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Thrombus Localization with Emergency Cerebral CT

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Purpose: To determine the prevalence of the hyperdense middle cerebral artery sign (HMCAS) in an acute stroke population (treated with intravenous tissue plasminogen activator (tPA) within 90 minutes of stroke onset); to correlate the presence/absence of the sign with arteriographic findings; and to correlate the HMCAS with the volume of subsequent infarction. **Patients and Methods:** 55 patients wtih acute ischemic stroke underwent CT to exclude cerebral hemorrhage and were then treated with intravenous tPA. The neuroradiologist, blinded to the clinical and arteriographic data, sought the HMCAS on the initial and subsequent scans. **Results:** The HMCAS was detected by CT in 19 of 55 (34.5%) patients (one false positive). Arteriograms in 14 of the 18 true positive patients confirmed the CT-predicted middle cerebral artery segment in 12. The 18 patients developed infarcts larger than patients not exhibiting the sign (132 cc vs 52 cc, $P < .002$). **Conclusion:** The HMCAS does predict middle cerebral artery occlusion and subsequent development of a large infarct.

Index terms: Arteries, cerebral, middle (MCA); Brain, infarction; Arteries, stenosis and occlusion

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The hyperdense middle cerebral artery sign (HMCAS) on computed tomography (CT) has been shown to be a marker for thrombus in the middle cerebral artery (MCA) (1–3). In two previous stroke therapy studies, six patients exhibiting the sign (HMCAS+ patients) developed larger infarcts, on average, than 44 patients not exhibiting the sign (HMCAS− patients) (4). Based on those observations, we hypothesized that the sign might occur frequently enough in an acute stroke population to allow some prediction of infarct volume. Furthermore, the sign might hold promise as a marker to predict patterns of response to thrombolytic therapy, including such adverse effects as hemorrhagic transformation (5, 6) in successfully recanalized vessels (7). If the HMCAS can offer this information, its status would be elevated from an observational curiosity to a useful clinical tool.

The purpose of this study was: 1) to determine the prevalence of the HMCAS in an acute stroke population; 2) to correlate the presence or absence of the sign with subsequent arteriographic findings where possible; and 3) to correlate the HMCAS with the volume of subsequent infarction.

Methods

Fifty-five patients with acute ischemic stroke had a CT scan to exclude cerebral hemorrhage and then were treated with intravenous tPA within 90 minutes of symptom onset. The tPA was administered over 60–90 minutes according to a dose-escalation design, and, accordingly, some patients received low doses and others received higher doses (mean dose 57.96 mg; interquartile range 45–70 mg). Patients were excluded from the study (8) if they were patients older than age 80, had severe hypertension, were using anticoagulants, or had only an isolated sensory deficit or ataxia. Patients were not excluded on the basis of the presumed ischemic stroke type (eg, Lacunar stroke patients were eligible), but those with only a sensory deficit or with isolated ataxia were excluded. The neuroradiologist, blinded to clinical and arteriographic data, sought the HMCAS on the initial scan, and examined subsequent scans for its

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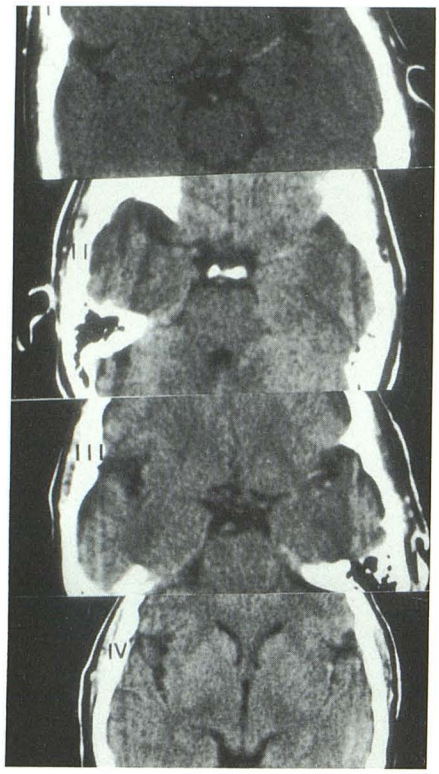


Fig. 1. CT categories I-IV on the left, from above downward, in patients 19, 13, 9, and 5, respectively.

persistence or disappearance. The initial scans were performed with a slice thickness of 10 mm in 39 patients, with 9 mm in one patient, with 8 mm in nine patients, and with 5 mm in six patients.

