ORIGINAL ARTICLE

Quantitative CT angiography predicts large artery occlusion types and successful thrombectomy in acute ischemic stroke

Chun Chien[a], Chun-Jen Lin[a,b], Feng-Chi Chang[b,c], Chih-Ping Chung[a,b], Chung-Jung Lin[b,c], Hung-Yu Liu[a,b], Nai-Fang Chi[a,b], Li-Chi Hsu[a,b],Chih-Wei Tang[d,e], Wan-Yuo Guo[b,c], Chao-Bao Luo[b,c], Yen-Jun Lai[f,*], I-Hui Lee[a,d,*]

[a]Division of Cerebrovascular Diseases, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]School of Medicine, National Yang-Ming University, Taipei, Taiwan, ROC; [c]Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [d]Institute of Brain Science, Brain Research Center, National Yang-Ming University, Taipei, Taiwan, ROC; [e]Department of Neurology, Far Eastern Memorial Hospital, New Taipei City, Taiwan, ROC; [f]Department of Radiology, Far Eastern Memorial Hospital, New Taipei City, Taiwan, ROC

Abstract

Background: Clinical and radiological outcomes of endovascular thrombectomy (EVT) are related to etiologies of large vessel occlusion (LVO) in acute stroke. However, preprocedural computed tomography angiography (CTA) or CT perfusion imaging can hardly distinguish embolic occlusion from atherosclerotic occlusion. We hypothesized that quantitative multiphase CTA (mCTA) of LVO may predict occlusion types and thrombectomy outcome.

Methods: We retrospectively evaluated the consecutive stroke patients who had undergone mCTA and EVT <6 hours of onset at two independent medical centers. The intra-arterial radiodensities of Hounsfield unit (HU) were measured to examine the $HU_{distal/proximal}$ ratio using receiver operating characteristic curve analysis. The derived cut-off value was re-examined in an independent cohort.

Results: In the derivation cohort (n = 102), 81 patients (79.4%) were embolic occlusion without severe residual intracranial atherosclerotic stenosis (ICAS[−]) and 21 patients were atherosclerosis-related occlusion (ICAS[+]) based on digital subtraction angiography (DSA). The optimal cut-off to predict embolic occlusion was HU ratio <0.6 measured at 2 mm from the occlusion site (maximum area under the curve = 0.87; sensitivity 96%; specificity 81%). This cut-off also independently predicted successful recanalization using stent-retrievers and/or contact aspiration (modified Treatment in Cerebral Ischemia score ≥2b; $p = 0.002$) after adjusting for age, atrial fibrillation, and collateral circulation score, but not predicted favorable outcome at 3 months post stroke. Importantly, in the validation cohort (n = 95, 80% embolic occlusion), this HU ratio cut-off similarly predicted occlusion types and recanalization outcome, respectively.

Conclusion: The mCTA-based quantitative radiodensities of acute LVO provides preprocedural predictive values of DSA-determined occlusion types and thrombectomy outcomes.

Keywords: Computed tomography angiography; Intracranial arteriosclerosis; Stroke; Thrombectomy

1. INTRODUCTION

Intracranial atherosclerotic stenosis (ICAS) is an important cause of large vessel occlusion (LVO)[1–4] and particularly prevalent in Asians, Hispanic, and Africans. A recent meta-analysis showed that LVO stroke caused by ICAS was associated with a lower recanalization and higher reocclusion rate following endovascular thrombectomy (EVT) compared with those etiologies other than ICAS. Alternatively, rescue therapies including intra-arterial glycoprotein IIb/IIIa inhibitor (tirofiban) dripping, balloon angioplasty, and/or stenting have been introduced.[5] Importantly, stroke patients caused by ICAS have relatively poor functional outcomes compared with those caused by embolic occlusion.[6] Baek et al[7] previously suggested a morphological dichotomy based on digital subtraction angiography (DSA) to distinguish occlusion etiologies as truncal-type occlusion versus branching-site occlusion of the proximal segment (M1) of the middle cerebral artery (MCA). In contrast to branching-site occlusion, truncal-type occlusion was associated with more reocclusion and a worse recanalization rate using stent retrievers (SR) in anterior circulation stroke. Although vascular morphological dichotomy might oversimplify heterogeneous or mixed occlusion etiologies, truncal-type occlusion has been associated with critical artherosclerotic stenosis, while branching-site occlusion being associated with mostly embolism at the distal

*Address correspondence. Dr. Yen-Jun Lai, Division of Medical Imaging, Department of Radiology, Far Eastern Memorial Hospital, 21, Section 2, Nanya South Road, Banqiao District, New Taipei City 220, Taiwan, ROC. E-mail address: yjlai@femh.org.tw (Y.J. Lai); Dr. I-Hui Lee, Division of Cerebrovascular Diseases, Neurological Institute, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC. E-mail address: ihlee@vghtpe.gov.tw (I.H. Lee).

