

Access this article online

Quick Response Code:



Website:

http://www.braincirculation.org

DOI:

10.4103/bc.bc_55_19

Regional leptomeningeal collateral score by computed tomographic angiography correlates with 3-month clinical outcome in acute ischemic stroke

D Chatterjee, K Nagarajan, Sunil K Narayan¹, R Lakshmi Narasimhan²

Abstract:

PURPOSE: The aim of the study is to assess the correlation between regional leptomeningeal collateral (rLMC) Scores calculated on computed tomography (CT) angiography following acute anterior circulation ischemic stroke, with 3-month clinical outcome measured as modified Rankin Scale (mRS) and Barthel Index (BI).

MATERIALS AND METHODS: A total of thirty patients were studied as per the exclusion and inclusion criteria and after informed consent. Multi-phase CT angiography was carried out within 24 h of stroke onset, and collateral scoring was done using rLMC score along with Alberta stroke programme early CT (ASPECT) scoring. At 3 months, patients were followed up to evaluate the clinical outcome using mRS and BI. Statistical analysis was performed to find out the correlation between rLMC score, ASPECT score, and clinical outcome and for association with demographic parameters and stroke risk factors.

RESULTS: A strong correlation was noted between ASPECT and rLMC scores ($P < 0.001$) and between rLMC scores and clinical outcome at 3 months (mRS and BI). Correlation with mRS ($P < 0.001$) was nearly as strong as that of BI on follow-up ($P < 0.001$). The ASPECT score also was a predictor of clinical outcome and showed correlation with mRS ($P < 0.001$) and BI ($P < 0.001$). No significant association was found between various stroke risk factors and demographic parameters with rLMC scores. The rLMC scoring system showed substantial inter-rater reliability with Kappa = 0.7.

CONCLUSIONS: rLMC score in CT angiography correlates with ASPECT Score and clinical outcome at 3 months. Hence, this scoring system can be used for collateral quantification as may be of use in predicting short-term clinical outcomes.

Keywords:

Collateral circulation, computed tomography angiography, ischemic stroke, regional leptomeningeal collateral score

Introduction

The therapeutic decision-making in patients presenting with acute ischemic stroke (AIS) is greatly influenced by ascertainment of prognosis, which, in turn,

depends on the vulnerability of the brain tissue to ischemia. This decision-making is based on information obtained from clinical and radiologic assessments. Status of collateral blood vessels is one such important radiological parameter. Following the onset of ischemic stroke, survival of the brain tissue distal to an arterial occlusion is dependent on the

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Chatterjee D, Nagarajan K, Narayan SK, Narasimhan RL. Regional leptomeningeal collateral score by computed tomographic angiography correlates with 3-month clinical outcome in acute ischemic stroke. *Brain Circ* 2020;6:107-15.

Departments of
Radio-Diagnosis and
¹Neurology, Jawaharlal
Institute of Postgraduate
Medical Education and
Research, Puducherry,
²Department of Neurology,
Institute of Neurology,
Madras Medical College
and Rajiv Gandhi
Government General
Hospital, Chennai,
Tamil Nadu, India

Address for correspondence:

Dr. K Nagarajan,
Department of
Radio-Diagnosis,
Jawaharlal Institute of
Postgraduate Medical
Education and Research,
Puducherry - 605 006,
India.
E-mail: lknagarajan1@
gmail.com

Submission: 27-11-2019

Revised: 27-12-2019

Accepted: 19-03-2020

Published: 26-06-2020

status of leptomeningeal collateral (LMC) pathways. These are small arteriolar connections between the terminal branches of larger cerebral vessels which open up following any proximal occlusion. It has been postulated that for any occlusion distal to the circle of Willis, tissue viability is dependent on blood flow via LMC pathways.^[1,2] A regional LMC score (rLMC score) has been devised based on the findings derived from multi-phase computed tomographic (CT) angiography. The rLMC score is a semi-quantitative system of scoring the pial collaterals, which is based on the major anatomic regions of anterior circulation of the brain, which have been delineated in accordance with the Alberta stroke programme early CT score (ASPECTS) method of scoring head CT.^[3-5] AIS interventions, either pharmacological or mechanical, have become a standard form of treatment in ischemic stroke patients within 6–8 h (extendable up to 24 h) of ictus. However, based on the tissue viability and vascular imaging, the modern trend is to extend this window to longer periods. The need for several invasive interventions will depend on the perceived outcome, and the degree of collateral circulation is an important factor which determines this. In this context, an objective assessment of rLMC scoring system will be essential and hence, the need to standardize rLMC scoring system and to determine its association with the outcome of stroke. The objective of this study was to correlate the rLMC score with the 3-month clinical outcome (modified Rankin Scale [mRS] and Barthel Index [BI]) in patients with M1 middle cerebral artery (MCA) and/or internal carotid artery (ICA) occlusion in AIS and also to evaluate the factors associated with baseline rLMC scores in AIS in the study population.

