Submitted: 31 August, 2021 Accepted: 12 October, 2021 Published: 08 January, 2023 DOI:10.22514/sv.2021.234

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ORIGINAL RESEARCH

Assessment of leptomeningeal collateral status using single-phase computed tomography angiography and its clinical value

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Abstract

At present, there is a lack of consensus regarding the high-cost performance method for evaluating the leptomeningeal collateral (LMC) status, and there are only few reports on the relationship between the LMC status and short-term neurological improvements in patients with acute middle cerebral artery (MCA) stroke. To evaluate the LMC status using single-phase computed tomography angiography (CTA) and assess the effect of the LMC status on short-term outcomes in patients with acute MCA regional ischemic stroke without reperfusion therapy. Thirty patients with acute MCA regional ischemic stroke without reperfusion therapy were sampled prospectively. Then, 256-layer single-phase CTA (using enhanced computed tomography, maximal intensity projection technology and multi-plane volume reconstruction) was used to measure each patient's LMC status using the MCA regional collateral score. The correlation between the LMC status and changes in the National Institutes of Health Stroke Scale (NIHSS) score was assessed. Differences in the modified Rankin scale score at 3 months after discharge between patients with a good (MCA territory collateral score $\geq$2) and those with a poor (MCA territory collateral score 0–1) LMC status were assessed. The NIHSS score change between admission and discharge correlated with the LMC status at admission ($r = 0.88$, $p = 0.03$). Three months after discharge, the mean modified Rankin scale scores in the poor and good LMC status groups were 1.91 ± 1.65 and 1.03 ± 1.36, respectively ($p = 0.0394$). The NIHSS scores at 3 months after discharge in the poor and good LMC status groups were 4.31 ± 4.29 and 2.16 ± 2.06, respectively ($p = 0.0489$). Our findings can further reinforce the understanding of the appropriate assessment of LMCs and its clinical value. A 256-slice single-phase CTA-maximal intensity projection can provide good assessment of the LMC status. In patients with MCA regional acute ischemic stroke, the LMC status may predict the short-term prognosis. Further research is needed to confirm these findings.

Keywords

Middle cerebral artery; Leptomeningeal collateral status; Modified Rankin scale score; Computed tomography angiography; Ischemic stroke

1. Introduction

Globally, stroke is the third leading cause of disability-adjusted life years [1] and imposes serious burdens on families and society. Assessment of collateral circulation is crucial for selecting therapeutic options and predicting prognosis after an acute ischemic stroke (AIS). However, there is a lack of consensus regarding the high-cost performance method for evaluating the leptomeningeal collateral (LMC) status. Meanwhile, there are only few reports on the effect of the LMC status on the prognosis of patients with middle cerebral artery (MCA) stroke without reperfusion therapy. Although there is increasing consensus that the prognosis is better in stroke patients with good collateral circulation [2–4], some controversies remain. Complete circle of Willis collateral circulation has been shown to independently predict functional independence and survival [5]. However, reports on the relationship between circle of Willis integrity and stroke prognosis are inconsistent [6]. Currently, the main methods for evaluating LMCs are digital subtraction angiography (DSA), magnetic resonance angiography (MRA), computed tomography angiography (CTA), and transcranial Doppler ultrasound (TCD). Each method has its own advantages and disadvantages. DSA is the gold standard for evaluating cerebral collateral circulation [7]; however, it is invasive [8], time-consuming, and expensive. Furthermore, TCD cannot directly analyze the morphology of intracranial vessels, and the results of TCD examination are affected by the technical skill of the operator. Although both CTA and MRA are used to evaluate the second-order collateral status of the brain, the anatomical evaluation by CTA is better than that by MRA [6]. LMCs are the main avenues for cerebral perfusion in the MCA blood supply region [9]. Hence, we aimed to evaluate the LMC status using CTA and to assess the effect of LMC status on short-term outcomes in patients with MCA regional AIS.