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M1 bifurcation. Subsequently, they reported computed tomography angiography (CTA) with reconstructive maximum intensity projections (MIPs) to distinguish between occlusion types with similar characteristics.[8] However, it remains unknown how occlusions beyond the distal M1 bifurcation could be predicted by CTA before thrombectomy decision in acute ischemic stroke.

Multiphase CTA (mCTA) of LVO and collateral backfilling of leptomeningeal arteries[9–12] is a commonly used preprocedural evaluation modality in acute ischemic stroke patients before EVT.[13] Multiphase CTA has been used to measure clot length by measuring the thick MIPs and illustrate three-dimensional renderings.[14] Accordingly, mCTA enables the determination of proximal and distal occlusion boundaries in an affected artery. In this study, we sought to provide a quantitative method using mCTA to predict occlusion types and successful recanalization before EVT. We hypothesized that abruptness of arterial occlusion by emboli leads to inadequate downstream blood flow from the proximal artery. Therefore, the distal/proximal radiodensity ratio in Hounsfield units (HU ratios = $HU_{distal/proximal}$) is lower in embolic occlusion than in atherosclerotic occlusion where chronic collateral circulation has been established as the severity of arterial stenosis developed.[15] Because the successful recanalization rate with SR and/or contact aspiration is highly related to occlusion types,[8] we hypothesized that the lower HU ratios is, the higher recanalization rate is achieved. Furthermore, we attempted to established best measurement position and a cutoff value of HU ratio considering both sensitivity and specificity.

2. METHODS

2.1. Patient baseline characteristics from two centers

We retrospectively evaluated clinical and radiological data of consecutive acute stroke patients with anterior circulation LVO stroke who had undergone mCTA and EVT at the Taipei Veteran General Hospital, Taiwan, between August 2015 and May 2019 as the derivation cohort. Regarding the independent validation cohort, acute stroke patients were retrospectively reviewed using the same inclusion criteria from the Far Eastern Memorial Hospital in New Taipei City, Taiwan, between January 2018 and December 2019. The inclusion criteria were as follows: (1) acute ischemic stroke within 6 hours of onset; (2) a National Institutes Health Stroke Scale (NIHSS) score ≥6 on admission (baseline); (3) an Alberta Stroke Program Early Computed Tomography Score (ASPECTS) ≥ 6 at the baseline by noncontrast brain CT; (4) moderate to good collateral circulation shown at mCTA (collateral circulation score 2-5, see below)[16]; and (5) normal or good premorbid function with a modified Rankin Scale (mRS) 0 to 1. We obtained written informed consent from each patient and/or family members or proxy for each patient before intravenous thrombolysis and/or EVT as recommended by Taiwan Ministry of Health and Welfare. Among them, intravenous thrombolysis was given to eligible patients with stroke onset within 4.5 hours. The Institutional Review Boards of Taipei Veteran General Hospital and Far Eastern Memorial Hospital approved this study.

2.2. Multiphase CTA protocols and measurements

In the derivation cohort, CT images were obtained using a 64-channel multidetector row computed tomographic system (Brilliance CT Scanners; Koninklijke Philips Electronics, The Netherlands). Axial 3-mm nonenhanced CT images were obtained first, and then 60 mL of nonionic contrast agent was administered, followed by 40 mL of normal saline chaser given through a power dual injector. For mCTA, arterial phase imaging acquisition was performed when the bolus-tracking marker reached the aortic arch region at 150 HU. The early venous and delayed venous phases were automatically obtained in 8 seconds after completing the arterial phase. The mCTA images were reconstructed into MIP images (8 mm/3 mm). In the validation cohort, CT images were obtained using a 64-channel multidetector row computed tomographic system (SOMATOM Definition AS; Siemens, Germany). The contrast administration protocol and delay phases acquisition were the same as that in the derivation cohort.