The HMCAS (MCA denser than its counterpart, and denser than any visualized artery or vein), was categorized according to the most proximal MCA segment thought to be involved on CT: CT category I, proximal M_1 segment; CT category II, distal M_1 or M_1-M_2 junction; CT category III, multiple M_2 segments; CT category IV, single M_2 segment (Figs. 1, 2A, 3A, 4A, and 5A). Subsequent arteriograms were examined for thromboembolism, and the segments of vessel occlusion were classified, modified according to the method of Saito: pattern 1, proximal MCA (M_1) occlusion; pattern 2, MCA trunk (M_1) distal to lenticulostriate arteries; pattern 3, two or more M_2 segment occlusions; pattern 4, single M_2 occlusion; pattern 5, single or multiple M_4 occlusions (9).

Infarct/edema volumes in surviving patients were measured using a pen-trace technique (10) on subsequent scans at 18–24 hours, 7–10 days, and 3 months (Fig. 6). Clinically, the subjects were examined neurologically with a standardized examination scale (NIH Stroke Scale) (11) prior to tPA treatment and six times following the initiation of treatment, including at seven days.

Statistical analysis was performed with nonparametric techniques, including the Wilcoxan rank sum test.

Results

The HMCAS was present in 19 patients (Table 1). One of the determinations was falsely positive, being localized to the hemisphere contralateral to the clinically involved hemisphere and the angiographically-identified M_1 thrombus. The mean infarct volume in the 18 true-positive HMCAS was 134 cc (interquartile range 78–218 cc). The mean infarct volume in the HMCAS− was 52 cc (interquartile range 0–46 cc). This difference is statistically significant ($P < .002$).

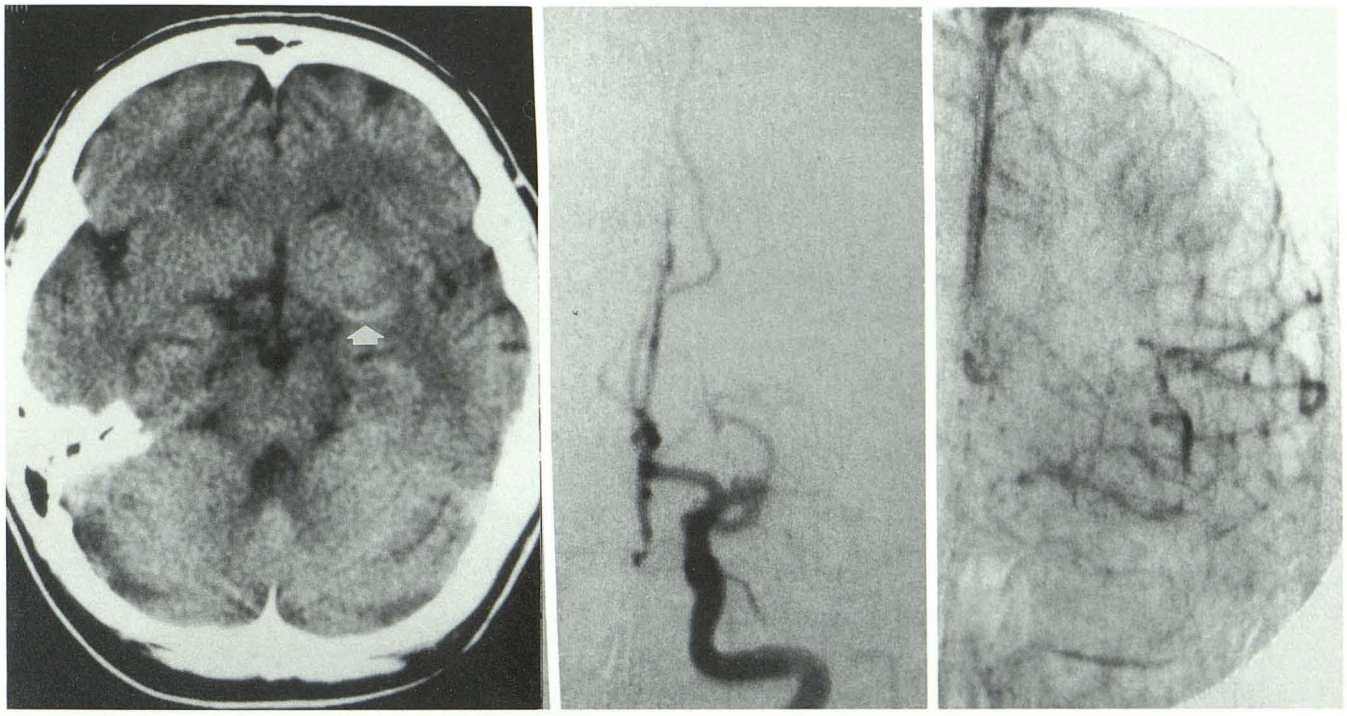
Table 2 summarizes infarct volumes according to CT category of MCA segment involved. Mean volumes were generally higher the more proximal the MCA segment involved, but statistical correlation could not be established.

