Poor Collateral Circulation Assessed by Multiphase Computed Tomographic Angiography Predicts Malignant Middle Cerebral Artery Evolution After Reperfusion Therapies

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Background and Purpose—Collateral circulation (CC) has been associated with recanalization, infarct volume, and clinical outcome in patients undergoing acute reperfusion therapies. However, its relationship with the development to malignant middle cerebral artery infarction (mMCAi) has not been evaluated. Our aim was to determine the impact of CC using multiphase computed tomographic angiography (during the acute stroke phase in the prediction of mMCAi.

Methods—Patients with consecutive acute stroke with <4.5 hours who were evaluated for reperfusion therapies and presented with an M1-MCA or terminal internal carotid artery occlusion by CTA were included. CC was evaluated on 6 grades by multiphase CTA according to the University of Calgary CC Scale; CC status was defined as poor (grades, 0–3) or good (grades, 4–5). The mMCAi was defined according to clinical and radiological criteria. Recanalization was assessed with transcranial Doppler at 24 hours and final Thrombolysis in Brain Ischemia score ≥2b in patients undergoing endovascular reperfusion treatment.

Results—Eighty-two patients were included. Mean age was 65.1±13.83 years, median baseline National Institutes of Health Stroke Scale score was 18 (interquartile range, 13–20), and 67.9% M1 and 32.1% terminal internal carotid artery occlusions. Fifty-three patients received endovascular reperfusion treatment. Fifteen patients developed mMCAi. In the univariate analysis, patients with mMCAi had lower CC scores (2.29 versus 3.71; P=0.001). Endovascular reperfusion treatment was associated with lower rate of mMCAi development than only intravenous reperfusion treatment (9.4% versus 29.6%; P=0.028). Patients with poor CC had higher risk of developing mMCAi (13% versus 2%; P=0.001). On the multivariate analysis adjusted by age, vessel occlusion, baseline National Institutes of Health Stroke Scale, and recanalization, the presence of poor CC by multiphase CTA was the only independent predictor of mMCAi (P=0.048; odds ratio, 9.72; 95% confidence interval, 1.387–92.53).

Conclusions—CC assessment by multiphase CTA independently predicts malignant MCA infarction progression. In patients with persistent occlusion after reperfusion therapies, the presence of poor CC may improve the early mMCAi detection and management. (Stroke. 2015;46:3149-3153. DOI: 10.1161/STROKEAHA.115.010608.)

Key Words: cerebral infarction ■ collateral circulation ■ infarction, middle cerebral artery ■ reperfusion ■ stroke

One of the most devastating complications of ischemic stroke is evolving to malignant middle cerebral artery infarction (mMCAi). The mMCAi evolution occurs in ≤10% of the patients with acute ischemic stroke, especially affecting young people. The mortality rate of mMCAi arises ≤80% in nonsurgery cases, with a high proportion of severe disability in the rest of cases.1

Early detection and management with praeox decompressive surgery within 48 hours may improve the vital and functional outcome of these patients.2,3 Therefore, early indicators of mMCAi evolution during the first hours after ischemic stroke symptoms onset are of high relevance.

Several predictors of mMCAi had been evaluated in the acute phase. Neuroimaging parameters as baseline...
diffusion-weighted imaging lesion volume has been shown to be a strong and accurate predictor of mMCAi. A diffusion-weighted imaging lesion volume >82 mL below 6 hours of stroke onset predicts, with low sensitivity, mMCAi evolution. This threshold of diffusion-weighted imaging volume raises 144 mL for patients imaged at 6 to 14 hours time-window.2,4 In noncontrast computed tomography (CT), ischemia that affects more than two thirds of the MCA territory predicts the development of mMCAi with a sensitivity of 91% and specificity of 94%.5 Recent studies have shown that some CT perfusion sequences (cerebral blood volume, cerebral blood flow, and cerebral blood volume/cerebrospinal fluid reserve volume) have shown positive correlation with mMCAi prediction.6,7 On the contrary, the degree of leptomeningeal or pial collateral circulation (CC) in acute stroke has been associated with clinical outcome, infarct volume, hemorrhage transformation risk, and recanalization rates.5–11 Single-phase CT angiography (CTA) is more widely used for CC status evaluation on acute stroke, but it lacks of temporal resolution and may mislabel CC status. In this perspective, a new time-resolved technique, multiphase CTA (mCTA) may improve CC evaluation, showing a better inter-rater reliability and clinical outcome prediction comparing with single CTA on patients with acute stroke.12–14 Moreover, a recent trial has proven the use of endovascular reperfusion treatment in patients selected by CC status determined by mCTA.15 However, the relationship with CC status and the development of mMCAi is less known.