We first evaluated collateral circulation score (0-5 grading system, where 0 means no visible collaterals in any phases and 5 means no filling delay of contrast and nearly normal prominence of pial collaterals compared with unaffected contralateral hemisphere)[16] and morphological dichotomy of branching-site occlusion or truncal-type occlusion.[7,8] We then measured HU levels by point analysis at the center of affected arteries. The proximal and distal occlusion sites were identified using arterial phase CTA and the intra-arterial HU levels were measured at the end, 1 mm, 2 mm, and 3 mm away from the proximal occlusion end ([HU_0], [HU_1], [HU_2], and [HU_3]), as well as at the distal occlusion end, 1 mm, 2 mm, and 3 mm away from the distal occlusion end ([$HU_{0'}$], [$HU_{1'}$], [$HU_{2'}$], and [$HU_{3'}$]). If the distal occlusion site was invisible at arterial phase CTA, we manually overlapped the venous phase CTA to determine the distal occlusion location and measured [$HU_{0'}$], [$HU_{1'}$], [$HU_{2'}$], and [$HU_{3'}$] from the distal occlusion end using arterial phase CTA (Fig. 1). If the occlusion site was at distal M1, we then measured the HU level at the dominant M2 branch. Finally, we analyzed the HU_n ratio, that is, $HU_{n\ distal/proximal}$, at n mm away from the occlusion end for each occluded artery per patient.

2.3. DSA and endovascular treatment

The diagnostic DSA was reviewed after EVT to classify occlusion types into either embolic occlusion without severe ICAS (ICAS[−]) or ICAS[+]–related occlusion, which was defined if any of the following criteria was met: (1) >70% residual arterial stenosis after thrombectomy,[17] (2) immediate or rapid re-occlusion within 15 minutes after EVT (SR and/or contact aspiration),[7,18] (3) EVT failure and having fixed degree of stenosis with flow impairment on angiography,[17] and (4) having rescue therapies including intra-arterial glycoprotein IIb/IIIa inhibitor (tirofiban), balloon angioplasty, and/or stenting.[18] Recanalization grading was classified using the modified Treatment in Cerebral Ischemia (mTICI) grade.[19] Successful recanalization was defined as mTICI grading above 2b using SR and/or contact aspiration (not rescue therapies).

In the derivation cohort, EVT was performed by at least two experienced interventional neurointerventionalists and mostly under general anesthesia, if available. In the validation cohort, endovascular treatment was performed by two experienced neurointerventionalists under conscious sedation. The protocols and procedures were generally similar in both hospitals. The strategy and tools of endovascular treatment were determined by neurointerventionalists' clinical judgment. Regarding EVT, contact aspiration, the Penumbra system (Penumbra, Inc., Alameda, CA), SOFIA (soft torqueable catheter optimized for intracranial access; MicroVention, Tustin, CA) and a stent-retriever system using the Solitaire SR (Medtronic Inc, Mansfield, MA) or Trevo SR (Stryker Neurovascular, Fremont, CA) were used. Rescue therapies were applied in few patients with ICAS[+]-related occlusion or arterial dissection.

2.4. Clinical outcome measurement

Clinical outcomes included NIHSS changes at 24 hours after EVT and the mRS at 90 days compared with those on admission (baseline), respectively. Symptomatic intracerebral hemorrhage (sICH) was defined as the presence of parenchymal hematoma accompanied by neurological deterioration as an increase in