Table 3 summarizes arteriographic correlation in the 14 HMCAS+ patients who underwent cerebral arteriography. Perfect correlation (presence of occlusion on arteriogram in the exact segment of MCA predicted) was present in 12/14 arteriograms performed a mean 2.2 days (range 1–7) post-treatment. Table 4 summarizes data on 24 arteriograms performed in 37 HMCAS− patients that exhibited: two vertebral and one basilar artery occlusion; two internal carotid artery (ICA) occlusions extending into the M_1 and M_3 segments, respectively; one embolic proximal M_1; four distal M_1; two M_2; and five M_4 occlusions.

Discussion

The prevalence of the HMCAS in this study was 34.5% (19/55). As previously shown, identification of the HMCAS by CT is a subjective exercise that lacks universal agreement. The specificity and positive predictive value have been shown to be high despite lack of total interobserver agreement (12). Certain individual case-examples provide clear, unequivocal evidence of thromboembolism.

Arteriographic correlation was obtained in 38 patients, including 14/18 true-positive HMCAS+ patients. Arteriographic occlusion correlated with HMCAS+ CT category in 12/14 arteriograms (Table 3). One discrepancy occurred in a CT category IV patient whose arteriogram on day 5 exhibited M_4 emboli, while her 7-day CT exhibited infarction, including the lenticulostriate distribution. The other exception occurred in a CT category I patient who exhibited distal M_1 narrowing and M_2 occlusions on day 3. It is postulated that the more proximal embolus suspected on CT



