ORIGINAL ARTICLE

Immediate CT change after thrombectomy predicting symptomatic hemorrhagic transformation

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Abstract

Background: The prognostic value of contrast accumulation from noncontrast brain computed tomography (CT) conducted immediately after intra mechanical thrombectomy (MT) in patients with acute ischemic stroke to predict symptomatic hemorrhage was studied.

Methods: Patients with acute ischemic stroke treated using MT between February 2015 and April 2019 were included. Contrast accumulation was defined as a high attenuation area observed on noncontrast brain CT conducted immediately after thrombectomy treatment, and the patients were categorized into (1) symptomatic hemorrhage, (2) asymptomatic hemorrhage, and (3) no hemorrhage according to the presence of hemorrhagic transformation and their clinical conditions. The pattern and extent of contrast accumulation were compared between patients with and without symptomatic hemorrhage. The maximal Hounsfield unit (HU) of cortical involvement in contrast accumulation was evaluated by calculating the sensitivity, specificity, odds ratio, and area under the receiver operating characteristic (ROC) curve.

Results: In total, 101 patients with anterior circulation acute ischemic stroke were treated by endovascular intervention. Nine patients developed symptomatic hemorrhage and 17 developed asymptomatic hemorrhage. Contrast accumulation was associated with all types of hemorrhagic transformation ($p < 0.01$), and cortical involvement pattern was more frequently associated with symptomatic hemorrhage ($p < 0.01$). The area under the ROC curve was 0.887. The sensitivity and specificity for HU > 100 in cortical involvement predicting symptomatic hemorrhage after endovascular treatment were 77.8% and 95.7%, respectively, with an odds ratio of 77.0 (95% CI, 11.94-496.50; $p < 0.01$).

Conclusion: Cortical involvement of contrast accumulation with a maximal HU > 100 predicts symptomatic hemorrhage after endovascular reperfusion treatment.

Keywords: Computed tomography; Hemorrhagic transformation; Mechanical thrombectomy; Stroke

1. INTRODUCTION

Mechanical thrombectomy (MT) has become an effective standard treatment for acute ischemic stroke (AIS) caused by large vessel occlusion (LVO).[1,2] However, reperfusion injury is the main complication of concern after the procedure, which may cause intracranial hemorrhage (ICH) and is associated with severe neurological deterioration.[3] Either hemorrhagic or transient contrast extravasation is frequently observed on noncontrast brain computer tomography (CT) after intra-arterial intervention. It is critical to distinguish these two imaging phenomenons.[3] A few studies have indicated that contrast extravasation with a hyperdense lesion with a maximum Hounsfield unit (HU) measurement >90 on the immediate brain CT after an intra-arterial intervention is highly associated with the occurrence of parenchymal hematoma.[4–6]

Yoon et al[6] assumed that contrast accumulation is associated with disruption of the blood-brain barrier,[5] and the patterns of contrast accumulation may differ between patients with and without further symptomatic ICH. In the current study, we evaluated the prognostic value of contrast accumulation in brain CT or magnetic resonance imaging (MRI) taken immediately after an MT for AIS, focusing on its location, distribution, and density to predict the onset of symptomatic ICH complications.

2. METHODS

2.1. Patient selection

Between February 2015 and April 2019, AIS patients who had just undergone MT were eligible to be included. When AIS

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patients were admitted to the emergency department, endovascular treatment was considered when the symptom onset was within 8 hours. Stroke patients with anterior circulation occlusion were also included, and their basic demographic and clinical data were reviewed. Vascular risk factor profile, blood test results, initial stroke severity in the National Institutes of Health Stroke Scale (NIHSS), and reperfusion treatment modalities were reviewed.

2.2. Imaging protocol and procedures

All patients underwent MR angiography using GE 1.5T or 3.0T scanner (Signa HDx; GE Healthcare, Milwaukee, WI, USA) with an eight-channel head-coil and with the following parameters: Spoiled gradient-echo sequence with TR/TE/FA, 24 msec/2.7 msec/20°; FOV/Matrix, 180 mm/384 × 224; slice thickness/slice overlap, 1.2 mm/50%; ASSET factor, 2; and actual bandwidth, 31 KHz. Endovascular recanalization treatment was performed using (1) stent retriever (Solitaire FR: ev3, Irvine, CA, USA), (2) aspiration thrombectomy (Penumbra system, Alameda, CA, USA), or (3) both stent retriever and aspiration techniques. Noncontrast brain CT (120 kVp, 140 mA, 5.0 mm section thickness) was performed immediately after the intra-arterial procedure and before transferring the patient to the intensive care unit. All patients took follow-up brain imaging 24 hours after the intervention, either brain CT or MRI (including susceptibility-weighted imaging depending on the patient status and decision of the attending physician).

