Early Imaging Prediction of Malignant Cerebellar Edema Development in Acute Ischemic Stroke

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Background and Purpose**—**Malignant cerebellar edema (MCE) is a life-threatening complication of acute ischemic stroke that requires timely diagnosis and management. Aim of this study was to identify imaging predictors in initial multiparametric computed tomography (CT), including whole-brain CT perfusion (WB-CTP).

Methods**—**We consecutively selected all subjects with cerebellar ischemic WB-CTP deficits and follow-up–confirmed cerebellar infarction from an initial cohort of 2635 patients who had undergone multiparametric CT because of suspected stroke. Follow-up imaging was assessed for the presence of MCE, measured using an established 10-point scale, of which scores ≥4 are considered malignant. Posterior circulation–Acute Stroke Prognosis Early CT Score (pc-ASPECTS) was determined to assess ischemic changes on noncontrast CT, CT angiography (CTA), and parametric WB-CTP maps (cerebellar blood flow [CBF]; cerebellar blood volume; mean transit time; time to drain). Fisher's exact tests, Mann–Whitney U tests, and receiver operating characteristics analyses were performed for statistical analyses.

Results**—**Out of a total of 51 patients who matched the inclusion criteria, 42 patients (82.4%) were categorized as MCE− and 9 (17.6%) as MCE+. MCE+ patients had larger CBF, cerebellar blood volume, mean transit time, and time to drain deficit volumes (all with $P<0.001$) and showed significantly lower median pc-ASPECTS assessed using WB-CTP (CBF, cerebellar blood volume, mean transit time, time to drain; all with $P<0.001$) compared with MCE− patients, while median pc-ASPECTS on noncontrast CT and CTA was not significantly different (both $P>0.05$). Receiver operating characteristics analyses yielded the largest area under the curve values for the prediction of MCE development for CBF (0.979) and cerebellar blood volume deficit volumes (0.956) and pc-ASPECTS on CBF (0.935), whereas pc-ASPECTS on noncontrast CT (0.648) and CTA (0.684) had less diagnostic value. The optimal cutoff value for CBF deficit volume was 22 mL, yielding 100% sensitivity and 90% specificity for MCE classification.

Conclusions**—**WB-CTP provides added diagnostic value for the early identification of patients at risk for MCE development in acute cerebellar stroke. **(*Stroke*. 2017;48:2597-2600. DOI: 10.1161/STROKEAHA.117.018237.)**

Key Words: brain edema ■ perfusion imaging ■ stroke

Malignant cerebellar edema (MCE) is a life-threatening complication that occurs in 10% to 40% of patients with acute cerebellar stroke.[1] MCE requires timely diagnosis because the mass effect causes obstructive hydrocephalus and direct damage to the brain stem. If the brain stem is spared from infarction, patients with MCE development can achieve good outcomes.[2]

The clinical diagnosis of cerebellar stroke is challenging because of nonspecific symptoms overlapping with benign conditions.[1] Early identification of patients at risk for MCE is no less challenging because symptom-based triage has been shown to be inadequate.[3] Imaging provides complementary information, but standard stroke protocols, including noncontrast computed tomography (NCCT) and computed tomography (CT) angiography (CTA), provide insufficient diagnostic accuracy for acute cerebellar stroke and the risk of MCE development.[1]

Contemporary whole-brain CT perfusion (WB-CTP) imaging enables entire brain coverage and provides considerable incremental value compared with NCCT and CTA alone in the detection of acute cerebellar stroke.[4] Moreover, WB-CTP imaging parameters enable to identify stroke patients developing malignant middle cerebral artery (MCA) infarction.[3]

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Therefore, our study aim was to identify imaging predictors in the initial multiparametric CT for MCE development.

Methods

Detailed methods are provided in the online-only Data Supplement.