A B C

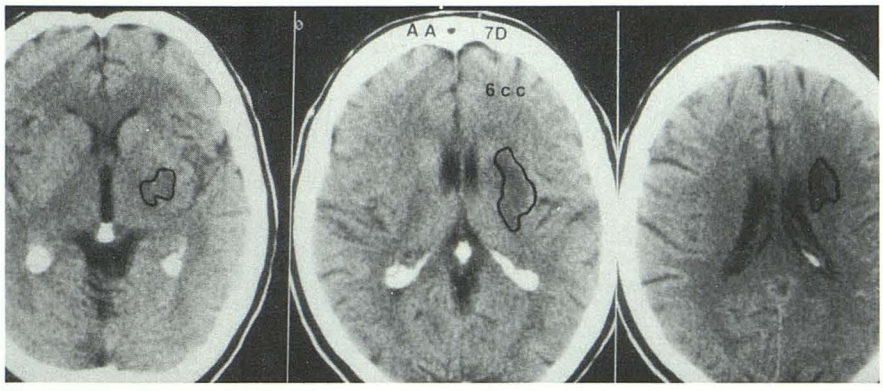


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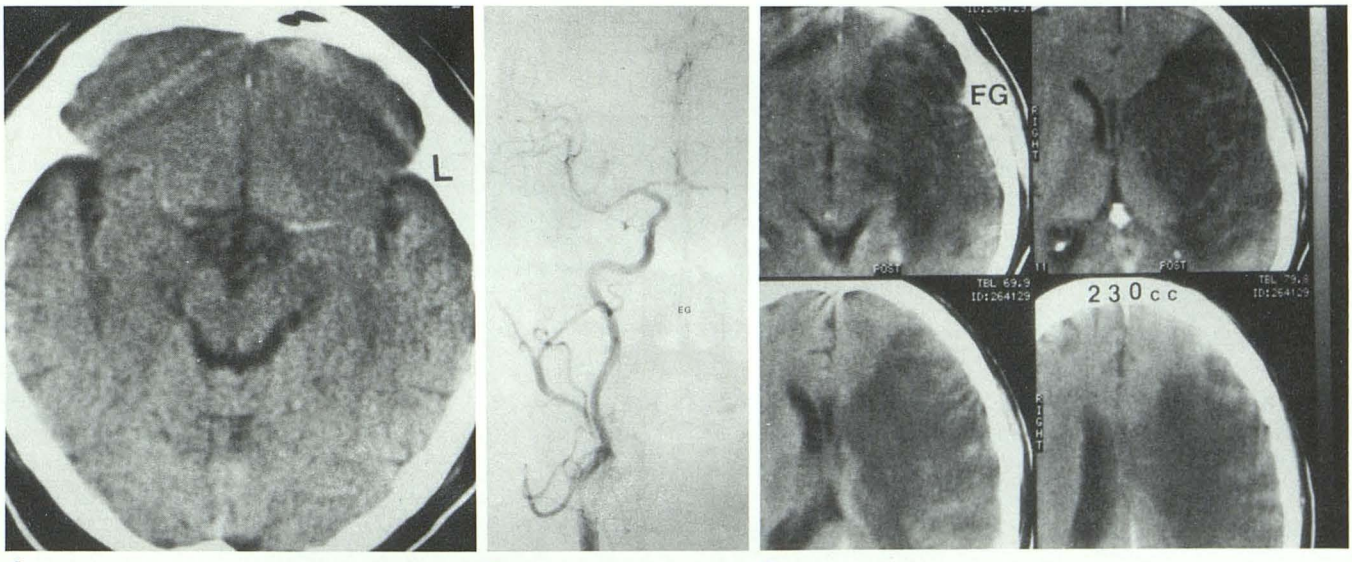
Fig. 2. *A*, CT category I HMCAS (*arrow*) on the left (patient 14).

B, Pattern 1 occlusion of proximal M_1 segment.

C, Corticocortical collaterals fill the M_2 segments within 5 sec.

D, Seven-day infarct in the lenticulostriate distribution of 6 cc.



A B C

Fig. 3. *A*, CT category I HMCAS on left (patient 3).

B, Anteroposterior RCC arteriogram documents poor collateral flow into the occluded MCA-ICA system at 24 hr.

C, Seven-day infarct of 227 cc.