2.3. Imaging analysis

The occluded vessels were determined by initial brain MR angiography. Angiographic successful recanalization was defined as complete or partial recanalization based on the modified Treatment in Cerebral Infarction (mTICI) scale. Cases suffering from significant intraprocedural contrast extravasation (ie, during contrast medium injection by hand push or injector, contrast medium leakage out of intracranial arteries can be observed during the procedure. It reflects the injury of arteries and iatrogenic brain hemorrhage, whether subarachnoid hemorrhage [SAH] or ICH) were excluded.

Cerebral hemorrhage, the major intracranial procedural complication, was classified according to the European Cooperative Acute Stroke Study (ECASS) criteria.[7] Symptomatic ICH is defined as any PH1, PH2, RIH, SAH, or intraventricular hemorrhage associated with a decline in NIHSS score 4 within 24 hours. PH1 indicates hematoma within an ischemic field with some mild pace-occupying effect but involving 30% of the infarcted area; PH2 indicates hematoma within an ischemic field with space-occupying effect involving 30% of the infarcted area; RIH indicates any intraparenchymal hemorrhage remote from the ischemic field. Immediate brain CT morphology was classified into one of the following five groups according to its presence and location: (1) negative, when contrast accumulation was absent; (2) cortical involvement (CO) with HU > 90, when contrast accumulation involved the cortex with HU > 90; (3) CO with HU > 100, when contrast accumulation involved the cortex with HU > 100; (4) noncortical involvement (NC) with HU > 90, when contrast accumulation presented with high attenuation region with a HU > 90 but not involving the cortex; and (5) NC > 100, when contrast accumulation presented with high attenuation region with a HU > 100 but not involving the cortex. Two radiologists independently performed the imaging analysis, and a neuroradiologist solved any discrepancy between the two. In the follow-up brain image, hemorrhage was defined as newly found high-density accumulation in brain CT and black spots accumulation visible in brain MRI SWI sequence.

2.4. Statistical analysis

The inter-rater agreement for discrimination between the symptomatic hemorrhage and the nonsymptomatic hemorrhage groups was calculated using the multirater J statistic. Statistical analyses between symptomatic hemorrhage and nonsymptomatic hemorrhage groups were performed using the Pearson's chi-square tests for dichotomous variables. Sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of the contrast accumulation findings in immediate CT in the prediction of symptomatic hemorrhage after thrombectomy were also calculated. Multiple logistic regressions with forward selection were concluded to include essential predictors of the disease. All statistical analyses were performed using SPSS version 24.0 (SPSS, Chicago, IL, USA). A p value < 0.05 was determined as statistically significant.

3. RESULTS

A total of 139 patients were treated by MT, among which 101 with anterior circulation stroke were included in the current study. All included patients were followed by noncontrast brain CT immediately after the intra-arterial reperfusion treatment. Contrast accumulation at this post-procedure immediate brain CT was detected in 42 patients (41.6%), including 18 patients with CO > 90 pattern (17.8%), (including 13 patients with CO > 100 pattern [12.9%]); 24 patients with NC > 90 pattern (23.7%) (including 20 patients with NC > 100 pattern [19.8%]) in terms of contrast accumulation location and densities.