Study Design

The initial cohort comprised 2635 consecutive patients who had undergone WB-CTP because of suspected ischemic stroke. We included subjects with (1) significant cerebellar perfusion deficits and (2) confirmed cerebellar infarction on follow-up within 72 hours. Main exclusion criteria were (1) basilar artery occlusion, (2)

Table 1. Characteristics of MCE− and MCE+ Patients

	Overall (N=51)	MCE− (n=42)	MCE+ (n=9)	*P* Value
Patient data				
Age	74 (58–81)	72 (55–82)	76 (73–78)	0.818
Male sex	32 (62.7%)	27 (64.3%)	5 (55.6%)	0.447
Time from symptom onset*	135 (105–225)	120 (105–165)	300 (165–735)	0.122
Admission NIHSS*	3 (2–6)	3 (2–6)	4 (3–10)	0.757
NCCT imaging data				
pc-ASPECTS NCCT	10 (9–10)	10 (9–10)	9 (9–10)	0.173
Cerebellar atrophy	21 (41.2%)	19 (45.2%)	2 (22.2%)	0.186
CTA imaging data				
pc-ASPECTS CTA-SI	9 (9–10)	9 (9–10)	9 (7–9)	0.086
VA occlusion	16 (31.4%)	9 (21.4%)	7 (77.8%)	0.002†
VA dissection	4 (7.8%)	3 (7.1%)	1 (11.1%)	0.552
WB-CTP imaging data				
Bilateral ischemia	13 (25.5%)	8 (19.0%)	5 (55.6%)	0.025†
pc-ASPECTS CBF	8 (6–9)	8 (7–9)	5 (3–6)	<0.001†
pc-ASPECTS CBV	9 (8–9)	9 (9–9)	8 (6–8)	<0.001†
pc-ASPECTS MTT	8 (7–9)	8 (8–9)	5 (3–7)	<0.001†
pc-ASPECTS TTD	8 (7–9)	8 (7–9)	5 (2–7)	<0.001†
CBF deficit volume	15 (4–23)	10 (4–18)	54 (35–67)	<0.001†
CBV deficit volume	4 (1–12)	3 (1–6)	23 (18–36)	<0.001†
MTT deficit volume	10 (4–19)	5 (3–15)	35 (17–55)	<0.001†
TTD deficit volume	10 (3–17)	8 (3–15)	39 (19–68)	<0.001†
CBF-CBV mismatch %	64 (40–81)	65 (48–86)	44 (32–66)	0.181
Follow-up imaging data				
Final infarction volume	5 (2–26)	4 (2–10)	53 (42–56)	<0.001†
Brain stem infarction	15 (34.1%)	10 (27.0%)	5 (55.6%)	0.036†
Supratentorial infarction	23 (45.1%)	16 (38.1%)	7 (77.8%)	0.035†
Cerebellar edema score	1 (0–3)	1 (0–2)	6 (6–8)	<0.001†
Functional data				
Admission mRS	3 (2–4)	2 (2–3)	3 (2–5)	0.389
Discharge mRS*	2 (1–5)	2 (1–3)	6 (6–6)	<0.001†
90-day mRS*	3 (1–6)	1 (0–3)	6 (6–6)	<0.001†

Values presented are number (percentage) for categorical and median (interquartile range) for ordinal and continuous variables. Statistical analysis for categorical variables was performed using the Fisher exact test and for ordinal and continuous variables using the Mann–Whitney U test. CBF/CBV indicates cerebellar blood flow/volume; CT, computed tomography; MCE, malignant cerebellar edema; mRS, modified Rankin Scale; MTT, mean transit time; NCCT, noncontrast CT; NIHSS, National Institutes of Health Stroke Scale; pc-ASPECTS, posterior circulation-Acute Stroke Prognosis Early CT Score; TTD, time to drain; VA, vertebral artery; and WB-CTP, whole-brain CT perfusion.

*Missing values: time from symptom onset, 19/51; admission NIHSS, 4/51; discharge mRS, 1/51; 90-day mRS, 17/51.

†*P* values indicate statistical significance.

nonischemic causes for cerebellar perfusion deficits, and (3) incomplete cerebellar coverage.

Definition of MCE

The mass effect of cerebellar infarction was graded using a 10-point score by Jauss et al (cerebellar edema score).[5] MCE was defined as a score of ≥4 as previously described.[2] All available follow-up imaging until discharge was assessed for MCE.

Multiparametric CT Imaging

Early ischemic changes were assessed using the posterior circulation-Acute Stroke Prognosis Early CT Score (pc-ASPECTS) on NCCT, CTA-source images, and parametric WB-CTP maps of cerebellar blood flow (CBF) and cerebellar blood volume, mean transit time, and time to drain. Perfusion deficits on WB-CTP maps were volumetrically assessed.