Materials and Methods

We conducted a prospective analytical study. A total of thirty patients with AIS were included in the study. All consecutive patients fulfilling the inclusion and exclusion criteria were included in the study.

Inclusion criteria

Patients of age >18 years with AIS who are diagnosed to have M1 MCA and/or ICA occlusion on multi-phase CT angiography within 24 h of the episode and who came for clinical follow-up for 3 months.

Exclusion criteria

Patients with known renal impairment, any hypersensitivity to CT contrast agents, any contraindication to radiation exposure, inability to give informed consent to the study by the patient/legally responsible attendant, those who are clinically unstable to withstand CT angiography, such as severe hypotension, on artificial ventilation, etc.

Study procedure

Patients presenting to the emergency medical services with AIS within 24 h of the episode were recruited in the study after obtaining informed consent and as per the inclusion/exclusion criteria. The clinical features were documented including patients' demographic factors such as age and gender, risk factors such as diabetes, hypertension, previous history of TIA or strokes, smoking, and alcoholism in the pro forma.

Imaging protocol

Standard nonenhanced CT of the brain was obtained within 24 h of the stroke episode followed by multi-phase CT angiography. Aortic arch to vertex CT angiography performed with helical technique using a multidetector CT scanner (Philips Brilliance 6 slice CT scanner, Philips Medical Systems, Netherlands) made up the first phase. Image acquisition was timed to occur during the peak arterial phase in the healthy brain and was triggered by bolus monitoring. Region of interest was kept at the arch of aorta. The remaining two phases from the skull base to the vertex were acquired in the equilibrium/peak venous and late venous phases. CT acquisition parameters were as follows: section thickness 1 mm at 120 kV and 175 mAs (collimation 6 × 1.5, rotation time 0.5 s, and pitch factor 1.389). A total of 60–80 ml of nonionic contrast agent was injected at a rate of 3 ml/s using a power injector. The CT angiogram so obtained was evaluated to obtain the rLMC and ASPECTS scores [Table 1]. rLMC score 0 indicates collateral artery is not seen, score 1 indicates artery is less prominent, and score 2 indicates artery is equal or more prominent when compared to the corresponding region in the contralateral hemisphere. In case of Sylvian sulcus, the scoring was done as 0 for artery not seen, 2 for artery less prominent, and 4 for artery equal or more prominent, when compared to opposite hemisphere. As these vessels are most distant from leptomeningeal ACA to MCA and

Table 1: Alberta stroke programme early computed tomographic score and Regional Leptomeningeal Collateral scores evaluated on computed tomography angiography

Aspects		rLMC score	
Caudate	/1	Sylvian sulcus	/4
Lentiform	/1	Basal ganglia	/2
Internal capsule	/1	M1	/2
Insula	/1	M2	/2
M1	/1	M3	/2
M2	/1	M4	/2
M3	/1	M5	/2
M4	/1	M6	/2
M5	/1	ACA	/2
M6	/1		
Total	/10		/20

rLMC: Regional Leptomeningeal Collateral score, CT: Computed tomography, ACA: Anterior cerebral artery, ASPECTS: Alberta stroke programme early computed tomographic score

PCA to MCA anastomoses, their opacification is a strong indicator of good retrograde flow via these collateral networks. Centricity Universal Viewer version 6 (GE Healthcare, Milwaukee, USA) image processing software, designed for multiplanar reconstruction and volume rendering, was used to reconstruct images in axial, coronal, and sagittal planes in 40-mm-thick slabs. The rLMC scores were obtained on these images [Figures 1 and 2]. The equilibrium or early venous-phase images were chosen for rLMC score calculation to ensure adequate time for retrograde opacification of the LMC-dependent slower filling MCA branches distal to the M1 occlusions. These rLMC scores were obtained by two radiologists (one of them, a third-year radiology trainee and an experienced neuroradiologist with 12 years of experience). The patients were prospectively followed up after 3 months in the

stroke clinic to assess the clinical outcome using the mRS and BI. Following this, the correlation of rLMC scores with ASPECTS scores and 3-month clinical outcome was determined. The demographic parameters and stroke risk factors that were evaluated in this study include age, sex, diabetes, hypertension, previous history of TIA or stroke, and smoking. These demographic variables and stroke risk factors were evaluated for any association with rLMC score.