2. Materials and methods

2.1 Participants

Thirty consecutive patients of Han ethnicity who were hospitalized at the Department of Neurology of the Third Affiliated Hospital of Shenzhen University following an AIS between January 2017 and November 2018 were prospectively enrolled in the study. The National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (MRS) scores were assessed on admission, discharge, and at 3 months after discharge. Of the study participants, 18 had hypertension, 9 had diabetes, 2 had impaired glucose regulation, 13 had hyperlipidemia, 7 had hyperuricemia, 4 had coronary heart disease, and 3 had arrhythmias.

2.2 Selection and exclusion criteria

Patients were included in the study if (1) they met the diagnostic criteria for AIS in the MCA region, as determined by head computed tomography (CT) and magnetic resonance imaging (MRI) [10]; (2) they were admitted to the hospital within one week after the onset of AIS; (3) they had an NIHSS score at admission of <20; and (4) obstruction of the MCA was confirmed in all cases at the time of MRI. Patients were excluded if they (1) had posterior circulation infarction or anterior cerebral artery infarction; (2) had lung, liver, kidney, or heart failure; (3) had a severe infection, peptic ulcer bleeding, or other non-treatable complications; (4) had advanced-stage cancer; and (5) could not cooperate with the examination or face-to-face follow-up.

2.3 Computed tomography angiography image acquisition

Head CTA scans were performed using a Philips 256-slice spiral CT scanner (Philips Company, Amsterdam, Netherlands). Patients were scanned in the supine position with their shoulders sagging as far backward as possible. The patient's head was fixed, and they were instructed to breathe calmly and not to swallow. A double-barrel high-pressure syringe was used to inject a bolus of 50 mL of the non-ionic contrast agent iopaconol (370 mg I/100 mL) through the median elbow vein at a flow rate of 4.5 mL/s, following which, 40 mL of saline was injected at the same rate. Using bolus tracking trigger technology, injections were tracked over a scanning range beginning from the aortic arch to the skull base (including the Willis ring). The scanning direction was from foot to head, and the region of interest was located at the aortic arch with an automatic trigger scanning threshold of 110 HU. Scanning was conducted using a tube voltage of 120 kV, a tube current of 60–200 mAs (automatic milliampere modulation technology), a scanning layer thickness of 0.9 mm, a pitch factor of 0.993, a rotation time of 0.5 s, and a reconstruction interval of 0.9 mm, with a standard reconstruction matrix of 512 $\times$ 512.

2.4 Image post-processing and reconstruction

Using the Philips Extended Brilliance Workspace workstation, Automated Vascular Analysis Software (Philips Company, Amsterdam, Netherlands) was used to automatically reconstruct blood vessels. Post-processing methods included volume rendering, maximal intensity projection (MIP), and volume reconstruction (VR). Processing allowed images to be rotated to any angle to obtain the best view of the lesion. The internal carotid artery and MCA and their branches could be observed and measured. The lumen size, course, and branch details of each segment of MCA could be clearly observed using CTA-MIP, and its results are consistent with those of DSA [11].

