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Basal Ganglionic Infarction Before Mechanical Thrombectomy Predicts Poor Outcome

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Background and Purpose—Use of mechanical thrombectomy for acute cerebrovascular occlusions is increasing. Preintervention MRI patterns may be helpful in predicting prognosis.

Methods—We reviewed all Merci thrombectomy cases of either terminal ICA or M1 occlusions and classified them according to diffusion MRI patterns of (1) completed basal ganglia infarct (pure M1a), (2) near-completed basal ganglia infarct (incomplete M1a), and (3) relative sparing of deep MCA field (M1b). We compared the M1a and M1b patients with respect to neurological deficit on presentation, recanalization rates, hospital length of stay, and disability on discharge. We also determined whether deep MCA compromise predicted hematoma hemorrhagic transformation (HT) and whether this correlated with worse clinical outcome at discharge.

Results—The M1a group had worse pre-Merci NIHSS (21 versus 14, $P=0.004$), worse discharge NIHSS (12 versus 4, $P<0.001$), longer hospital length of stay (11.5 versus 6.4 days, $P=0.003$), and higher rates of discharge mRS ≥ 3 (OR 8.4, 95% CI 2.1 to 44.7) despite equivalent recanalization rates when compared to the M1b group. The M1a group had a higher rate of parenchymal hematoma HT (OR 6.7, 95% CI 1.02 to 183.3). Patients with such hematoma HT had higher rates of death or dependency discharge (100% versus 60%, OR=infinite).

Conclusions—Among patients with ICA and M1 occlusions, preintervention diffusion MRI evidence of advanced injury in the basal ganglia bodes worse dysfunction and disability at discharge, longer hospital stays, and higher rates of hemorrhage after intervention when compared to other diffusion patterns. (*Stroke*. 2009;40:3315-3320.)

Key Words: Merci ■ thrombectomy ■ hemorrhage ■ basal ganglia

The Merci Retrieval System (Concentric Medical Inc) is the first device cleared by the FDA for intracranial mechanical thrombectomy.^{1,2} It is designed to recanalize large vessel occlusions attributable to thromboembolism. Because experience with the Merci retriever remains limited, we do not know which patients receive the most benefit. Whether patients with certain preintervention MRI patterns have better outcomes after revascularization is currently under investigation.^{3,4} One commonly encountered preintervention MRI pattern of injury consists of completed or near-completed basal ganglionic infarct with a large penumbra in the ipsilateral hemispheric cortex. This pattern is likely the result of sufficiently prolonged occlusion of the prebifurcation M1 segment of the middle cerebral artery (MCA) and the lenticulostriate artery (LSA) ostia.⁵ This yields disproportionately profound deep versus superficial MCA territory ischemia as the LSAs do not possess leptomeningeal collat-

erals as the distal MCA branches do. Early completed infarction in the entire lenticular nucleus, portions of the caudate, and internal and external capsule may substantially impede long-term functional recovery, as key nodes and connecting tracts for cognitive large-scale neuronal networks are irreversibly injured.⁶ Thus, basal ganglionic and deep white matter infarction may result in severe disability despite cortical preservation.

Materials and Methods

All consecutive patients undergoing Merci clot retrieval for large arterial occlusions from August 2002 to December 2007 were prospectively entered into our institution's database according to protocol approved by our local Institutional Review Board. We retrospectively reviewed only terminal internal carotid artery (ICA) and M1 segment occlusions, or tandem lesions if at least 1 of the occlusions involved the terminal ICA or M1. Reviewed patients had to demonstrate diffusion weighted (DWI)-perfusion weighted (PWI)