Statistical analysis

rLMC score was trichotomized as poor (0–10), medium (11–16), and good (17–20), according to the study conducted by Menon *et al.*^[4] The ASPECTS^[3] score was categorized as low (0–7) and high (7–10). The mRS score was categorized as good (mRS 0–2) and poor outcome (mRS 3–6). The BI was categorized as total dependence (0–20), severe dependence (21–60), moderate dependence (61–90), and slight dependence (91–100).^[6] Inter-rater reliability in the assessment of rLMC scores was analyzed using Kappa statistics. Spearman's correlation was used for exploring associations between rLMC score, ASPECTS score, mRS, and BI. $P < 0.05$ was considered statistically significant. Univariate analysis was done to look for any association between confounding demographic parameters and stroke risk factors and rLMC scores.

Table 2: Relationship of Regional Leptomeningeal Collateral score and Alberta stroke programme early computed tomographic score

	rLMC score (%)			Total (%)
	Poor	Medium	Good	
High ASPECTS (>7)	0 (0)	3 (50)	3 (50)	6 (100)
Low ASPECTS (≤7)	11 (45.8)	9 (37.5)	4 (16.7)	24 (100)
Total	11	12	7	30

rLMC: Regional Leptomeningeal Collateral score

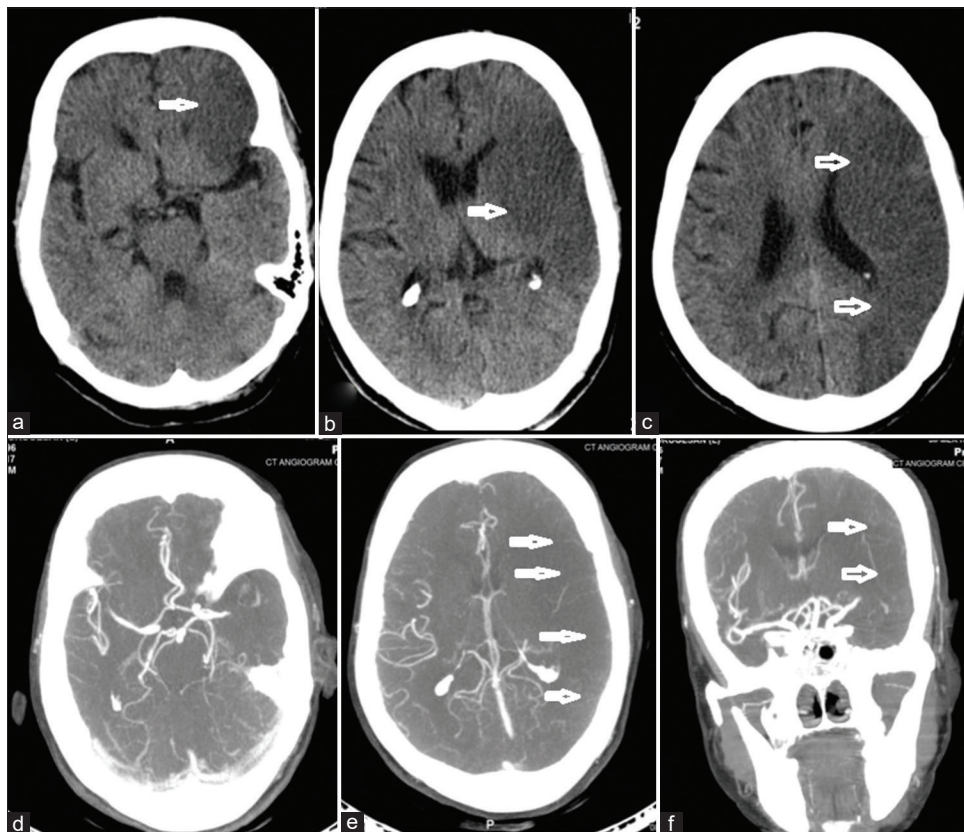


Figure 1: Axial noncontrast computed tomography sections (a-c) show a large acute infarct in the left middle cerebral artery territory (arrows). Alberta stroke programme early computed tomographic score was 3. Computed tomography angiography axial (d and e) and coronal (f) sections show abrupt cutoff of M1 segment of the left middle cerebral artery with paucity of collaterals in the left cerebral hemisphere as compared to the opposite side (arrows in e and f). The Regional Leptomeningeal Collateral score was 6