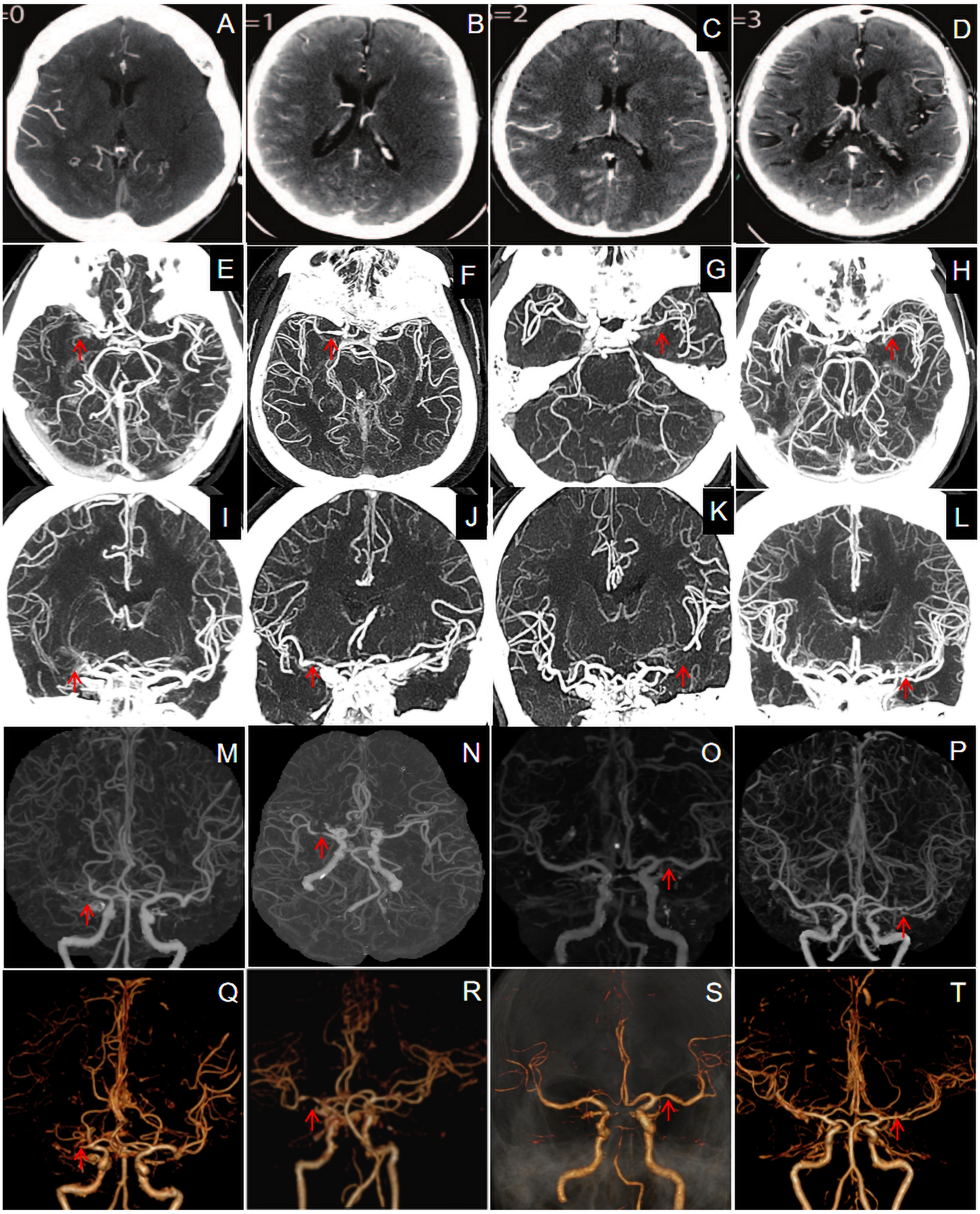
The LMC status for each patient was assessed using 256-slice CTA within 1 week of admission. All patients were examined by the same radiologist, and their LMC status was assessed by the same neurologist based on the Tan score system/MCA regional collateral score [12].

2.5 Assessing LMC status and neurological function

Single-phase CTA with enhanced CT was used for evaluating LMC status using a 0 to 3 scoring system (Fig. 1A–D, Ref. [12], based on the Tan score system). The description of the scoring system is as follows: 0 point, no LMC; 1 point, the leptomeningeal anastomosis collateral pathway filled $<50\%$ of the occlusive blood supply area; 2 points, collateral circulation by leptomeningeal anastomoses filled 50%–99% of the occlusive blood supply area; and 3 points, collateral circulation by leptomeningeal anastomoses filled 100% of the occlusive blood supply area [12]. The poor collateral circulation group was considered to have a score of 0 or 1, while the good collateral circulation group had scores of 2 and 3. To confirm the results of single-phase CTA with enhanced CT evaluation, LMC status was evaluated with CTA-MIP (Fig. 1E–L), three-dimensional MIP (Fig. 1M–P), and VR (Fig. 1Q–T). The NIHSS and the MRS were used to assess the neurological function. Patients were divided into a good prognosis (MRS $\leq$2) group and a poor prognosis (MRS $>$2) group. All MRS scores were determined by face-to-face interviews by specialists trained in the use of the scale.