Statistical Analysis

Analyses were performed in SPSS Statistics 23 (IBM, Armonk, NY). The Fisher exact test was applied for categorical and the Mann–Whitney *U* test for ordinal or continuous variables. Receiver operating characteristic analyses compared the diagnostic performance of clinical and imaging parameters. *P* values <0.05 indicated statistical significance.

Results

Patient Characteristics

Among the study population, 9 patients (17.6%) were classified as MCE+, while 42 patients (82.4%) were classified as MCE− (Table 1 and the Figure for patient examples). No statistically significant differences were present in initial functional status and early ischemic changes on NCCT or CTA-source images (all *P*>0.05). MCE+ patients had worse pc-ASPECT scores and larger perfusion deficit volumes on all WB-CTP parameter maps (all *P*<0.001).

Diagnostic Performance of Clinical and Imaging Parameters for MCE

Clinical parameters on initial presentation and early ischemic changes on NCCT and CTA-source images had no significant diagnostic value for MCE classification in a receiver operating characteristics analysis (all *P*>0.05). In contrast, WB-CTP parameters evaluating early ischemic changes using pc-ASPECTS and hypoperfusion volumes allowed a significant classification of MCE for all WB-CTP parameter maps (all *P*<0.001). The analysis yielded the highest AUC values for CBF deficit volume (0.979), cerebellar blood volume deficit volume (0.956), and pc-ASPECTS CBF (0.935). For the CBF deficit volume, the cutoff value with the highest Youden's Index, indicating the highest discriminative power, was 22 mL (sensitivity, 100%; specificity, 90%). Detailed results are presented in Table 2.

Additional patient characteristics and statistical analyses are provided in the online-only Data Supplement.

Discussion

In this study on acute cerebellar stroke, multiparametric CT, including WB-CTP, allowed for an identification of patients who subsequently developed MCE. The sizes of the CBF and cerebellar blood volume perfusion deficit and pc-ASPECTS CBF were the most accurate predictors. A CBF deficit volume of 22 mL, ≈40% of 1 cerebellar hemisphere, was the diagnostic threshold with the highest combined sensitivity (100%) and specificity (90%).

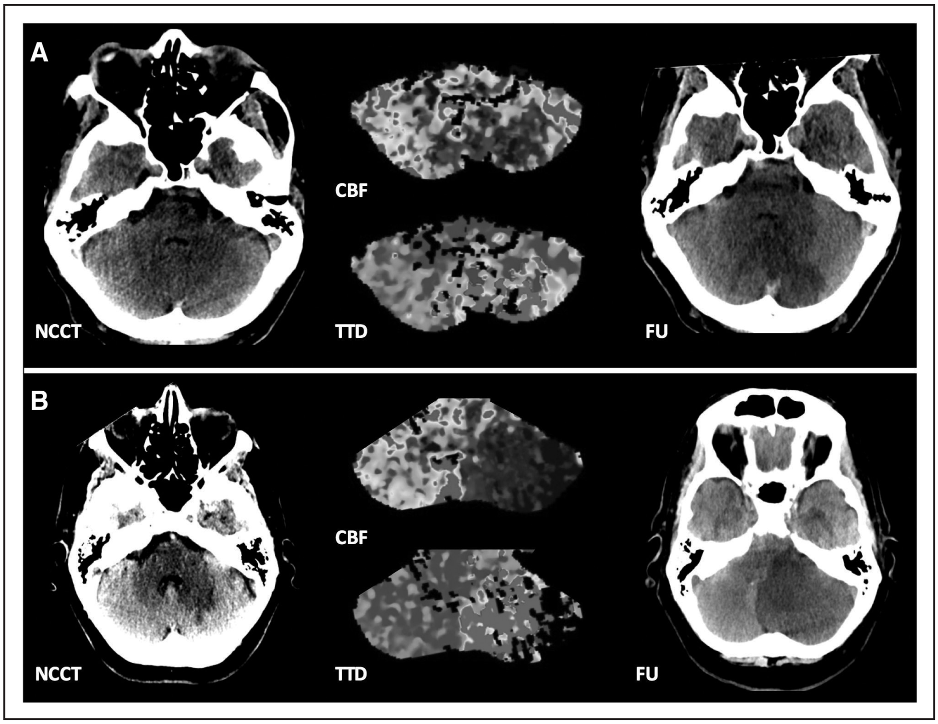

Figure. Examples of MCE− and MCE+ patients. Patient examples of acute cerebellar stroke without (**A**) and with (**B**) subsequent development of malignant cerebellar edema (MCE) on day 3 follow-up imaging (FU). CBF indicates cerebellar blood flow; CT, computed tomography; NCCT, noncontrast CT; and TTD, time to drain.