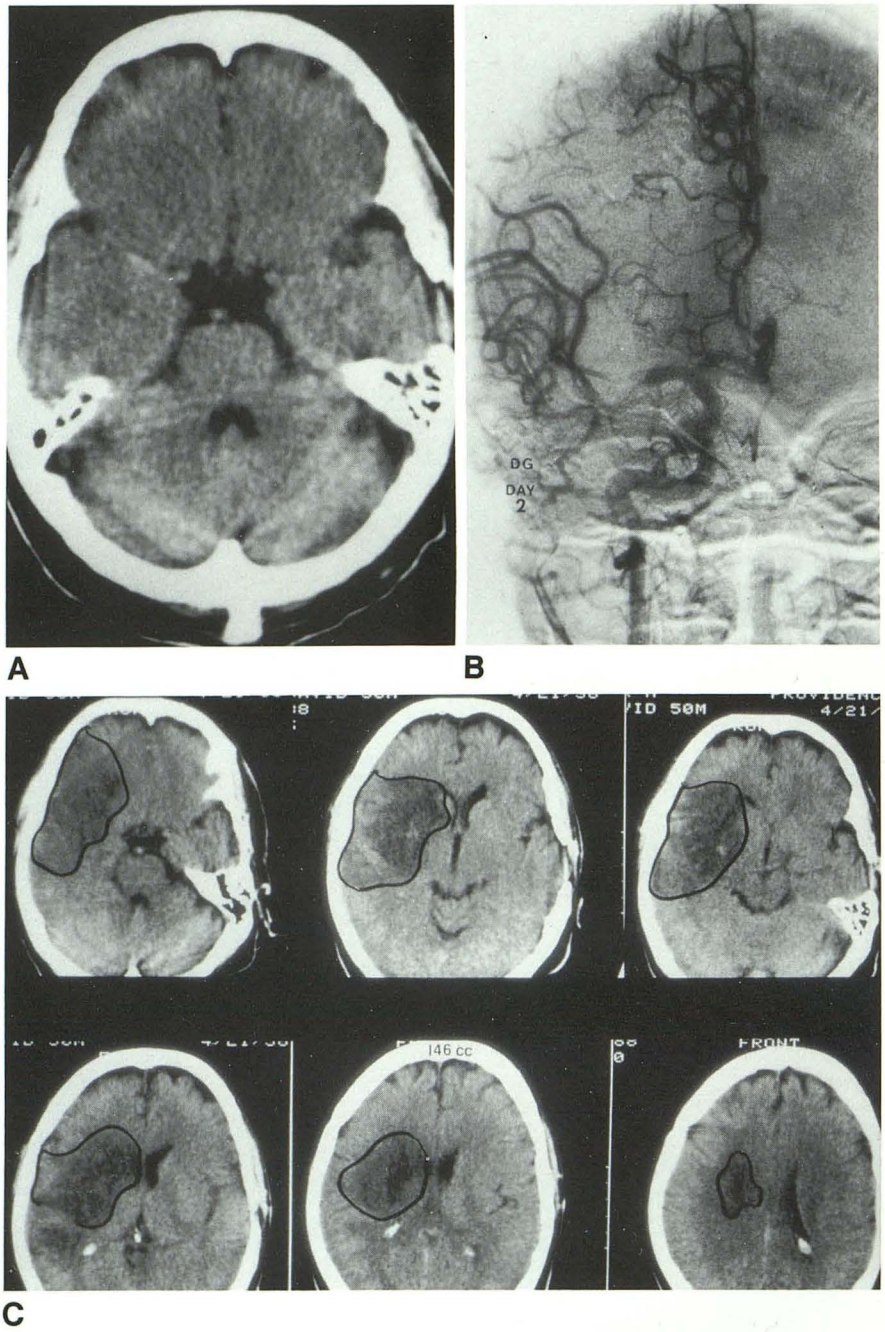


Fig. 4. *A*, CT category II HMCAS on right (patient 10).

B, Anteroposterior RCC arteriogram shows near complete distal M_1 occlusion, extending into M_2 segments, on day 2. Some lenticulostriate branches opacify, while others are occluded.

C, Seven-day infarct volume of 146 cc includes the lenticulostriate distributions, with minimal petechial hemorrhagic change.

either lysed or passed distally prior to arteriography in both these patients.