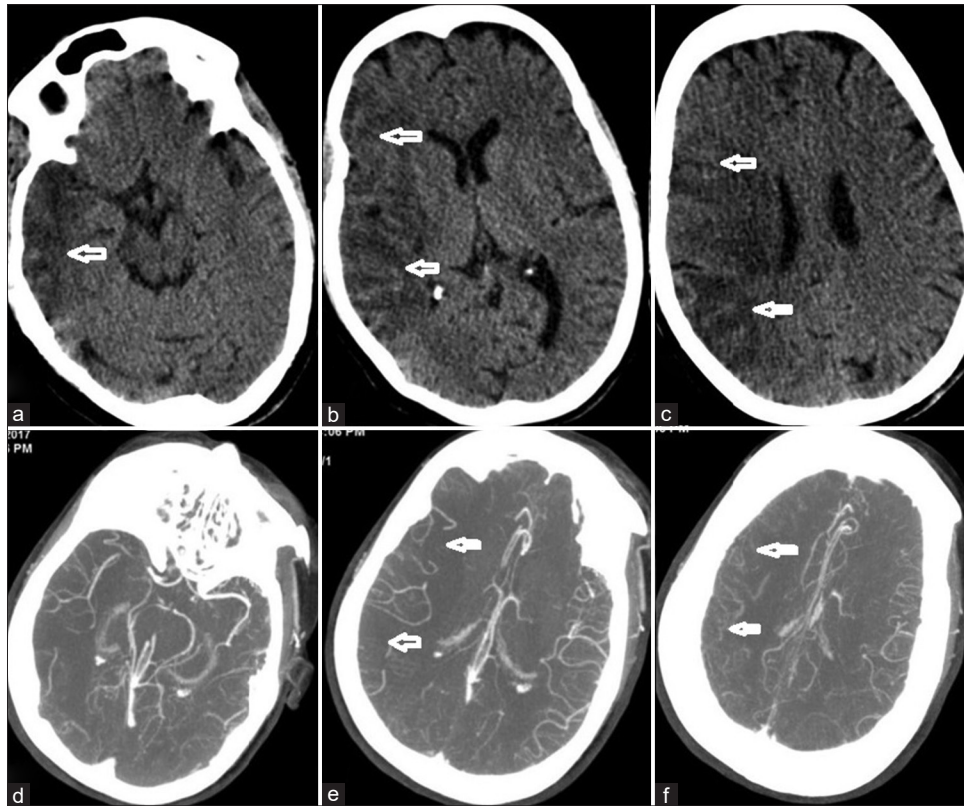


Figure 2: Axial noncontrast computed tomography sections (a-c) show a large acute infarct in the right middle cerebral artery territory (arrows). Alberta stroke programme early computed tomographic score was 4. Computed tomography angiography axial sections (d-f) show abrupt cutoff of M1 segment of right middle cerebral artery with moderate collateralization in the right cerebral hemisphere as compared to the opposite side. The Regional Leptomeningeal Collateral score was 16

Results

A total of thirty patients were included in the study. The statistical analysis was carried out using SPSS (Statistical Package for Social Sciences) version 20.0 (IBM, New York, USA).

Age distribution

The minimum age of patients included in the study was 21 years and maximum age was 86 years. The mean age was calculated to be 47 years, with a standard deviation of 15.9.

Sex distribution

Among the included patients in our study, the number of males was 19 (63.3%) and number of females was 11 (36.7%).

Site of occlusion

Nineteen (63.3%) patients had M1 MCA occlusion and the remaining 11 (36.3%) patients had intracranial ICA ± MCA occlusion.

Alberta stroke program early computed tomographic score

In our study, six (20%) patients had a high ASPECTS score and the remaining 24 (80%) patients had a low ASPECTS score at the time of presentation.

Regional Leptomeningeal Collateral score

The rLMC score was trichotomized into poor (0–10), moderate (11–16), and good (17–20).^[4] In our study, 7 (23.3%) patients had good score, 12 (40%) patients had medium score, and the remaining 11 (36.7%) patients had poor rLMC scores. Of the 19 patients with MCA occlusion, six patients had a good rLMC score, 5 had moderate, and 8 had a poor score. Of the 11 patients with intracranial ICA ± MCA occlusion, 7 had a medium score, 3 had poor score, and only one patient had a good rLMC score. There was no statistically significant association between rLMC score and site of occlusion ($P = 0.11$, >0.05). Of the six patients with ASPECTS score >7 , three patients had a good rLMC score, 3 had medium, and none had a poor score [Table 2]. Of the 24 patients with ASPECTS ≤ 7 , 11 had a poor score, 9 had medium score, and 4 had a good rLMC score. There was a positive correlation between rLMC score and ASPECTS score (Spearman's $\rho = 0.8$, bias-corrected 95% confidence interval [CI] = 0.7–0.9; $P < 0.001$) [Figure 3]. On performing univariate analysis, no significant association was found between various stroke risk factors and demographic parameters with rLMC scores.

