion-perfusion indices, angiographic collateral grade, and infarct growth in 44 patients who underwent endovascular recanalization therapy: angiographic collateral grade and penumbral volume interactively shape tissue fate in these patients.²⁶ In the present study, the extent of collaterals evident at catheter angiography correlated strongly with the HIR. This finding indicates that collaterals may protect the brain not only by reducing the volume of tissue experience any hypoperfusion, but also by reducing the intensity of hypoperfusion within altered perfusion fields. By permitting a greater proportion of tissue to experience benign oligemia that is tolerable indefinitely rather than severe oligemia that is rapidly injurious, collateral flow can ameliorate the effect of loss of anterograde flow though an acute oc-

Table 2 Odds ratios (95% CIs) for having lowest quartile for hypoperfusion intensity ratio

	Model 1: Preangiographic state			Model 2: Postangiographic state		
	Crude	Multivariate	p Value	Crude	Multivariate	p Value
Clinical findings						
NIHSS score on admission, per 1-point increase	0.947 (0.835-1.073)			0.980 (0.852-1.128)		
Hypertension	2.112 (0.534-8.355)			1.717 (0.397-7.433)		
Atrial fibrillation	0.530 (0.104-2.699)			0.864 (0.139-5.381)		
Premorbid antiplatelet use	1.892 (0.497-7.198)			1.789 (0.406-7.878)		
Never smoked	2.551 (0.573-11.356)			3.472 (0.665-18.131)		
Diastolic blood pressure, per 1-mm Hg increase	0.946 (0.902-0.992)	0.959 (0.922-0.998)	0.039	0.935 (0.882-0.992)	0.955 (0.917-0.995)	0.027
Glucose on admission, per 1-mg/dL increase	0.986 (0.966-1.006)	0.987 (0.970-1.003)	0.113	0.977 (0.951-1.004)	0.982 (0.964-1.001)	0.060
Cardioembolic stroke	1.613 (0.375-6.946)			0.961 (0.178-5.198)		
MRI findings						
DWI lesion volume	0.969 (0.908-1.034)	0.950 (0.894-1.009)	0.098	0.966 (0.905-1.032)	0.947 (0.890-1.007)	0.082
DWI lesion pattern						
Large cortical	Ref	Ref		Ref	Ref	
Border zone	11.814 (0.555-251.6)	5.921 (0.408-85.936)	0.193	6.941 (0.295-163.5)	5.216 (0.350-77.625)	0.231
Small cortical	13.044 (0.640-265.8)	7.516 (0.579-97.591)	0.123	9.284 (0.372-231.7)	6.944 (0.529-91.230)	0.140
Predominantly deep	30.354 (2.296-401.3)	18.004 (1.855-173.8)	0.012	32.835 (1.969-547.6)	20.524 (2.069-203.6)	0.010
Angiographic findings						
T-zone occlusion				1.179 (0.047-29.785)		
Collateral grading						
Poor (0 or 1)				Ref		
Intermediate (2 or 3)				2.774 (0.139-55.318)		
Excellent (4)				4.263 (0.265-68.631)		

NIHSS = NIH Stroke Scale; DWI = diffusion-weighted imaging.

cluded artery. Collaterals likely mediate, in several ways, the association noted in this study between the HIR and DWI lesion patterns. Most patients with large cortical DWI topographic patterns had poor collaterals and a high V_{T8s}/V_{T2s} ratio, indicating that poor leptomeningeal collaterals with occlusion of proximal vessels result in large cortical lesion patterns, whereas cortical areas are spared through collaterals and reduced V_{T8s}/V_{T2s} ratio in most patients with a predominantly deep DWI lesion pattern. Large cortical pattern is a common DWI topographic finding in patients with atrial fibrillation or cardioembolic sources. Atrial fibrillation and cardioembolic stroke mechanism were univariate predictors for the intensity of hypoperfusion within the affected field in the present study. The sudden onset of ischemia in cardioembolic occlusion as opposed to intermittent or chronic onset that may occur in atherosclerotic lesions is likely associated with a paucity of previously evoked collaterals, and subsequent hypoperfusion in much of the affected territory.

We found an association of elevated diastolic pressure on presentation with a greater intensity of hypoper-

fusion within the affected field. This finding is consistent with emerging evidence that acute hypertension in cerebral ischemia patients is related to the extent of brain ischemia. It was recently reported that higher pretreatment blood pressure levels are associated with poor recanalization in patients with acute stroke treated with IV tissue plasminogen activator.²⁷ Patients with adequate collaterals do not need highly elevated perfusion pressures to protect the threatened field; in contrast, blood pressure elevations may increase collateral flow in passive pressure-dependent ischemic fields in patients with inadequate collateral. Early hypertension after ischemic stroke was associated with increased mortality.²⁸ Successful recanalization induces substantial decreases in systolic blood pressure, probably due to elimination of the need for this blood pressure elevation.²⁹

Strengths of our study included the consecutive, prospective recruitment of patients who underwent comprehensive workups, including vascular, laboratory, and cardiologic studies; catheter angiographic evaluation in a large proportion of subjects, includ-

ing collateral grading and site of occlusion; and analysis of a variety of MRI findings. However, the results of this study should be interpreted with caution because of the modest sample size and retrospective nature. In addition, relatively few patients with large DWI lesion volumes were included in this study. Multicenter studies with a large sample will be required to prove or disprove our results. In addition, only pretreatment MRI findings were studied, and follow-up diffusion-weighted images were not evaluated in the present study.

APPENDIX

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