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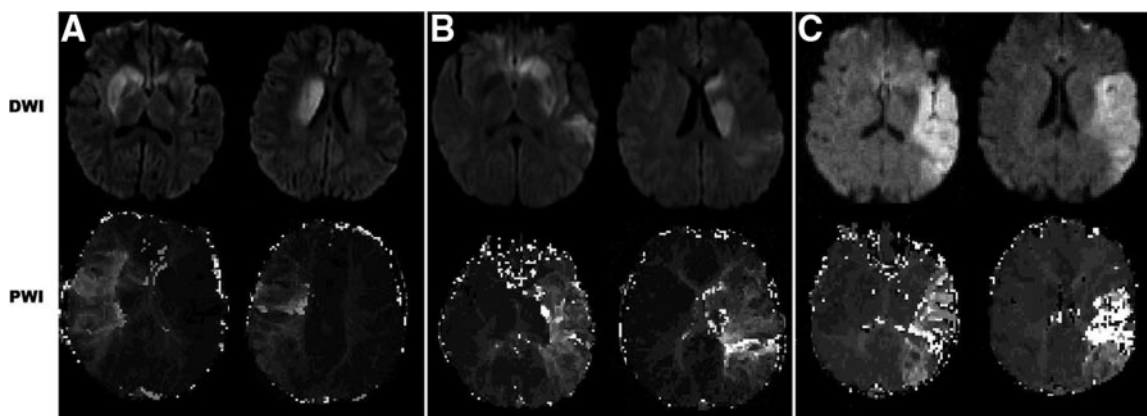


Figure. Three different preintervention DWI and PWI (MTT) MRI sets illustrating the 3 various patterns. A, Pure M1a, demonstrating diffusion restriction in the entire globus pallidus and caudate body, with DWI/PWI mismatch throughout the hemisphere. B, Incomplete M1a, demonstrating patchy diffusion restriction in the globus pallidus and caudate body with DWI/PWI mismatch throughout the hemisphere. C, M1b, demonstrating preservation of the globus pallidus and caudate body with infarction of the insula, temporal, and frontal opercula with DWI/PWI mismatch in the posterior temporal lobe.

mismatch on MRI before thrombectomy, and either a documented neurological examination or NIH stroke scale (NIHSS) on discharge. We recorded the final revascularization of the primary arterial occlusive lesion (AOL) from the angiogram. This has been described previously,⁷ and in summary a score of 0 represents no recanalization; a score of 1, incomplete or partial recanalization with no distal flow; a score of 2, incomplete or partial recanalization with any distal flow; and a score of 3, complete recanalization with any distal flow.

Two reviewers then independently analyzed the preintervention MRI scans and identified a group with diffusion abnormality throughout the deep MCA territorial basal ganglia and white matter (pure M1a pattern), diffusion abnormality in more than 50% but less than 80% of the deep MCA territorial basal ganglia and white matter (incomplete M1a pattern), and those with all other mismatch patterns with relative sparing of the deep MCA territory (M1b). The defining ranges of diffusion abnormality in this region of interest were chosen to best distinguish these three anecdotally distinct MRI patterns. Volumetric estimation was subjective. Examples of the 3 different MRI patterns are shown (Figure). The interrater agreement was calculated. Together, both reviewers reassessed any MRI pattern disagreements and assigned patients after consensus.

We compared patients with both M1a patterns to those with the M1b pattern with respect to demographic data on sex and age; the presence of premorbid hypertension, diabetes, dyslipidemia, cardiac disease, pulmonary disease, peripheral vascular disease, prior stroke, and suspected or demonstrated cardioembolic source for stroke; aspects of the intervention to include dominant hemispheric injury, time to MR imaging, time to first Merci pass, delay from MR imaging to first Merci Pass, good primary arterial occlusive lesion (AOL score 2 or 3) recanalization, persistence of DWI-PWI mismatch on postintervention MRI, concomitant use of intraarterial thrombolytic or preintervention administration of intravenous thrombolytic; and clinical outcome measures including preintervention NIHSS, hospital length of stay (LOS), discharge modified Rankin score (mRS), discharge NIHSS, and change in NIHSS by discharge. We then analyzed the proportion of patients within each group with death or dependency at discharge.