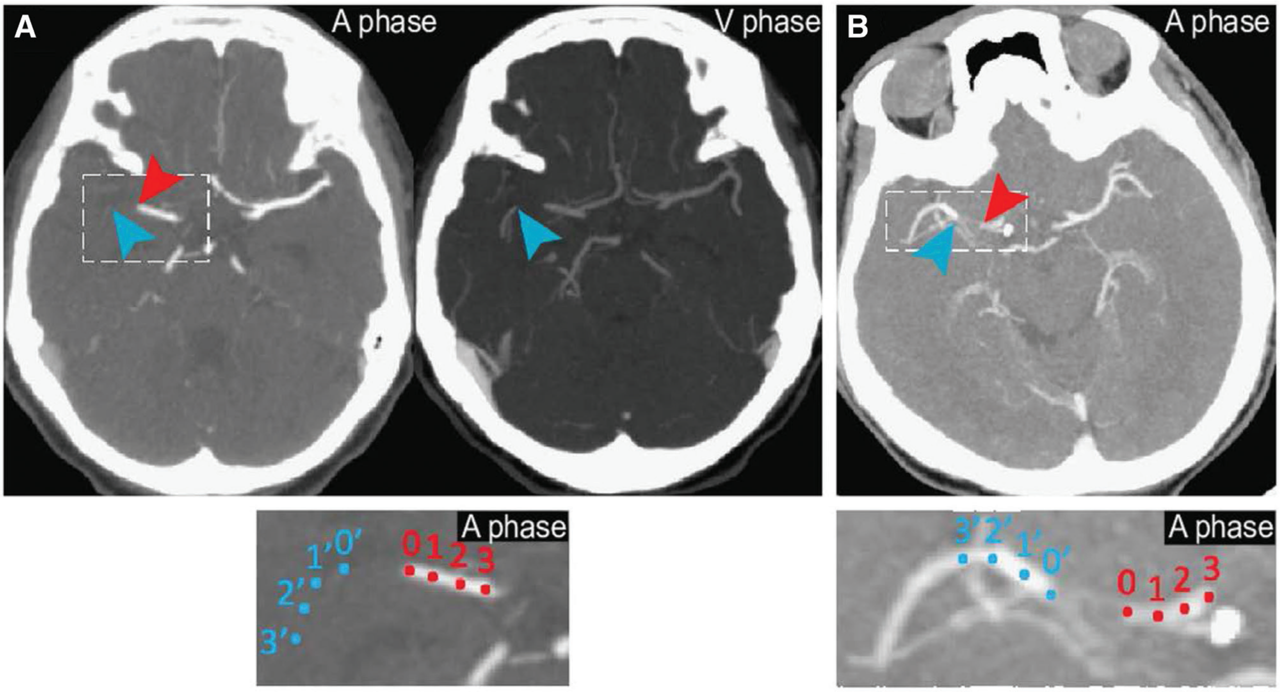

Fig. 1 Measurements of the intra-arterial Hounsfield units (HU) (A) at the central point of proximal artery end [HU_0], 1 mm [HU_1], 2 mm [HU_2], and 3 mm [HU_3] (red dots and numbers at high magnification) after determination of the proximal occlusion site in arterial phase (A phase) computed tomography angiography (CTA; red arrow head). When the distal occlusion end could not be identified in the A phase CTA, we manually overlapped the venous phase (V phase) CTA to determine the distal occlusion site (blue arrow head) onto the A phase CTA to measure [$HU_{0'}$], [$HU_{1'}$], [$HU_{2'}$], and [$HU_{3'}$] (blue dots and numbers). (B) When the distal occlusion site was visible in the A phase CTA, we measured the HU level of the distal occlusion site (blue arrow head) at the distal end [$HU_{0'}$] and at 1 mm [$HU_{1'}$], 2 mm [$HU_{2'}$], and 3 mm [$HU_{3'}$] (blue dots and numbers).

NIHSS of ≥4 within 36 hours after the procedure according to the safe implementation of thrombolysis in stroke monitoring study criteria.[20]

2.5. Statistical analysis

Statistical analysis was performed using the SPSS software (IBM SPSS Statistics for Windows, version 25.0; International Business Machines Corporation, Armonk, NY). The demographic clinical profiles, risk factors, imaging measurements, procedural variables, and outcomes were compared between the DSA-determined ICAS[+] and ICAS[−] groups in the derivation cohort. The Mann-Whitney *U* test was used for continuous variable comparison. χ^2 test or Fisher's exact test was used for categorical variable comparison. A p value <0.05 was considered statistically significant. To determine an optimal cut-off value with the best predictive power of HU ratios among different measurement locations, we performed receiver operating characteristic (ROC) curve analyses and compared the area under the curve (AUC) values. For the optimal HU ratio cut-off, we calculated the sensitivity, specificity, and positive and negative predictive values (PPV and NPV, respectively) for occlusion types and successful recanalization in both the derivation and validation cohorts. Moreover, multivariate logistic and linear regression analyses were performed in the derivation cohort to investigate independent predictors for occlusion types, successful recanalization, NIHSS change within 24 hours after EVT, and favorable outcomes (mRS 0-2) at 90 days, respectively.