Of the 24 HMCAS− patients who underwent arteriography, seven showed no intracranial occlusion, and three had vertebrobasilar occlusions. Thus proven thrombi/emboli in the MCA of 14 patients evaded CT detection. Therefore the negative predictive value of an absent HMCAS in excluding MCA thrombus is low (10/24 = 41.6%). Mean CT infarct volume of 14 HMCAS− patients with proven MCA occlusive disease was 50 cc (range 0–313 cc).

The frequencies of arteriographically documented ICA occlusion (7/38, 18.4%) and MCA occlusion (21/38, 55.2%) in all patients who underwent arteriography are within the range of occurrence in other stroke studies (7, 13, 14, 15).

The presence of the HMCAS does predict development of a large infarct with few exceptions, despite treatment with intravenous tPA. CT category I (proximal M_1) involvement predicted an infarct of 100 cc or greater in eight of nine patients. Infarct patterns involved the central

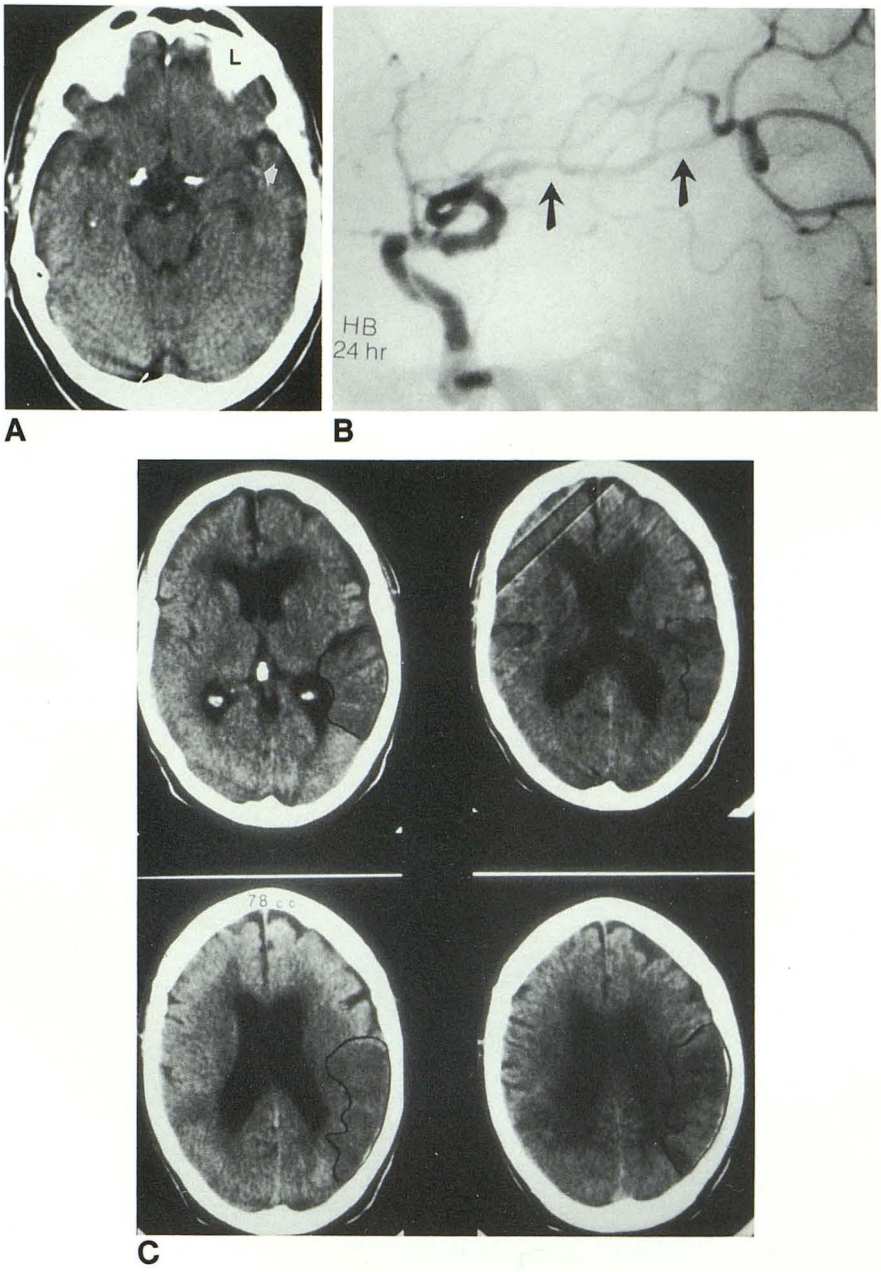


Fig. 5. *A*, CT category IV HMCAS on left (*arrow*) (patient 23).

B, Recanalizing occlusion in angular artery (*arrows*) at 24 hr.

C, Seven-day infarct = 78 cc.