2.6 Treatment of AIS

All patients were routinely treated with antiplatelet medication (aspirin or clopidogrel), cholesterol-reducing medication (atorvastatin or rosuvastatin), medication for control of blood pressure and blood sugar, and rehabilitation exercises for limb dysfunction.



F I G U R E 1. Leptomeningeal collateral (LMC) status score assessed using enhanced computed tomography based on the Tan score system: (A) 0 point; (B) 1 point; (C) 2 points; (D) 3 points [12]. LMC status assessed using axial (E–H) and coronal (I–L) maximal intensity projection (MIP) corresponds to the Tan score system; LMC status assessed using three dimensional MIP (M–P) and multi-plane volume reconstruction (Q–T) corresponds to the Tan score system. The red arrows all point to the middle cerebral artery stenosis.

2.7 Statistical methods

Data were collected from electronic medical records. The integrity and consistency of the data were checked manually and the data were stored in a study database. SAS (SAS Institute Inc., Cary, NC, USA) 9.0 was used to perform the data analysis. Variables that conformed to a normal distribution were expressed as the mean ± the standard deviation. Between-group differences were assessed using two-sample *t*-tests. The correlation between neurological function recovery and the LMC status score was analyzed using Pearson correlation analysis. The chi-square test was used to analyze the differences in prognosis among the various LMC status groups. For all analyses, $p < 0.05$ was considered statistically significant.

3. Results

This study included 17 males and 13 females aged 31–86 years (mean age, 62.65 ± 11.78 years). The AIS focus of all the patients was in the MCA blood supply area, the watershed of MCA and anterior cerebral artery, and the watershed of

TABLE 1. Relationship between leptomeningeal collateral status and NIHSS score difference at discharge and admission.

Leptomeningeal collateral status score at admission*	NIHSS score at admission$	NIHSS score at discharge&	NIHSS score difference at discharge and admission#
1.62 ± 1.16	7.74 ± 4.96	4.39 ± 4.29	3.76 ± 3.17

*Note: There was a correlation between # and *; Pearson correlation (r = 0.8844, p < 0.05); p-values were determined by t-tests, $ and & p = 0.03 < 0.05.*

TABLE 2. Patient NIHSS/MRS scores disaggregated by leptomeningeal collateral status.

Grouping (number)	NIHSS score at admission	NIHSS score at discharge	NIHSS score at 3 months after discharge	MRS score at 3 months after discharge
Tan score system 0–1 Group (15)	$7.60 \pm 5.56^{\$}$	$5.59 \pm 4.65^{*}$	$4.31 \pm 3.69^{\#}$	$1.91 \pm 1.65^{\&}$
Tan score system 2–3 Group (19)	$7.91 \pm 5.96^{\$}$	$3.01 \pm 4.03^{*}$	$2.16 \pm 3.21^{\#}$	$1.03 \pm 1.36^{\&}$
p-values	$0.4389^{\$}$	0.0464^{*}	$0.0394^{\#}$	$0.0489^{\&}$

*Note: p-values were determined using t-tests; $ > 0.05, *, # and & are all <0.05.*

the posterior cerebral artery and MCA. In the poor collateral circulation group (n = 15), 10 patients had basal ganglia infarction and 13 patients had cortical or subcortical infarction of the frontal, parietal, and temporal lobes. In the good collateral circulation group (n = 19), 15 patients had basal ganglia infarction and 18 patients had cortical or subcortical infarction of the frontal, parietal, and temporal lobes. No significant difference was noted in the number and location of lesions between the two groups (all $p < 0.05$). There was a significant association between the LMC status and the change in NIHSS score difference between admission and discharge ($p = 0.03$, Table 1, Pearson correlation (r) = 0.88). Three months after discharge, the MRS scores in the poor (MCA territory collateral score 0–1) and good LMC status (MCA territory collateral score ≥ 2) groups were 1.91 ± 1.65 and 1.03 ± 1.36 (Fig. 2), respectively ($p = 0.0394$, Table 2). NIHSS scores at 3 months after discharge in the poor (MCA territory collateral score 0–1) and good LMC status (MCA territory collateral score ≥ 2) groups were 4.31 ± 4.29 and 2.16 ± 2.06 (Fig. 3), respectively ($p = 0.0489$, Table 2).