3. RESULTS

In the derivation cohort, 102 patients with anterior circulation stroke and EVT were included (median age: 76 years old, interquartile range: 66.8-84.3; 50% were male), after excluding those with posterior circulation stroke (n = 22), no available mCTA (n = 15), distal artery occlusion at the M2 segment of MCA (n = 5) and proximal ICA occlusion with difficulties in approaching intracranial anterior circulation arteries (n = 2). According to DSA-based diagnosis, 81 out of 102 patients were classified as the embolic occlusion ICAS[−] group (79.4%) and 21 patients (20.6%) as the ICAS[+]-related occlusion group (Table 1). Compared with the ICAS[+]-related occlusion group, the embolic occlusion ICAS[−] group revealed significantly older (77 vs 68, p = 0.009) and had a higher frequency of atrial fibrillation (75.3% vs 42.9%, p = 0.007). No significant differences were found in the other vascular risk factors, baseline NIHSS, and ASPECTS. Furthermore, the embolic occlusion ICAS[−] group had an insignificantly worse collateral circulation than the ICAS[+]-related occlusion group (p = 0.063). Regarding occlusion location, the embolic occlusion ICAS[−] group had a higher frequency of distal M1 bifurcation occlusion than the ICAS[+]-related occlusion group (42% vs 4.8%, p = 0.001). Patients in the embolic occlusion ICAS[−] group were more likely to have successful recanalization (mTICI grade ≥2b) using SR and/or contact aspiration than those in the ICAS[+] occlusion group (70.4% vs 33.3%, p = 0.003). Therefore, a greater attenuation in the NIHSS by 24 hours after EVT was found in the embolic occlusion ICAS[−] group than in the ICAS[+] occlusion group (−4 vs 0, p = 0.009). No significant difference was found in the onset to puncture time and the percentage of symptomatic ICH after the procedure between the groups. However, the proportion of favorable outcomes (mRS 0-2) at 90 days were insignificantly different between the groups (33.3% vs 19%, p = 0.289), suggesting that other crucial variables (eg, age) may counteract the effects of occlusion types and successful thrombectomy. Because additional rescue therapies were differently adopted

Table 1

Comparisons of the clinical and radiological features between intracranial atherosclerotic steno-occlusion and embolic occlusion without severe intracranial artery stenosis determined with digital subtraction angiography in the derivation cohort

Characteristics	Intracranial artery stenosis[+] (N = 21, 20.6%)	Intracranial artery stenosis[−] (N = 81, 79.4%)	p
Age	68 (50-75)	77 (69-85)	**0.009**
Sex (male)	9 (42.9%)	42 (51.9%)	0.625
Hypertension	10 (47.6%)	54 (66.7%)	0.132
Diabetes mellitus	6 (28.6%)	21 (25.9%)	0.787
Atrial fibrillation	9 (42.9%)	61 (75.3%)	**0.007**
Dyslipidemia	3 (14.3%)	20 (24.7%)	0.391
Smoking	3 (14.3%)	10 (12.3%)	0.728
Alteplase administration	7 (33.3%)	44 (54.3%)	0.141
CT ASPECTS	8 (7-9)	8 (7-9)	0.738
Collateral circulation score	4 (3-4)	3 (3-4)	0.063
Onset to puncture time (min)	257 (168-324)	216 (157-296)	0.224
Distal ICA occlusion	6 (28.6%)	15 (18.5%)	0.365
Proximal M1 occlusion	8 (38.1%)	16 (19.8%)	0.090
Middle M1 occlusion	6 (28.6%)	16 (19.8%)	0.384
Distal M1 occlusion	1 (4.8%)	34 (42.0%)	**0.001**
HU_0 ratio	0.78 (0.63-0.88)	0.515 (0.39-0.68)	**<0.001**
HU_1 ratio	0.67 (0.56-0.80)	0.352 (0.26-0.47)	**<0.001**
HU_2 ratio	0.70 (0.60-0.83)	0.318 (0.24-0.42)	**<0.001**
HU_3 ratio	0.61 (0.55-0.80)	0.312 (0.23-0.47)	**<0.001**
Dissection	2 (9.5%)	0	**0.041**
mTICI grading 2b/3	7 (33.3%)	57 (70.4%)	**0.003**
Symptomatic ICH	4 (19%)	5 (6.2%)	0.084
NIHSS on admission	16 (13-20.5)	17 (13.5-21)	0.534
△NIHSS at 24 hours	0 (6-3)	−4 (1-10.5)	**0.009**
Good outcome $_{3m}$ (mRS 0-2)	4 (19%)	27 (33.3%)	0.289

The results are expressed as the number of patients (%) or median (interquartile range). Bold values indicates $p < 0.05$.

ΔNIHSS = change of National Institutes of Health Stroke Scale at 24 hours compared with that on admission; ASPECTS = Alberta stroke program early computed tomography score; DSA = digital subtraction angiography; HU = Hounsfield unit; ICA = internal cerebral artery; ICH = intracranial hemorrhage; M1 = first portion of middle cerebral artery; mRS = modified Rankin Scale; mTICI = modified treatment in cerebral infarction;

between the derivation (3/102, 2.9%) and validation (14/95, 15.7%) cohorts, we did not count successful recanalization by rescue therapies for ICAS[+]-related occlusion.