Twelve cases received brain CT, and 89 cases received brain MRI in 24 hours after treatment. Symptomatic hemorrhage occurred in 9 patients (8.8%) and asymptomatic hemorrhage

Table 1

Analysis of factors associated with symptomatic hemorrhage

Patient characteristics	Symptomatic hemorrhage (+), N (%)	Symptomatic hemorrhage (−), N (%)	*p*
Number of patients	9	92	
Age > 70	3 (33.3)	49 (53.3)	0.254
Female patients	4 (44.4)	48 (52.2)	0.658
Intravenous thrombolysis	4 (44.4)	36 (39.1)	0.756
Hypertension	4 (44.4)	41 (44.6)	0.994
Diabetes mellitus	3 (33.3)	18 (19.6)	0.331
Previous stroke	1 (11.1)	11 (12)	0.940
ESRD	0 (0.0)	4 (4.3)	0.523
Heart failure	2 (22.2)	7 (7.6)	0.142
Cardioembolic source	4 (44.4)	52 (56.5)	0.487
Dyslipidemia	1 (11.1)	22 (23.9)	0.382
Cancer history	1 (11.1)	11 (12)	0.940
Coronary artery disease	1 (11.1)	11 (11.9)	0.940
mTICI 3	8 (88.9)	64 (69.6)	0.221
Initial NIHSS > 20	4 (44.4)	39 (39)	0.905
Cortical contrast accumulation HU > 90	8 (88.9)	10 (10.9)	<0.01[a]
Cortical contrast accumulation HU > 100	8 (88.9)	5 (5.4)	<0.01[a]
Non cortical contrast accumulation HU > 90	1 (11.1)	23 (25.0)	0.350
Non cortical contrast accumulation HU > 90	0 (0.0)	20 (21.7)	0.118

ESRD = end-stage renal disease; HU = Hounsfield unit; mTICI = modified Treatment in Cerebral Infarction; NIHSS = National Institute of Health Stroke Scale.

[a]statistically significant.

Table 2

Sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of contrast accumulation findings in predicting symptomatic hemorrhage

CT finding	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	Accuracy (%) (95% CI)	Positive predictive value (%) (95% CI)	Negative predictive value (%) (95% CI)
Cortical contrast accumulation HU > 90	88.9 (51.7-99.7)	89.1 (80.9-94.6)	89.1 (81.3-94.4)	44.4 (29.9-60.0)	98.8 (92.8-99.8)
Cortical contrast accumulation HU > 100	88.9 (51.7-99.7)	94.6 (87.8-98.2)	94.1 (87.5-97.8)	61.5 (39.8-79.5)	98.9 (93.2-99.8)

The 95% CI was calculated by Clopper-Pearson method.
CT = computed tomography; HU = Hounsfield unit.

Table 3

Results of multiple logistic regressions with forward selection to include significantly important predictors of symptomatic hemorrhage

Variable	Odds ratio (95% CI)	*p*
Cortical contrast accumulation HU > 100	139.20 (14.4-1341.9)	<0.01

HU = Hounsfield unit.

in 17 patients (16.5%). Table 1 illustrates the factors associated with symptomatic hemorrhagic transformation after endovascular treatment. Intravenous (IV) thrombolysis treatment, risk factors, initial NIHSS and laboratory variables showed no differences between the symptomatic hemorrhage and nonsymptomatic hemorrhage groups. Contrast accumulation with cortical involvement has a higher incidence of symptomatic hemorrhage after thrombectomy ($p < 0.01$). Table 2 shows the sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio for CO > 90 and CO > 100 in predicting symptomatic hemorrhage. CO > 100 pattern independently predicted symptomatic hemorrhage with an odds ratio of 139 (95% CI, 14.4-1341.9; $p < 0.01$) (Table 3). The AUC was 0.887 (Fig. 1).

4. DISCUSSION

In the context of thrombectomy therapy in acute stroke, contrast accumulation has been reported with a wide variation between 20% and 80% in the study populations.[5,6,8] The clinical significance and physiopathology of these lesions were first described in 1994 by Wildenhain et al[9] in six patients. They noticed that the