Inter-rater reliability of Regional Leptomeningeal Collateral score

The rLMC score for CT angiography (CTA) was assigned for each patient by two independent

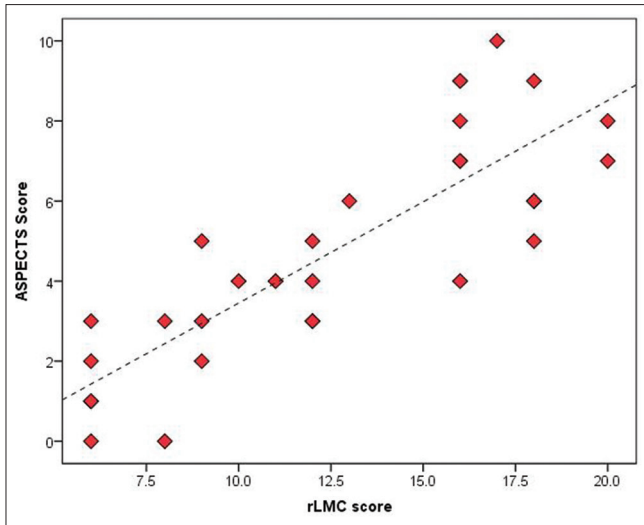


Figure 3: Scatter diagram showing correlation between Regional Leptomeningeal Collateral score and Alberta stroke programme early computed tomographic score

radiologists. The inter-rater reliability using kappa statistics showed statistically significant reliability with $\text{Kappa} = 0.7$ ($P < 0.001$).

Modified Rankin Scale score

The mRS was categorized into good (0–2) and poor outcomes (3–6). Out of the thirty patients included in our study, 12 (40%) patients had a good outcome and 18 (60%) patients had a poor outcome [Table 3]. Of the 12 patients with mRS score 0–2, five patients had a good rLMC score, 7 had medium, and none had a poor score. Of the 18 patients with mRS score 3–6, 11 had a poor score, 5 had a medium score, and 2 had a good rLMC score. There was a significant correlation between rLMC score and mRS score (Spearman’s rho = -0.80 , bias-corrected 95% CI = -0.9 to -0.5 ; $P < 0.001$). There was a significant correlation between ASPECTS score and mRS with Spearman’s rho = -0.75 (bias-corrected 95% CI = -0.8 to -0.5 ; $P < 0.001$) [Figure 4].

Barthel Index

BI was categorized into total dependence (0–20), severe dependence (21–60), moderate dependence (61–90), and slight dependence (91–100).¹⁶ Of the thirty patients included in our study, 1 (3.3%) was totally dependent, 10 (33.3%) were severely dependent, 19 (63.3%) were moderately dependent, and none were slightly dependent on follow-up [Table 4]. One patient was totally dependent on follow-up and had a poor rLMC score. Of the ten patients with BI 21–60, eight patients had a poor rLMC score, 2 had medium, and none had a good score. Of the 19 patients with BI 61–90, 2 had a poor score, 10 had medium score, and 7 had a good rLMC score. There was a significant association between rLMC score and BI (Spearman’s rho = 0.82 , bias-corrected 95% CI = 0.5 – 0.9 ; $P < 0.001$) [Figure 5]. There was a significant

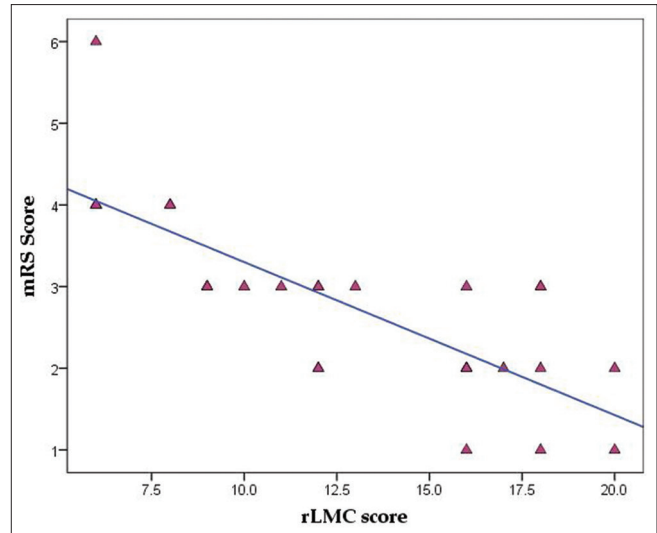


Figure 4: Scatter diagram showing correlation between Regional Leptomeningeal Collateral score and modified Rankin Scale score

Table 3: Correlation between Regional Leptomeningeal Collateral score and modified Rankin Scale score

	rLMC score (%)			Total (%)
	Poor	Medium	Good	
Good mRS score (0-2)	0 (0)	7 (58.3)	5 (41.7)	12 (100)
Poor mRS score (3-6)	11 (61.1)	5 (27.8)	2 (11.1)	18 (100)
Total	11	12	7	30

mRS: Modified Rankin Scale, rLMC: Regional Leptomeningeal Collateral score

Table 4: Correlation of Regional Leptomeningeal Collateral score with Barthel Index

	rLMC score (%)			Total (%)
	Poor	Medium	Good	
Totally dependent	1 (100)	0 (0)	0 (0)	1 (100)
Severely dependent	8 (80)	2 (20)	0 (0)	10 (100)
Moderately dependent	2 (10.5)	10 (52.6)	7 (36.8)	19 (100)
Total	11	12	7	30

rLMC: Regional Leptomeningeal Collateral score

correlation between ASPECTS score and BI (Spearman’s rho = 0.8 , bias-corrected 95% CI = 0.6 – 0.8 ; $P < 0.001$).