As expectedly, we disclosed that the HU ratios (=$HU_{distal/proximal}$) of the ICAS[+]-related occlusion group were significantly higher than those of the embolic occlusion ICAS[−] group at 0 to 3 mm from the occlusion end (Table 1), which were likely attributed to the availability of collaterals and making a distinction between the groups. Hence, we analyzed the ROC curve and the AUC of each HU_n ratio at the end [HU_0], 1 mm [HU_1], 2 mm [HU_2], and 3 mm [HU_3], which were 0.76, 0.85, 0.87, and 0.84, respectively (Fig. 2). The largest AUC occurred at the HU_2 ratio with the maximum sum of sensitivity (96.3%) plus specificity (81.0%) being 177.3%. Additionally, the HU_2 ratio cut-off was 0.594. The predictive power using an HU_2 ratio <0.6 to predict embolic occlusion in the derivation cohort was as follows: sensitivity 96.3%, specificity 81.0%, PPV 95.1%, and NPV 85.0% (Table 2). A similar but lower predictive specificity of morphological dichotomy of branching-site occlusion was sensitivity 92.6%, specificity 57.1%, PPV 89.2%, and NPV 66.7% (Table 2). Additionally, we applied the HU_2 ratio <0.6 to predict successful recanalization using SR and/or contact aspiration, revealing a sensitivity of 72.0%, specificity 75.0%, PPV 92.2%, and NPV 39.5%, which was superior to the predictive value using a morphological dichotomy of branching-site occlusion (sensitivity 67.9%, specificity 61.1%, PPV 89.1%, and NPV 28.9%) (Table 2). Importantly, after adjusting for confounding variables including age, history of atrial fibrillation, collateral circulation score, and branching-site occlusion using a multivariate logistic analysis (Table 3), HU_2 ratio <0.6 independently predicted both embolic occlusion ICAS[−] type ($p < 0.001$) and successful recanalization ($p = 0.002$). However, the HU_2 ratio of the occlusion artery itself did not predict clinical outcomes, neither NIHSS improvement within 24 hours after thrombectomy nor favorable outcomes (mRS 0-2) at 90 days. The multivariate regression analysis of significant predictors for favorable outcomes at 90 days were age ($p = 0.017$), NIHSS on admission ($p < 0.001$), and NIHSS improvement within 24 hours ($p < 0.001$).

To validate the predictive value of HU_2 ratios in an independent cohort of consecutive patients who undergone EVT, 95 patients were included in the analysis after excluding those lack of mCTA imaging (n = 27), posterior circulation stroke (n = 25), M2 occlusion (n = 13), and proximal ICA total occlusion (n = 16). Among them, 76 patients were embolic occlusion ICAS[−] (80%) and 19 patients were ICAS[+]-related occlusion (20%). The predictive power of HU_2 <0.6 to predict embolic occlusion ICAS[−] was sensitivity 93.4%, specificity 63.2%, PPV 91.0%, and NPV 70.5%; for successful recanalization after EVT, sensitivity 93.8%, specificity 85.7%, PPV 97.4%, and NPV 70.5%. Both predictive values were good and supportive of the findings in the derivation cohort (Table 2).

4. DISCUSSION

Our study provides novel mCTA-derived quantitative criteria of a single LVO for preprocedural evaluation in acute ischemic stroke: HU_2 ratio <0.6 from mCTA predicts more likely embolic occlusion and successful recanalization after adjustment for age, presence of atrial fibrillation, collateral circulation score, and branching-site occlusion dichotomy. Thus, this HU_2 ratio radiodensity criteria is useful in the early differentiation of occlusion types before EVT and helps preprocedural planning before the initiation of the procedures. These results are in line with the previously report that DSA- or CTA-defined morphological dichotomy of branching-site occlusion of the distal M1 segment of MCA as a good predictor of successful recanalization utilizing SR, because embolic occlusion usually occurs at the distal M1 branching site.[7,8] The mCTA-derived HU_2 ratios have an advantage to be applicable to various occlusion locations from intracranial internal carotid artery to proximal MCA, beyond the limitation of the morphological dichotomy that depends on the visibility of distal M1 bifurcation.