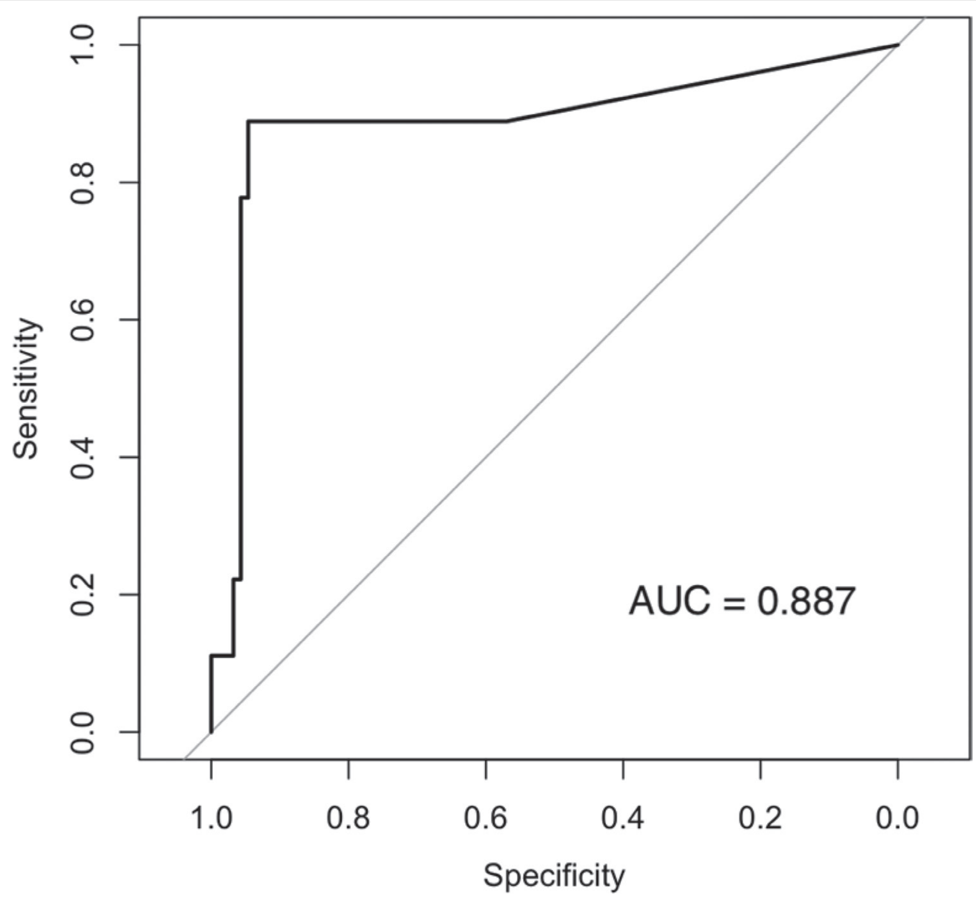

Fig. 1 ROC curve of cortex HU and symptomatic hemorrhage. AUC = area under the curve; HU = Hounsfield unit; ROC = receiver operating characteristic.

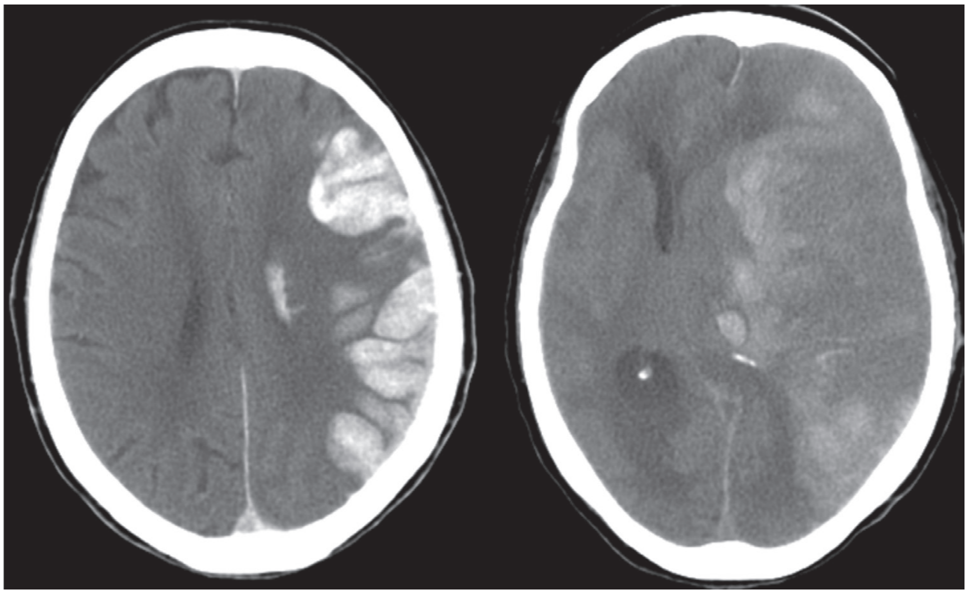

Fig. 2 An 82-y-old female with left distal ICA acute occlusion underwent endovascular thrombectomy. The immediate brain CT after the procedure showed contrast accumulation (HU > 100) at left frontal and parietal cortical area. Pupil dilatation was noted 20h after the procedure. Brain CT showed prominent hemorrhagic transformation and diffuse swelling, which causing rightward midline shifting. The hemorrhagic transformation did not locate at specific location. CT = computed tomography; HU = Hounsfield unit; ICA = internal carotid artery.