We determined whether there was an association between the varying preintervention MRI patterns, any hemorrhagic transformation (HT), and HT with parenchymal hematoma (PH).⁸ We defined PH and "hematomal HT" as $HT \geq PH1$, to include all types of parenchymal hematomas (PH1 and PH2). We then assessed whether PH worsened clinical outcome at discharge. We also determined whether there was a relationship between PH and baseline demographics, the presence of premorbid medical conditions, peak and mean glucose levels in the 72 hours after ictus, and aspects of the intervention.

Statistical analyses for categorical variables included χ^2 , Fisher exact test when cell sizes were small, and odds ratios for selected comparisons. We examined continuous variables using analysis of variance with post hoc Tukey comparisons, and applied the Mann-Whitney and Kruskal-Wallis tests with appropriate post hoc comparisons to measures with uneven distributions. All analytic procedures were conducted in R version 2.8.0.⁹

Results

We initially identified a total of 52 patients meeting inclusion criteria. Two patients were excluded from our study because of early (<24 hour) transfer back to the initial referring institution after thrombectomy, leaving 50 patients. Among these patients, the average age was 64 years old, 46% were male, and median pretreatment NIHSS was 19. On preintervention MRI, 14 patients had the pure M1a, 12 had the incomplete M1a, and 24 had the M1b pattern. Consequently, 26 patients constituted the M1a group. Because of premorbid disability, 1 patient was excluded solely from the mRS analysis. One patient was diagnosed with an atrial myxoma as the cause of stroke and was excluded solely from hospital LOS comparisons because of a prolonged hospital stay involving cardiac surgery. Three patients with the M1a pattern and 4 with the M1b pattern either did not undergo post-Merci MR imaging or had uninterpretable DW-PW images to determine whether there was persistent mismatch after thrombectomy.

Of the initial 52 patients, there was initial disagreement on the group assignment of 5 patients, which represents 90% interrater agreement. Consensus was then reached on the final group assignments for these 5 discordant designees.

Baseline demographics and aspects of the intervention were similar between groups (Table 1). The use of concomitant intravenous or intraarterial recombinant tissue plasminogen activator (rt-PA) was similar between groups, as was the distribution of cardioembolic strokes. The M1a group fared worse clinically than the M1b cohort on multiple comparisons (Table 2). Patients with M1a patterns had worse preintervention NIHSS compared to the M1b group (21 versus 14, $P=0.004$). Similarly, when compared to the M1b patients, the M1a patients had worse discharge NIHSS (12 versus 4,

Table 1. Demographics of Patients With Pre-Merci M1a and M1b MRI Patterns

Characteristic	M1a n=26	M1b n=24	P
Age, y	63.8±21.1	65.5±16.2	0.75
Male sex, n (%)	11 (42)	12 (50)	0.77
Premorbid history of: n (%)			
Hypertension	14 (54)	16 (67)	0.40
Diabetes	6 (23)	6 (25)	1
Prior stroke	1 (4)	2 (8)	0.60
Cardiac history	11 (42)	13 (54)	0.57
Dyslipidemia	11 (42)	6 (25)	0.24
Pulmonary disease	4 (15)	4 (17)	1
Peripheral vascular disease	2 (8)	2 (8)	1
Dominant cerebral injury, n (%)	18 (69)	15 (65)	0.77
Cardioembolic source, n (%)	11 (42)	13 (54)	0.57
Time to MRI, h	5:06±2:52	5:17±2:38	0.30
Time to clot retrieval, h	6:17±2:50	6:24±2:28	0.89
Time from MR to Merci, h	1:20±0:57	1:13±1:03	0.68

P<0.001), worse discharge mRS (5 versus 2, *P*=0.003), and longer hospital LOS (11.5 versus 6.4 days, *P*=0.003).

The M1a group had higher rates of death or dependency at discharge (88% versus 46%, OR 8.4, 95% CI 2.1 to 44.7). All deaths in this cohort were stroke-related, and mortality rates were similar between both groups (27% versus 14%, OR 2.2, 95% CI 0.5 to 12.4).