Table 2. ROC Analysis of Clinical and Imaging Parameters for MCE

	AUC (95% CI)	*P* Value	Youden's Index	Cutoff Value
Admission NIHSS	0.549 (0.256–0.843)	0.748	0.224	13
Admission mRS	0.553 (0.281–0.825)	0.732	0.105	2
pc-ASPECTS NCCT	0.648 (0.448–0.848)	0.166	0.286	9
pc-ASPECTS CTA-SI	0.684 (0.473–0.895)	0.086	0.397	7
pc-ASPECTS CBF	0.935 (0.869–1.000)	<0.001*	0.810	6
pc-ASPECTS CBV	0.898 (0.812–0.984)	<0.001*	0.762	8
pc-ASPECTS MTT	0.929 (0.851–1.000)	<0.001*	0.758	7
pc-ASPECTS TTD	0.905 (0.805–1.000)	<0.001*	0.627	7
CBF deficit volume	0.979 (0.944–1.000)	<0.001*	0.905	22 mL
CBV deficit volume	0.956 (0.895–1.000)	<0.001*	0.841	15 mL
MTT deficit volume	0.862 (0.732–0.993)	<0.001*	0.611	16 mL
TTD deficit volume	0.897 (0.783–1.000)	<0.001*	0.706	19 mL
CBF-CBV mismatch %	0.646 (0.475–0.816)	0.174	0.333	77%

A receiver operating curve (ROC) analysis was performed; the maximum value of the Youden's Index and its associated parameter cutoff value are shown. AUC indicates area under the curve; CBF/CBV, cerebellar blood flow/volume; CI, confidence interval; MCE, malignant cerebellar edema; mRS, modified Rankin Scale; MTT, mean transit time; NCCT, noncontrast CT; NIHSS, National Institutes of Health Stroke Scale; pc-ASPECTS, posterior circulation-Acute Stroke Prognosis Early CT Score; and TTD, time to drain.

**P* values indicate statistical significance.

MCE has been investigated in imaging studies using follow-up NCCT to identify parameters that correlate with the development of brain stem symptoms in the subacute phase.[6] In cerebellar stroke, the only baseline imaging parameter reported to predict MCE is hypodensity of >2/3 of the posterior inferior cerebellar artery territory,[3] which is only observed in a small subset. To date, no further predictive parameters in the admission CT or magnetic resonance imaging examination have been reported for MCE.[1,3]

In MCA stroke, as opposed to cerebellar stroke, previous studies could identify reliable clinical and baseline NCCT and CTA imaging predictors for the occurrence of space-occupying edema, for example, National Institutes of Health Stroke Scale scores ≥15 to 20 or >50% hypodensity of the MCA territory.[7] In contrast, NCCT and CTA were not able to reliably identify patients at risk for MCE development in our study. Yet, lessons learned from MCA stroke also highlight the incremental value of CT perfusion imaging for the prediction of brain swelling.[8,9] In line with our observations in the setting of cerebellar stroke, previous CT perfusion studies in MCA stroke identified larger ischemic lesion volumes, as well as lower CT perfusion-based ASPECTS, as risk factors for edema development.

There are limitations to this study that need to be considered when interpreting the results. First, this is a single-center retrospective study with a limited number of patients. Yet, our study represents the largest cohort of cerebellar stroke analyzed by multiparametric CT to date. Second, only patients with cerebellar perfusion deficits who had undergone WB-CTP were included, thereby, not considering patients with confirmed infarction but unremarkable WB-CTP. However, as WB-CTP has a high sensitivity for cerebellar stroke,[4] large infarcts at risk for MCE development were unlikely to be missed. Moreover, all patients were recruited from a prospectively collected registry with standardized imaging protocols. Third, manual volumetric assessment of the perfusion deficits was applied because no quantitative thresholds for cerebellar stroke are established.

In conclusion, initial multiparametric CT has a considerable diagnostic value for the early identification of cerebellar stroke patients at risk for MCE development.

Disclosures

None.

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