density of the lesions might be secondary to hemorrhage and/or contrast extravasation and suggested a possible relation between the image findings and clinical prognosis. Nakano et al[8] concluded that contrast accumulation is a significant risk factor for hemorrhagic transformation after intra-arterial reperfusion treatment. However, the hemorrhagic transformation could be clinically nonspecific. Meanwhile, we did not observe symptomatic hemorrhage in the patients without contrast accumulation in the current study, and this was compatible with the previous study.[8]

The pathophysiology of contrast accumulation after intra-arterial reperfusion therapy is a disruption of the blood-brain barrier and basal lamina by initial ischemic insult, reperfusion injury, and the toxic effect of contrast media or thrombolytic agent.[6,10] With existence of contrast accumulation in an immediate CT, basal ganglia were the most frequently enhanced location because most contrast media injection to evaluate endovascular treatment response is carried out around the origin of the lenticulostriate arteries. Because a contrast accumulation restricted to basal ganglia might not predict symptomatic hemorrhage,[5,6,11] we explored the contrast medium accumulation at the cortex beyond the basal ganglia to evaluate the further possibility of hemorrhagic transformation and found an increased risk of symptomatic hemorrhagic, reflecting more widespread blood brain barrier disruption and reperfusion injury. In our study, we observed significant cortical contrast medium extravasation with high HU deposition in one case (Fig. 2). Within 24 hours, the patient suffered from severe hemorrhagic transformation and brain swelling.

Our study did not find evidence supporting the predictability of IV thrombolysis, initial NIHSS, laboratory variables, and recanalization conditions (mTICI 2c and 3) in post-MT symptomatic ICH. Only contrast accumulation in the cortex with HU > 90 predicted symptomatic hemorrhage with a sensitivity and a specificity greater than 88.9%. For contrast accumulation in the cortex with HU > 100, the specificity was 94.6%, and the odds ratio was 139.20. The CO > 100 sign could be helpful in proactive management, such as strict blood pressure (BP) control or preventive craniotomy for patients with a high risk of symptomatic hemorrhage after thrombectomy. One study demonstrated that a higher initial NIHSS and larger infarction volume increased the risk of hemorrhagic transformation.[12] However, we found no significant difference between symptomatic and nonsymptomatic hemorrhage groups in the initial NIHSS. As part of a standard protocol in our department, we carry out further comprehensive stroke surveys using MRI when the initial MRI shows a large infarction volume (such as diffusion weighted image [DWI] volume > 100 cc or all cortical involvement). The treatment trend is a conservative medical treatment to avoid the recanalization of hemorrhage. This selection decreases the post-endovascular thrombectomy (EVT) brain hemorrhage rate. Although a dual-energy CT can be used to divide the iodine deposition and hemorrhage to predict hemorrhagic complications,[13,14] this technique is not widely available like single-energy CT. Alternatively, serial MRI examinations mentioned in the current study demonstrated a similar function as dual-energy CT.

There are some limitations in the current study. First, we used retrospective data from a single center with a relatively small number of patients. These undoubtedly resulted in limited statistical power, and potential selection bias is possible. Because of the retrospective nature, more stricted BP control was arranged in CO > 90 patient group which might slightly decreased the hemorrhagic transformation rate. Second, essential factors, such as onset to recanalization time or initial collateral condition, were not evaluated. A separate cohort may be required to validate our prediction model.

In conclusion, cortical involvement of contrast medium pooling with HU > 100 may be used to predict further symptomatic ICH in AIS patients who had just undergone MT. The image assessment procedures are simple and cost-effective. The clinical findings observed in the post-MT brain CT remind further attention and careful management in specific patients to avoid potentially fatal complications.

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