Post hoc comparison of the M1a subgroups (Table 3) demonstrated that the discharge NIHSS scores in both the pure and incomplete M1a subgroups were worse than the M1b cohort (*P*=0.04 for both comparisons). In comparing discharge mRS and rates of hematoma HT, only the pure M1a cohort differed from the M1b group (5 versus 2, *P*=0.02; 42.9% versus 4.5%, *P*=0.007, respectively). The only clinical measure that differed between the pure and incomplete M1a subgroups was the hospital LOS (14.7 versus 7.1 day, *P*=0.006).

For the HT analysis (Table 2), 2 patients who did not have imaging by 72 hours were excluded. The occurrence of any HT was similar between groups (27% versus 14%, OR 2.2, 95% CI 0.5 to 12.4). However, patients with the M1a pattern showed a higher rate of PH transformation than the M1b group (27% versus 5%, OR 6.7, 95% CI 1.02 to 183.3). Patients with PH transformation had worse discharge mRS (5 versus 4, *P*=0.03). There were no other predictors of PH transformation among baseline demographics, premorbid medical conditions, and aspects of the intervention. The concomitant use of intravenous or intraarterial thrombolytic was not related to HT.

Discussion

Because mechanical thrombectomy is still a relatively new procedure, optimum patient selection remains ill-defined. Our series demonstrates that preintervention diffusion MRI evidence of advanced injury in the basal ganglia and white

Table 2. Clinical Outcomes of Patients With Pre-Merci M1a and M1b MRI Patterns and Those With and Without Hematoma Transformation (HT≥PH1) After Thrombectomy

Characteristic	Primary Comparison			Post Hoc HT Analysis*		
	M1a n=26	M1b n=24	P†	No HT or HT<PH1 n=40	HT≥PH1 n=8	P‡
Pre-Merci NIHSS	21 (18–27)	14 (10–38)	0.004	19 (12–38)	18 (15–21)	0.69
Intravenous rt-PA, n (%)	7 (27)	5 (21)	0.74	9 (23)	3 (38)	0.39
Intra-arterial rt-PA, n (%)	2 (8)	1 (4)	0.07	1 (3)	2 (25)	0.07
Good recanalization, n (%)‡	22 (85)	16 (67)	0.19	31 (78)	7 (88)	1
Persistent mismatch, n (%)§	16 (70)	10 (50)	0.23	19 (54)	5 (63)	1
Mean serum glu, mmol/L	7.4±1.3	6.8±1.5	0.12	6.9±1.5	7.5±1.2	0.32
Peak serum glu, mmol/L	9.5±3.1	8.5±2.5	0.22	9.1±3.1	8.7±1.4	0.74
Discharge NIHSS	12 (6–25)	4 (2–15)	<0.001	5 (2–25)	12 (8–14)	0.09
Change in NIHSS	7.8±7.6	8.8±6.5	0.67	8.3±7.1	6.2±5.0	0.48
Discharge mRS	5 (4–6)	2 (1–6)	0.003	4 (1–6)	5 (4–6)	0.03
Length of stay, d ¶	11.5±7.4	6.4±4.1	0.003	9.2±6.7	5.8±3.8	0.25
OR, discharge mRS≥3	23 (88)	11 (46)	8.4 (2.1–44.7)	24 (60)	8 (100)	Inf
OR, discharge mRS≥3, ≠6	16 (84)	8 (38)	7.3 (1.9–45.0)	17 (52)	6 (100)	Inf
OR, death during stay	7 (27)	3 (14)	2.2 (0.5–12.4)	7 (18)	2 (25)	0.6 (0.1–3.8)
OR, any HT*	14 (54)	9 (41)	1.7 (0.5–5.3)			
OR, HT≥PH1*	7 (27)	1 (5)	6.7 (1.02–183.3)			

*Two patients did not undergo imaging by 72 hours to determine HT.

†Odds ratios (95% CI) are shown for selected comparisons.