Discussion

Collateral circulation refers to an alternate route of blood supply, bypassing a blocked artery or vein via nearby minor vascular channels. The LMCs are an auxiliary network of small blood vessels that act as anastomotic channels between major vascular territories in conditions where cerebral blood flow is pathologically altered. These subsidiary collateral pathways remain closed in physiological conditions, but they open up when collateral flow through the circle of Willis is inadequate.¹⁷ Collateral vessels predominantly develop in the prenatal

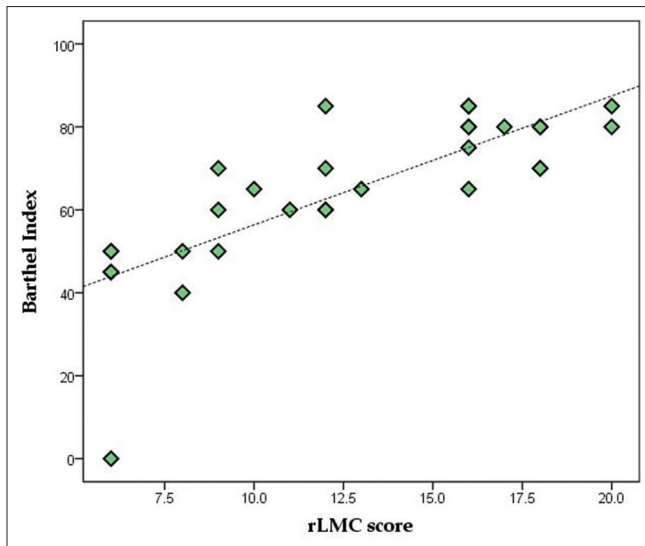


Figure 5: Scatter diagram showing correlation between Regional Leptomeningeal Collateral score and Barthel Index

period. In usual circumstances, intracranial vascular occlusions cause collateral blood supply to occur through large vessels, which are medium-sized arteries forming the circle of Willis. LMCs are pial-based vascular channels which act as small connecting arteries between the terminal cortical branches of major cerebral arteries along the surface of the brain.^[8] Heubner first discovered the existence of LMCs in cadaveric brains.^[7] Fay suggested that LMCs were “points of fusion” in the peripheral zones of MCA, ACA, and PCA.^[1] Other studies have described LMCs as a continuous vascular network in the brain with interconnections at the capillary, arteriolar, and pial artery level.^[9]

Modern imaging modalities such as conventional cerebral angiography, CTA, and magnetic resonance imaging have given us considerable insight regarding the role of LMCs in preserving brain tissue until recanalization is achieved. Like other collaterals, these vessels are dormant under physiological conditions when there is unimpeded blood flow from all major cerebral arteries, but are recruited when any one major artery is either chronically or acutely occluded. LMCs of varying numbers have been noted in nearly 80% of the patients with acute MCA occlusion in CTA images obtained within few hours of stroke. In humans, LMCs have been found to show considerable variation in their distribution, size, number, and compensatory capacity in ischemic stroke.^[10] Taking into account the inter-individual variability in the magnitude of collaterals, multiple collateral scoring systems have been devised. These LMC scoring systems have been calculated based on CTA, and they have shown potential in predicting clinical outcomes. One major limitation of these scoring systems is that they do not consider into account the considerable regional variability in

the presence of these intercommunicating arteries. Furthermore, there is nonuniformity in the CTA-based imaging protocols used in various studies.^[4] Hence, with a robust scoring system and optimal imaging protocols, it is possible to achieve standardization in the assessment of LMCs. This will lead to better understanding of the physiology of LMCs in AIS related to their mechanism of action and temporal profile of their development and enhance our existing knowledge regarding the preferable modes of delivery of thrombolytic drugs.

The rLMC score is based on the extent of contrast opacification of pial and lenticulostriate arteries distal to an M1 MCA ± ICA occlusion on CTA. It is semi-quantitative and is based on the major anatomic regions of the anterior circulation in the brain, which have been delineated in accordance with the ASPECTS method of scoring head CTs.