We postulate that poor CC status may represent an early predictor of mMCAi evolution. Therefore, we aimed to determine their relationship in the setting of patients with acute stroke evaluated by multiphase CTA (mCTA).

## Methods

This was an observational, prospective, single-center study. Between March 2013 and July 2014, patients with consecutive acute stroke with <4.5 hours from symptoms onset who were evaluated for
reperfusion therapies and presented with proximal anterior circula-

tion occlusion were included.

According to our radiological acute stroke protocol, approved by
the local ethics committee, all patients received a noncontrast CT
to rule out hemorrhage and a mCTA to determine large-vessel occlusion
and CC status. All scans were obtained with the patient in supine
position by using a 128-slice CT scanner (Definition AS; Siemens,
Erlangen, Germany). Collaterals were measured with a multiphase
CTA and the following parameters, collimator of 128×0.6 mm, 120
kVp, and 250 mAs, covering the first phase from the carina until the
vertex and the second and third phases from the foramen magnum to
the vertex. Acquisition was triggered using a bolus tracking (100 HU)
in the aortic arch after 60 mL of intravenous injection contrast, then
the second a third phases started 4 second after the previous phase.14
Collaterals were measured comparing backfilling arteries beyond the
occluded artery to similar arteries in the opposite unaffected hemi-
sphere in three different phases. MCA vascular enhancement distal to
occlusion was rated by using Calgary Scoring on mCTA.12 Scores 0
to 3 were categorized as poor CC status, in contrast with scores 4 and
5, which were considered as good CC. When endovascular reperfu-
sion treatment (ET) was performed, CC was also evaluated by digital
suction angiography using a previous published scale.16

Neurological status was assessed by a certified neurologist on
patient’s arrival, at 24 hours, and at discharge using the National
Institutes of Health Stroke Scale (NIHSS).

Recanalization was defined by transcranial Doppler (TCD) when
Thrombolysis in Brain Ischemia score 4 or 5 was detected on a 24-hour
TCD. In patients treated with ET, Thrombolysis in Brain Ischemia
score ≥2b was considered as recanalization too. At 24 to 48 hours, a
noncontrast CT scan was performed to evaluate infarct volume and
presence of hemorrhagic transformation.

The modified Rankin Scale score was used to assess functional
outcome at 3 months. Good outcome was defined as modified Rankin
Scale 0 to 2. Malignant MCA infarction was defined according to
previously published clinical and radiological criteria.1,2,5

The primary outcome was the presence of mMCAi. CC score
was analyzed as a dichotomic variable (poor and good CC status) for
analysis. Univariate comparisons were performed by Fisher exact test
or Pearson χ² as appropriate. Univariate correlations between the CC
score and baseline NIHSS, age, and infarct volume were determined
by Spearman correlation coefficients. Logistic regression models
with backward elimination of nonsignificant variables (P=0.05) were
used to identify variables independently associated with mMCAi.

Results

Eighty-one patients with acute stroke with large-vessel ante-
crior circulation occlusion were included in the study. The mean
age of the series was 65.1±13.8 years, and the median baseline
NIHSS was 18 (interquartile range, 13–20). On mCTA, 81.7% of
patients had a M1 middle cerebral artery (MCA) occlusion and
19.2% an intracranial distal or terminal carotid occlusion. Fifty-seven
(69.5%) patients received intravenous tissue-type plasminogen activator and 53 (64.6%) ET (primary intra-arterial therapy, 9.7%). Seventeen patients did not receive reper-
fusion therapies because extensive early ischemic signs on baseline
CT (Alberta Stroke Program Early CT [ASPECTS] score <5) or either contraindication according to protocol. Fifteen patients (18.2%) developed mMCAi, and 5 underwent
decompressive hemicranectomy according to local protocols.