‡Good recanalization defined as AOL score of 2 or 3.

§Three M1a, 4 M1b, and 5 No HT or HT<PH1 patients did not undergo post-Merci MR imaging or had uninterpretable DW-PW images.

||Patients that expired were not analyzed in these comparisons.

¶One patient from the M1b group underwent cardiac surgery and was excluded from LOS analysis.

Median (interquartile range, IQR) reported for NIHSS and mRS values. OR indicates Odds ratio.

Table 3. Post Hoc Analysis of M1a Subgroups

Clinical Outcome Measure	Group			Post Hoc Comparison		
	Pure M1a	Incomplete M1a	M1b	Pure M1a vs M1b	Incomplete M1a vs M1b	Incomplete vs Pure M1a
Pre-Merci NIHSS	21 (18–27)	20 (19–25)	14 (10–38)	0.04	ns	ns
Discharge NIHSS	12 (7–21)	14 (3–25)	4 (2–15)	0.04	0.04	ns
Change in NIHSS	7.5±8.0	8.3±7.6	8.8±6.5	ns	ns	ns
Discharge mRS	5 (4–6)	5 (3–6)	2 (1–6)	0.02	ns	ns
Length of stay, d	14.7±8.1	7.1±2.9	6.0±3.2	<0.001	ns	0.006
HT≥PH1, n (%)	6 (42.9)	1 (8.3)	1 (4.5)	0.007	ns	ns

matter of the deep MCA field bodes poorly for clinical outcome at hospital discharge. Patients with extensive deep MCA diffusion lesions have substantially worse neurological function at discharge, higher rates of disability, and longer hospital stays when compared to other preintervention MRI patterns.

One likely contributing factor to the increased rate of parenchymal hematoma among pure M1a patients is the development of ischemia-induced permeability derangement before intervention. The deep MCA field in particular may be susceptible to blood–brain barrier failure after ischemia.¹⁰ Successful reperfusion in the setting of the deep MCA field may thus pose an even higher risk of hemorrhagic transformation.

Patients with deep MCA compromise likely have more disability at discharge for several reasons. Although some milder degrees of diffusion abnormality are reversible with early reperfusion,^{11–15} the M1a pattern may identify those patients who already have advanced injury in large portions of the basal ganglia and internal capsule before the start of intervention. Successful revascularization will not avert the functional deficits that accrue from these established lesions. Moreover, patients with complete deep MCA diffusion lesions are more prone to parenchymal hematomas after intervention, likely because of reperfusion of a profoundly infarcted deep field, which may further decrement their functional outcome.

Limitations of our study include modest sample size. As a result, we focused mostly on comparing the combined pure and incomplete M1a group with the M1b group and less on separately analyzing the pure and incomplete M1a groups. Post hoc analysis yielded mixed results. Although the incomplete M1a and M1b groups both had shorter hospital LOS than the pure M1a group, the neurological dysfunction and clinical outcomes of the incomplete M1a subgroup more closely resemble the pure M1a than the M1b cohort. Larger samples are needed to confirm this observation.

We analyzed the mRS in a dichotomized fashion. This discards the full range of outcome information, but does protect against the confounding of mortality analyses by family variations in the decision to withdraw care for critically ill patients with poor prognoses. We did not analyze reperfusion using the Thrombolysis in Myocardial Ischemia Scale, as this scale is not appropriate for the cerebral circulation, as demonstrated by its application in mutually contradictory ways in past cerebral clinical trials.^{16,17} The

AOL scale was specifically developed for the cerebral circulation and has a more stable meaning across studies. Despite similar overall rates of recanalization between groups, it is still possible that the combination of deep MCA field injury and successful reperfusion may contribute to HT and subsequently poor outcome in the subset of M1a patients with good reperfusion. We intend to further investigate the M1a population for any relationship between reperfusion, HT, and clinical outcome. From the variable permeability perspective, it is possible that the natural history of the M1a cohort may be better than the clinical course after successful reperfusion because of less HT and subsequent clinical deterioration.