Saito *et al.*,^[11] way back in 1987, studied the site of occlusion and the findings on CTA of forty cases with MCA occlusion and correlated the findings with the 3-month clinical outcome. They studied serial carotid angiograms obtained within 24 h after stroke onset to assess the conduction time of contrast medium from the Carotid siphon (IC) to M2 MCA through the anterior cerebral arteries and LMCs. In cases with IC–M2 time of <5 s, it was found that extensive CT hypodensity did not develop. Qureshi^[12] devised a formal grading scheme for angiographic evaluation of LMCs in acute stroke patients before and after intra-arterial thrombolysis based on the anatomic location of occlusion and presence of LMC pathways in the affected distribution. The pre- and post-thrombolysis angiograms were independently graded, and it was found that interobserver agreement was higher using this angiographic grading and correlated with 7-day mortality. Higashida *et al.*^[13] proposed another new 5-point grading system for scoring of collaterals on Digital Subtraction Angiography based on the extent and delay of retrograde filling (ASITN/SIR collateral grade scale) to provide a semi-quantitative assessment of collateral status. Kim *et al.*^[14] evaluated the baseline cerebral angiograms of 42 patients enrolled in the PROACT II Trial for the degree of regional collateral circulation. A 4-point scale was used to grade the LMCs using ASPECTS model. Collateral grade on baseline angiography moderately predicted final infarct volume and good correlation with follow-up NIHSS scores for those who received thrombolysis, but not for control patients.

Christoforidis *et al.*^[15] carried out conventional angiography and described five grades of collateral reperfusion considering the position of the last reperfused arterial segment in relation to the site of occlusion. It was found that both infarct volume and

discharge mRS scores were significantly lower for patients with better pial collateral scores regardless of the success of recanalization after thrombolysis independent of other predictive factors. Miteff *et al.*^[16] studied whether collateral vessel status, as seen on CTA, can predict the fate of penumbral tissue identified on perfusion CT and thereby influence clinical outcome. It was found that good collateral status (51/92) was significantly associated with reduced infarct expansion and more favorable functional outcomes (mRS 0–2) and concluded that in proximal vessel occlusion, perfusion CT mismatch and good collateral status are critical determinants associated with favorable clinical outcome, particularly if major reperfusion occurs. Maas *et al.*^[17] prospectively studied 741 patients with CTA for AIS. Leptomeningeal collaterals in the affected hemisphere were graded in comparison to that in the normal contralateral hemisphere. Between cases and controls, patients with adequate collaterals had similar clinical outcomes. They found that patients with poor Sylvian leptomeningeal collateralization had worse clinical outcomes when compared with controls. They also showed a temporal relationship in the recruitment of collaterals, with nearly three-fourths collaterals activated within the first of stroke and a slower secondary recruitment of collaterals then happens, which may extend till 24 h. The rLMC system also provides higher score for good Sylvian collaterals taking into account the regional importance of Sylvian fissure LMCs.

Tan *et al.*^[18] proposed two novel grading systems: the Clot Burden Score (CBS) to define the extent of thrombus and Collateral Score (CS) for scoring the pial collaterals and correlated them with the 3-month clinical outcome. They found that patients with higher CBS and CS demonstrated smaller pretreatment perfusion defects and final infarct volume and better clinical outcome. Their collateral scoring system was confined only to MCA territory and was not based on ASPECTS model.

It was Menon *et al.*^[4] who proposed the new 20-point scoring system called the rLMC score on multi-phase CTA as a strong and reliable imaging predictor of good clinical outcomes in acute anterior circulation ischemic strokes. They retrospectively studied 138 patients with AIS and M1 MCA ± intracranial ICA occlusions. The rLMC score was based on scoring pial and lenticulostriate arteries (0 = no artery seen; 1 = artery less prominent; and 2 = artery equal or more prominent compared with matching region in opposite hemisphere) in six ASPECTS regions (M1–6) plus anterior cerebral artery region and basal ganglia. Pial arteries in the Sylvian sulcus are scored 0, 2, or 4. Good clinical outcome was defined as mRS ≤ 2 at 90 days after the stroke episode. It was found that 37.6% had a good (17–20), 40.5% a medium (11–16), and 21.7% a poor (0–10) rLMC score. Higher total scores

indicated better collateralization. Interrater reliability was high, with an intraclass correlation coefficient of 0.87. Good rLMC score was found to be an independent predictor of 3-month good clinical outcome, along with age (<80 years), baseline ASPECTS (≥ 8), and CBS (≥ 8). The investigators could not find any single vascular risk factor that was associated with the presence of poor rLMCs. It was concluded that the rLMC score is a strong imaging parameter on CTA for predicting clinical outcomes in patients with AISs.

Leng *et al.*^[19] performed a systematic review and meta-analysis of the pretreatment role of collaterals in predicting the efficacy and safety of endovascular treatment in AIS and concluded that good pretreatment collateral status is significantly associated with favorable functional outcome and lower rates of symptomatic intracranial hemorrhage and mortality in patients with AIS undergoing endovascular therapies.