basal ganglia region in all patients, indicating lenticulostriate-distribution occlusion, and infarct patterns involved the cortical regions, indicating cortical branch-distribution involvement with inadequate cortical collaterals, in eight of nine patients. The smallest infarct (6 cc) developed in a patient with an M_1 embolus and excellent corticocortical anastomoses from both the anterior cerebral artery and posterior cerebral artery (Fig. 2). The largest infarct occurred in a patient with ICA occlusion extending into the M_1 segment and poor corticocortical anastomoses (Fig. 3). Positive correlation of arteriographic findings with infarct location and size has been previously noted (9, 16).

CT category II (distal M_1-M_2 junction) involvement in four patients also presaged a large infarct (124-cc mean volume, range 27–282 cc). Again infarct volume was smallest with incomplete M_1 occlusion, combined with good distal corticocortical anastomosis (Figs. 1 and 4).

CT category III (multiple M_2) involvement occurred in only one patient, but the volume of 130 cc is virtually identical to the CT category II (distal M_1) mean volume (Figs. 1 and 6). Four CT category IV patients developed mean infarct volume

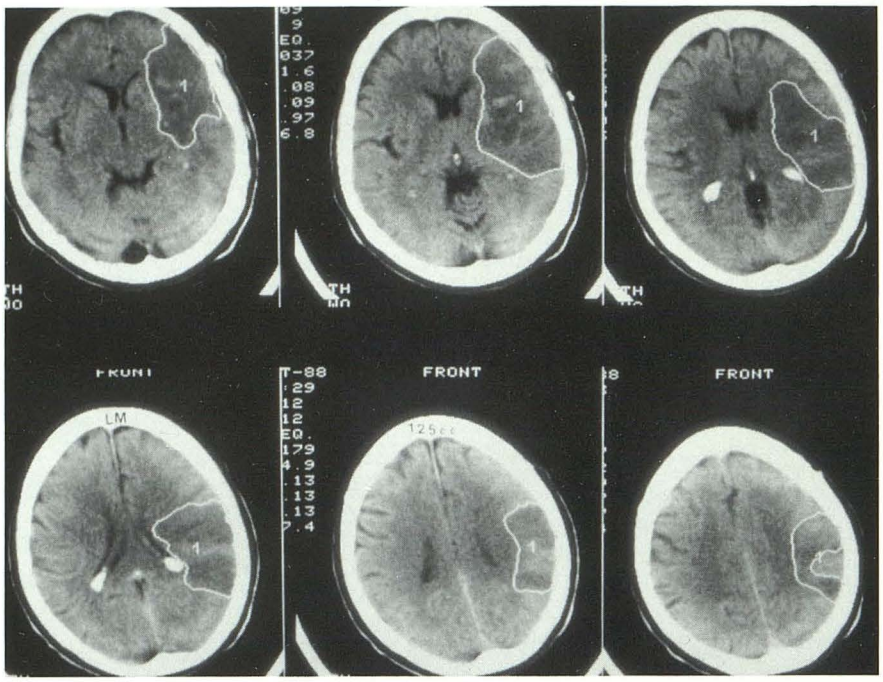


Fig. 6. CT category III patient 29 (Fig. 1), demonstrates 7-day volume = 130 cc, with petechial hemorrhagic change.