Our small sample sizes may have prevented the detection of any subtly increased resistance to thrombectomy in the M1a group's occlusions. Although good target recanalization rates were similar in both groups, others have shown that the more proximal the MCA occlusion, the less likely it is to recanalize.¹⁸ Because the M1a pattern is merely a preintervention MRI that represents a terminal ICA or very proximal M1 thrombus, it may predict poor outcome solely attributable to a potential association with higher rates of residual occlusion, an independent risk factor for postthrombotic sICH,¹⁹ and persistent postthrombectomy DWI–PWI mismatch.²⁰

There were several aspects of the pre- and postintervention radiographic data that were not analyzed in our comparison. We did not correlate the angiographic absence of contrast opacification of the LSA with the M1a subtype MR pattern, nor did we assess the angiographic collateral grade, which has been shown to influence tissue fate, both in the presence and absence of thrombolytic therapy.^{21,22} We also did not compare the preintervention perfusion mismatch volume, the postintervention infarct core volume, or the final infarct volume at 30 days which may have more impact on the functional disability and rehabilitative potential of the patient than the preintervention infarct volume and location.^{23,24}

Hyperglycemia is an independent risk factor for poor outcome after ischemic stroke and for HT after thrombolysis,^{25,26,27} possibly because it serves as a marker of longstanding microvascular damage.^{28,29} In our comparisons of peak and mean glucose levels in the immediate 72 hours after stroke, there was no relationship between HT and higher blood glucose levels. Hyperglycemia may have less of an impact on HT in embolectomy-treated cases. Alternatively, we may have been underpowered to detect a bivariate relationship between HT and higher blood sugar levels.

Admittedly, several other postintervention clinical aspects that have an independent impact on outcome were beyond the scope of our study, namely systolic blood pressure and temperature after intervention.^{30,31,32} Our study also does not describe longer-term clinical outcome. Because this study only compared the immediate hospital discharge outcomes and disability, these findings are not applicable to long-term morbidity and mortality. We intend to study whether the predictive value of the M1a MRI pattern has long-term applicability as well.

We are not proposing that patients with the M1a preintervention MRI pattern be denied mechanical thrombectomy as a treatment option. Only a randomized trial can determine whether this pattern predicts lack of benefit from treatment. However, our study confirms that it is a poor prognostic indicator that can inform family discussions about patient prognosis. One should bear this in mind when reviewing previous stroke treatment data, as uneven distribution of M1a patients may have affected study outcome, and it should be considered in future acute stroke trial designs.³³ The modified natural history of occlusions after thrombectomy of M1 or ICA terminus occlusions cannot be compared without attention to this preintervention MRI pattern. In future trials, classifying placebo and treated patients according to this scheme is essential to further compare the natural history of the M1a cohort with that after successful recanalization.

Summary

The preintervention diffusion MRI pattern of deep MCA territory basal ganglionic and white matter compromise with hemispheric cortical penumbra predicts worse outcome, neurological function and disability, and longer hospital stays. Patients with this pattern have worse neurological function before any intervention and may be prone to hemorrhage after intervention. Future clinical studies of acute MCA or ICA terminal thrombectomy should account for such preintervention MRI patterns.

Disclosures

All authors are or have been employees of the University of California, which holds several patents on retriever devices for stroke. Dr Duckwiler is a Scientific Advisor for and shareholder in Concentric Medical, Inc. Dr Liebeskind is a consultant for Concentric Medical. Dr Starkman has received grant funding for clinical trials from Concentric Medical, and Genentech Inc. Dr Saver is a scientific consultant for CoAxia, Concentric Medical, Talecris, Ferrer, AGA Medical, BrainsGate, PhotoThera, and Cygnis; has received lecture honoraria from Ferrer and Boehringer Ingelheim; received support for clinical trials from Concentric Medical; and is a site investigator in multicenter trials sponsored by AGA Medical and the NIH for which the UC Regents received payments based on the number of subjects enrolled.

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