There is currently no consensus on diagnosing different occlusion etiologies.[21,22] The diagnosis of ICAS[+]-related occlusion in acute stroke patients who failed to recanalization using EVT could be oversimplified, which was based on several clinical suggestions including rapid reocclusion and additional rescue therapy applications. In contrast to embolic occlusion ICAS[−] group, the etiologies of ICAS[+]-related occlusion vary more widely, including atherosclerotic plaque rupture with in situ thrombosis, atherosclerotic stenosis mixed with embolic occlusion, or dissecting occlusion. Hence, thrombectomy outcomes may be affected by such different etiologies, which possibly compromise our NPV of the recanalization rate in those predicted as ICAS[+]-related occlusion. Moreover, there is no standard endovascular management of ICAS[+]-related occlusion, and the application of rescue therapies vary among different neurointerventionalists. Previously, Baek et al[18] reported that high recanalization rates could be achieved in the ICAS[+] patients, similar to that in ICAS[−] patients, with incorporating advancement in rescue therapies, including intra-arterial glycoprotein

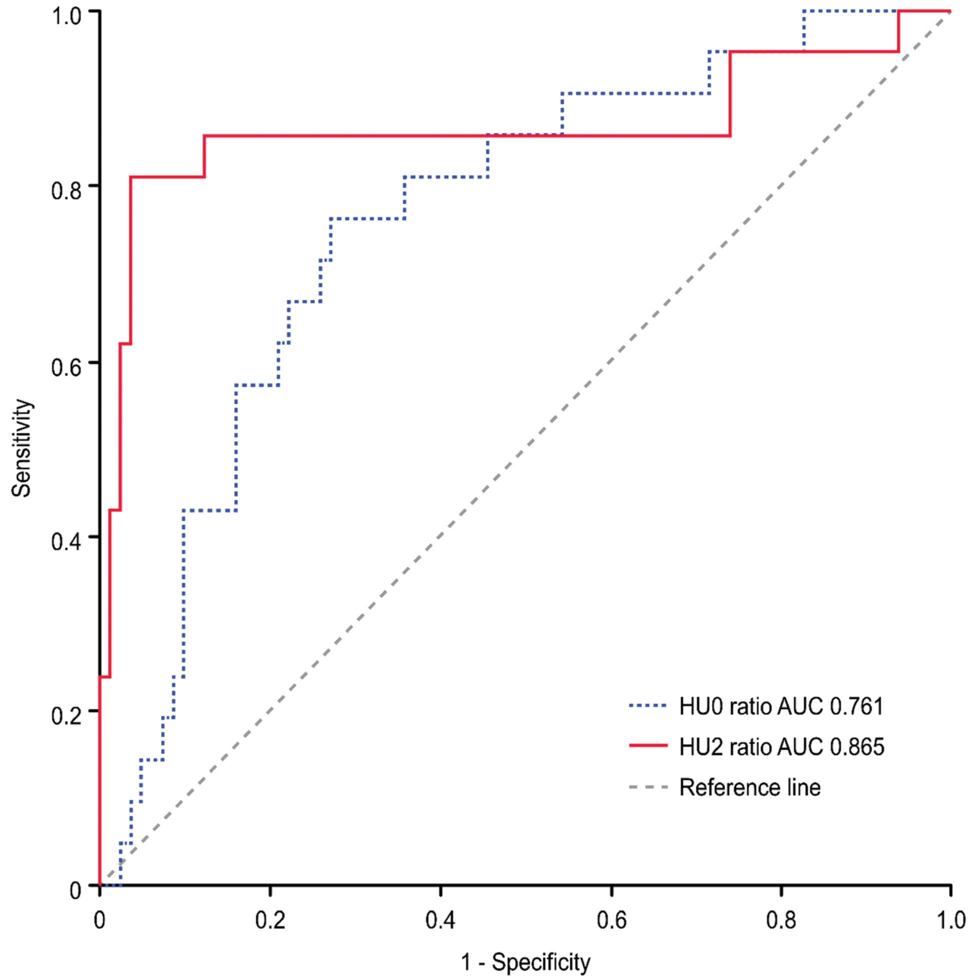

Fig. 2 Receiver operating characteristic curves of Hounsfield unit (HU) ratios ($HU_{distal}/HU_{proximal}$) at arterial occlusion ends (HU_0, area under the curve [AUC] = 0.761; 95% CI, 0.651-0.872) and 2 mm away from the occlusion ends (HU_2, AUC = 0.865; 95% CI, 0.744-0.986) for predicting occlusion types determined with digital subtraction angiography. The maximum sensitivity plus specificity was achieved by the HU_2 ratio (the sensitivity was 81.0%, and the specificity was 96.3%), and the HU_2 ratio cut-off was 0.594.