TABLE 1: 7-Day infarct volume and arteriographic findings in 19 HMCAS patients

Patient	Scan Section Thickness	7-Day Infarct Volume (cc)	Pattern Arteriographic Occlusion	Arteriogram Day
1. SB	10	287	N/A	N/A
2. MP	10	64	4	5
3. EG	10	227	ICA+ 1	7
4. MM	10	125	ICA+ 3	2
5. WS	10	78	2	5
6. JV	10	218	2	2
7. JB	10	78	3	1
8. NE	8	285	N/A	N/A
9. LM	8	130	3	1
10. DG	8	146	2	2
11. SC	10	43	ICA+ 3	1
12. JP	10	148	ICA+ 1	1
13. NC	5	26	N/A	N/A
14. AA	10	6	1	1
15. WH	10	241	N/A	N/A
16. AB	10	85	4	1
17. JC[a]	8	8	1	1
18. VB	5	113	ICA+ 1	1
19. AE	8	112	3	1

Note.—Outline of patient population: CT slice thickness; infarct volume within 7 days; pattern of arteriographic occlusion (ICA = internal carotid artery occlusion; 1 = M_1 proximal; 2 = M_1 distal to lenticulostriates; 3 = multiple M_2; 4 = single M_2; 5 = distal M_3, M_4; PCA = posterior cerebral artery); arteriogram day (N/A = no arteriogram).

[a] False+: HMCAS suspected on side opposite MCA occlusion.

of approximately half that of CT category III, as might theoretically be expected (Figs. 1 and 5). Therefore, a predictable pattern of infarct volumes do occur depending on the MCA segment involved (Table 2), as well as on the collateral flow.

This analysis suggests that the relatively frequent HMCAS correlates with arteriographic findings and is associated with development of large infarcts despite tPA therapy, volumetrically predictable based on identification of the MCA segment involved on CT. That such excellent angio-

TABLE 2: Summary of mean and range volumes of infarct/edema at 7–10 days in each HMCAS category

Category	Number	Mean Volume (cc)	Range (cc)
I	9	164	6–287
II	4	124	27–282
III	1	130	0
IV	4	76	64–85

TABLE 3: Arteriographic correlation indicating the number of arteriograms performed in each CT category and the number confirming the CT-predicted location of the filling defect

CT Category	No. of Arteriograms	Correlation
I	7	6
II	2	2
III	1	1
IV	4	3

TABLE 4: Arteriographic findings in 24 arteriograms performed in 37 HMCAS-patients

MCA occlusion	
Pattern 1 and ICA occlusion	1
Pattern 3 and ICA occlusion	1
Pattern 1	1
Pattern 2	4
Pattern 3	1
Pattern 4	1
Pattern 5	5
ICA stenosis (dissection)	1
Vertebrobasilar occlusion	3
Normal	6
Total	24

graphic correlation was obtained raises the question that intravenous tPA in doses used may be inefficient in recanalizing occluded cerebral arteries. Other questions that need to be answered regarding the HMCAS and thrombolytic therapy include: Is there any differences between HMCAS+ and HMCAS− patients in their response to treatment? Does the HMCAS, as prima facie evidence of arterial occlusion, predispose to hemorrhagic transformation in the recanalization phase (5)? Several randomized trials of thrombolytic therapy for acute ischemic stroke are underway. The radiographic and clinical comparisons of the treated patients to the control patients may provide some answers.

The concept that an immediate CT finding can help predict infarct size and possibly predict response to therapy has important implications. This might allow selection of a subgroup of stroke patients less likely to achieve a satisfactory outcome with standard therapy, or even with experimental intravenous thrombolysis. The HMCAS combined with an immediate arteriogram to demonstrate inadequacy of collateral flow may indicate the need for more aggressive therapy, such as intraarterial thrombolysis.

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