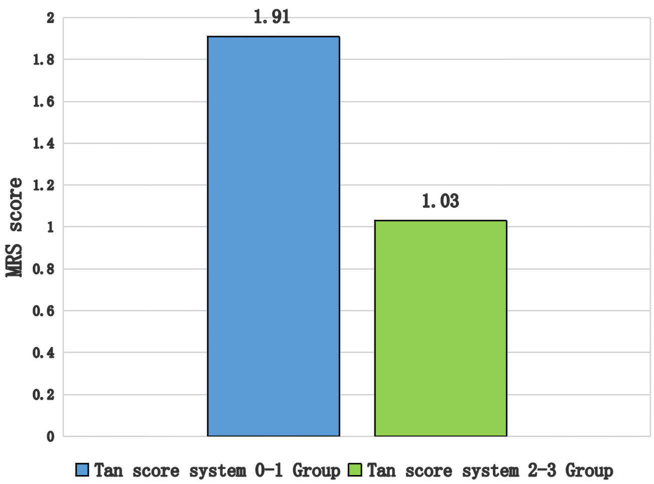


FIGURE 2. Modified Rankin Scale scores at 3 months after discharge among the different leptomeningeal collateral status groups ($p < 0.05$).

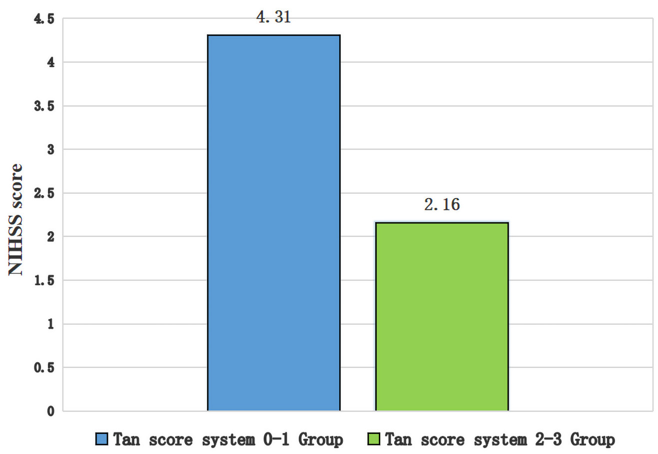


FIGURE 3. National Institutes of Health Stroke Scale scores at 3 months after discharge among the different leptomeningeal collateral status groups ($p < 0.05$).

4. Discussion

Our study data suggest that better LMC status is associated with better short-term clinical prognoses in patients with a cerebral infarction in the MCA region. Based on the MCA regional collateral scoring method, 256-slice single-phase CTA-MIP provided a good assessment of LMC status in patients with acute MCA regional infarction.

Collateral flow is the basis for AIS treatment, since neurons will only survive long enough to be rescued by reperfusion therapies if there is a sufficient collateral flow [13]. Blood supply to the brain is secured by an extensive collateral circulation system. Cerebral collateral circulation can be divided into 3 levels: first-order collateral circulation (Willis ring), second-order collateral circulation (leptomeningeal collaterals, ophthalmic artery), and third-order collateral circulation (collateral branches by neovascularization). The first-order cerebral collateral circulation (Willis ring) grows quickly, but with a development integrity rate of only 13% [14]. The brain tissue in the cerebral ischemic penumbra may develop ischemic necrosis before the growth of third-order cerebral collateral circulation. Second-order collateral circulation may compensate in time with cerebral perfusion in ischemic areas. MCA involvement accounts for about 70% of the stenosis or occlusion of intracranial arteries [8], and an assessment of the collateral circulation might help predict clinical results after recanalization in patients undergoing endovascular treatment for AIS [15]. Hence assessment of MCA regional LMC is crucial.