Baseline characteristics of all, non-mMCAi, and mMCAi
patients are shown in the Table. mMCAi patients presented
more often with internal carotid artery occlusion than with M1
occlusion (71% versus 11.9%; P=0.033), and had higher base-
line median NIHSS (19.86 versus 15.70; P=0.016), but similar
ASPECTS score in the baseline CT scan.

In the univariate analysis, patients with mMCAi had sig-
nificantly higher infarct volume (230.42 versus 55.58 mL; 
P<0.001) in the 24-hour CT control.

In patients who received reperfusion therapies (n=64), no significant association was detected between recanaliza-
tion evaluated after 24 hours by TCD and mMCAi evolution
(52.3% mMCAi patients recanalized versus 47.7% who did
not; P=0.22). However, in patients treated with ET, we could
find a significant correlation between lower Thrombolysis in
Brain Ischemia scores and mMCAi evolution (P=0.005).

Figure 2. Graphic bars that shows the
number of patients with good and bad
collaterals according to malignant middle
cerebral artery infarction (mMCAi) and
non-mMCAi patients in the no-recanaliza-
tion group.
therapies when compared with intravenous thrombolysis was significantly associated with absence of mMCAi development (9.4% versus 29.6%; P=0.021). No significant differences were found on ASPECTS score and proximal site occlusion between these groups, being baseline median NIHSS higher in the ET group than in only intravenous thrombolysis group (median, 17 versus 13; P=0.032).

From the global series, 43 (52.4%) patients presented with good CC score by mCTA. In those patients treated with ET, CC evaluation by mCTA was significantly correlated with the digital sustraction angiography pial CC score (P=0.437; P=0.004). The presence of poor CC status evaluated by mCTA was significantly associated with mMCAi evolution n=13 (86.6%). A receiver operating characteristic curve shows a cutoff point ≤2 CC score for malignant progression with a specificity of 85% and a sensitivity of 65% with a positive predictive value of 35% and negative predictive value of 63%. Moreover, patients with poor CC n=13 (34.2%) evolved to mMCAi versus patients with good CC n=2 (3.03%; P=0.001; Figure 1). Neither patient with good CC developed mMCAi in no-recanalization patients (0 versus 6; P=0.68; Figure 2).

In the multivariate analysis adjusted by age, vessel occlusion, baseline NIHSS and recanalization, the presence of poor CC status by mCTA emerged as the only independent predictor of mMCAi (odds ratio, 9.72; 95% confidence interval, 2.11–44.08; P=0.001). No significant differences were found on ASPECTS score and proximal site occlusion after reperfusion therapies, the presence of persistent occlusion after reperfusion therapies, the presence of poor CC may help in the early malignant MCA detection and management.

Moreover, the presence of baseline parenchymal lesion defined by ASPECTS score was not related to mMCAi evolution; the precocity of acquisition parenchymal imaging (<4.5 hours) and the relative small sample could explain this finding. CC status has emerged as the only independent predictor of mMCAi evolution. Especially in patients who did not achieved recanalization, CC status was strongly associated with malignant outcome. This finding could be useful to the early assessment of patients with risk of mMCAi, especially in those patients undergoing reperfusion therapies when recanalization is not achieved. Therefore, predictive models adding CC assessment could improve the accuracy of predictors as volume lesion (ie, diffusion-weighted imaging lesion),1–4 If our results could be confirmed by further research, CC score would emerge as an early predictor of mMCAi evolution. On this way, early identification of candidates for neuro-intensive care unit admission and early hemicranectomy could be performed, which could potentially improve the prognosis of these patients.

Our study has some limitations. The short number of patients of the series precludes conclusions. In relation with baseline findings, our percentage of mMCAi (18%) is higher than the usual reported in the literature.1,2 However, our series is focused on severe stroke (median NIHSS, 18) with proximal anterior circulation occlusions.6–21

Another limitations are the lack of information on early recanalization in those patients who did not received reperfusion therapies and our time frame for determine recanalization. However, on the analysis of the influence of recanalization on mMCAi evolution, these patients were excluded.

In conclusion, CC assessment by mCTA is feasible and predicts malignant MCA progression. In patients with persistent occlusion after reperfusion therapies, the presence of poor CC may help in the early malignant MCA detection and management.

Disclosures

None.

References


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