Table 2

Predictive power of the HU_2 ratio <0.6 for embolic occlusion type and successful recanalization using stent retrievers and/or contact aspiration in the derivation and validation cohorts

Predictive variables	Sensitivity, %	Specificity, %	PPV, %	NPV, %	AUC	*p*
Embolic occlusion						
Derivation cohort						
Branching-site occlusion	92.6	57.1	89.2	66.7	0.75	**<0.001**
HU_2 ratio <0.6	96.3	81.0	95.1	85.0	0.89	**<0.001**
Validation cohort						
HU_2 ratio <0.6	93.4	63.2	91.0	70.5	0.84	**<0.001**
Successful recanalization						
Derivation cohort						
Atrial fibrillation	61.4	34.4	67.2	28.9	0.48	0.826
Hyperdense artery sign	59.6	33.3	53.1	39.5	0.46	0.539
Branching-site occlusion	67.9	61.1	89.1	28.9	0.59	**0.031**
HU_2 ratio <0.6	72.0	75.0	92.2	39.5	0.66	**<0.001**
Validation cohort						
HU_2 ratio <0.6	93.8	85.7	97.4	70.5	0.89	**<0.001**

Bold values indicates $p < 0.05$.

AUC = area under the receiver operating characteristic curve; HU = Hounsfield unit; NPV = negative predictive value; PPV = positive predictive value.

Table 3

Multivariate regression analysis for independent predictors of intracranial occlusion types and successful recanalization in the derivation cohort

	Embolic occlusion type		Successful recanalization	
Predictors	**Adjusted OR (95% CI)**	***p***	**Adjusted OR (95% CI)**	***p***
Age	1.035 (0.97-1.11)	0.310	0.99 (0.96-1.04)	0.959
HU_2 ratio <0.6	151.6 (14.32-1605.4)	**<0.001**	15.66 (2.82-86.84)	**0.002**
Branching-site occlusion	3.460(0.398-30.043)	0.260	1.21(0.25-5.90)	0.816
Collateral circulation score	2.65 (0.88-8.01)	0.083	1.15 (0.66-2.02)	0.616
Atrial fibrillation	0.62 (0.07-5.83)	0.676	0.28 (0.07-1.10)	0.067

Bold values indicates $p < 0.05$.
HU = Hounsfield unit; OR = odds ratio.

IIb/IIIa inhibitor infusion, balloon angioplasty, and stenting. However, aggressiveness in achieving successful recanalization may come at a price of increasing sICH rate.[23] Our patients with ICAS[+]-related occlusion, despite lower recanalization rate and less initial NIHSS improvement, were younger and having established collateral circulation compared with those with embolic occlusion ICAS[−], which uncontrolled variables may explain why there was no group difference in favorable outcome at 90 days. In line with others' report,[24] we found that age, baseline NIHSS, and NIHSS change within 24 hours were independent predictors of favorable outcome at 90 days.

There are several potential reasons causing misprediction based on the mCTA-derived HU ratios. First, there are possible comorbidities that delayed contrast filling including lower cardiac output (eg, congestive heart failure and dehydration), proximal ICA severe stenosis or tandem occlusion, and bilateral proximal ICA steno-occlusion. We might underestimate the HU_2 ratio under these clinical conditions and misclassify ICAS[+]-related occlusion for embolic occlusion. Second, in acute stroke patients with good and excellent collateral circulation, ultra-early pial collateral backfilling might atypically elevate HU_2 ratios in embolic occlusion, which usually has lower HU_2 ratio. Third, clot or thrombus histology might influence contrast infiltration and flow velocity. The thrombus permeability is correlated with fibrin and red blood cell compositions. More permeable thrombi are associated with cardioembolic origin,[25] which could lead to higher HU ratios in some embolic occlusion.

In conclusion, the quantitative radiodensities of intracranial arteries based on mCTA may help early prediction of different occlusion etiologies in acute ischemic stroke. The optimal cut-off value of the HU_2 ratio <0.6 predicts embolic occlusion and successful recanalization using stent-retrievers and/or contact aspiration. The patient representativeness was acceptable and the derived cut-off values of the HU_2 ratio was well validated in two independent cohorts. Further studies with more large sample sizes and examining different approaches to different occlusion types are warranted.

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