This study shows that 256-slice single-phase CTA-MIP provided a good assessment of LMC status in patients with acute MCA regional infarction. In this study, we considered that the three-dimensional MIP (Fig. 1M–P) and CT multi-plane VR (Fig. 1Q–T) have partial information distortion of the LMC circulation, indicating that the VR and three-dimensional MIP cause omissions of the LMC circulation. The original MIP image (Fig. 1E–L) can reflect more realistic information of the LMC circulation. In stroke patients, CTA can further be used for evaluating LMC opening and collateral flow [16]. In multiphase CTA scans, patients receive a greater dose of radiation than that in single-phase CTA. A previous study [17] used single-phase CTA-MIP to evaluate collateral circulation and prognosis of acute MCA occlusion in cerebral infarction. The total extent of collateral flow was best visualized using MIP [18]. The lumen size, course, and branch details of each MCA segment can clearly be visualized using CTA-MIP, and the results obtained are highly consistent with those of DSA [11]. This study found that LMC status could be successfully evaluated using 256-layer single-phase CTA-MIP, the CTA-MIP could distinguish different levels of LMC status, and the morphology of leptomeningeal collaterals could easily be identified during the clinical evaluation.

This study also demonstrated that better LMC status is associated with better short-term clinical prognoses in patients with AIS in the MCA region. The NIHSS score change between admission and discharge was correlated with the LMC status on admission. Three months after discharge, the neurological status of the good LMC group was better than that of the poor LMC group. One study [9] demonstrated that LMC opening is the main mechanism of collateral circulation in cerebral infarction in the MCA blood supply area. Poor LMC status is independently associated with greater cerebral edema at 24 hours after AIS in patients who have undergone reperfusion treatment [19]. Good LMC status predicts a favorable outcome in patients who have undergone intra-arterial treatment [20]. The status of the leptomeningeal collaterals can not only affect the clinical efficacy, but also estimate prognosis of patients with AIS.

This was a single-center study, and participation was restricted to patients with acute MCA infarction. Thus, the generalizability of our study conclusions is limited. We hope to further increase the sample size and conduct multi-center and long-term follow-up studies.

5. Conclusions

Our findings can further reinforce the understanding of the appropriate assessment of LMC and its clinical value. Based on the MCA regional collateral scoring method, 256-slice single-phase CTA-MIP provided a good assessment of LMC status in patients with acute MCA regional infarction. LMC status may independently predict the short-term recovery of neurological function in patients with acute MCA regional infarction. Further research is needed to confirm these findings.

AUTHOR CONTRIBUTIONS

LC, LR and HJ—designed the study, performed the research, wrote the manuscript and revised the manuscript. JL—performed the research, provided advice on the discussion. GQ and FC—provided some constructive opinions. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study design was approved by the ethics review board of The Third Affiliated Hospital of Shenzhen University (No: 2019-SZLH-LW-004). Informed consent was obtained from all included participants.

ACKNOWLEDGMENT

We would like to thank Editage [www.editage.cn] for English language editing.

FUNDING

This study was supported by Shenzhen city of science and technology planning projects (No. JCYJ20180507184647636 and KJYY20180703165202011), Shenzhen healthcare research project (SZLY2017012) and Shenzhen medical cure and prevention integration program of nervous system disease. The funders provided the article processing charge for this study, but had no other role.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

CONSENT FOR PUBLICATION

We obtained written consent for publication from the patients.

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How to cite this article: Liming Cao, Lijie Ren, Hongliang Jiang, Jiahua Li, Guozhen Qiu, Feng Chi. Assessment of leptomeningeal collateral status using single-phase computed tomography angiography and its clinical value. Signa Vitae. 2023; 19(1): 130-135. doi: 10.22514/sv.2021.234.