Various CTA-based studies have shown that collateral status predicts clinical outcome.^[16,17] The rLMC score is a less subjective ordinal scale for scoring collaterals, and all areas of anterior circulation are taken into consideration. Though rLMC scoring systems are in the evolving stage and the question of the best method for evaluation of collaterals is yet to be answered, the evaluation of LMCs using any of the scoring system should probably part of the CT imaging in AIS.^[20] The currently proposed methods of assessing collaterals are still somewhat semi-quantitative, and this might have a bearing on the overall underappreciation of the fundamental role of collateral circulation in clinical outcomes following AIS.

We included thirty patients with anterior circulation AIS in our study, who presented to the hospital within 24 h of onset and underwent CTA for collateral assessment with rLMC scoring system. Collateral recruitment can occur till 24 h after stroke onset as suggested by Maas *et al.*^[17] Our results support the findings of Ryu *et al.*^[21] that ASPECTS is a good independent predictor of clinical outcome because there was a statistically significant correlation with mRS and BI ($P < 0.001$). There was a significant correlation between the rLMC score at baseline and 3-month clinical outcomes. Correlation with mRS was as strong as that of BI on follow-up. The scoring system also showed a high inter-rater reliability (kappa = 0.7 with $P < 0.001$). The rLMC score also showed a good correlation with baseline ASPECTS with a Spearman's rho of 0.8. This is in agreement with the study conducted by Miteff *et al.*^[16] which concluded that good collateral status correlates well with reduced infarct volumes. Higher ASPECTS scores were also a strong predictor of good clinical outcome and showed good correlation with mRS ($P < 0.001$) and

BI ($P < 0.001$). Our study corroborates the findings of Menon *et al.* that rLMC score can show a stronger correlation with final clinical outcome as compared to other collateral scoring systems. We, therefore, suggest that the infarct core, measured in accordance with the ASPECTS scoring system, along with a trichotomized rLMC score, will allow rapid grading of collaterals and easier decision-making in the management of patients with AISs due to large-vessel occlusions. In agreement with the study conducted by Menon *et al.*,^[4] we were unable to find any significant association between collateral status in AIS and various vascular risk factors such as smoking, alcoholism, diabetes, hypertension, or previous stroke or TIA using univariate analysis. Age and gender distribution also showed no obvious association with collateral scores. Multivariate analysis could not be done due to limited sample size of thirty patients. NIHSS scores varied from 8 to 16, but it was recorded by different clinical fellows (from emergency medicine, internal medicine, and neurology) and hence was not taken into final statistical evaluation. Of the study population done, only five patients underwent intravenous thrombolysis, and rest of the patients were under similar standard stroke treatment.

Factors affecting the variability of LMCs have not yet been conclusively understood. Studies have suggested genetic as well as vascular risk factors such as prior hypertension, statin use, age, metabolic syndrome, and circle of Willis completeness as potential contributors to variability of collaterals. Recently, van Seeters *et al.*^[22] studied the determinants of LMCs and their effect on clinical outcome in 484 patients from Dutch stroke study with MCA occlusion, used multivariate analysis and Poisson regression, and found that the glucose level at admission, proximal MCA occlusion, and an incomplete ipsilateral posterior circulation in the circle of Willis were predictors of adverse LMC flow following AIS. However, these factors did not affect the final clinical outcome. This raises the possibility that a combination of factors – hereditary and acquired – may have a role in the determination of the final collateral status. Hemodynamic parameters may have a role in collateral functioning. Recent reports mentioned about higher baseline blood pressure in AIS patients with large-vessel occlusion/stenosis associated with better collateral flow and also that high pulse pressure and increased arterial stiffness may contribute to the impairment of cerebral collateral circulation.^[23,24] Zhang *et al.*^[25] studied the collateral status to stroke subtype as per the TOAST classification. They found that the baseline collateral showed a strong relationship with good clinical outcome in all patients and in cardio-embolic stroke but not in large artery atherosclerotic stroke. All studies with collaterals would invariably be of large artery atherosclerotic type, and hence there is a need

for study in a large sample of stroke subtypes to see whether the subtype of stroke has a role in the prediction of collaterals.

Limitations of our study

Limited number of patients, noninclusion of posterior circulation stroke, exclusion of those < 18 years, inherent chance of CTA variations in volume of flow within these collateral vessels that may be induced by occlusion, and principal investigator not blinded to the CTA findings and clinical outcomes were the study limitations. Multivariate logistic regression analysis of various stroke risk factors on rLMC scores could not be carried out due to limited number of patients in the study. Correlation with clinical NIHSS score and hemodynamic parameters was not part of the study.

Conclusions

Our study of thirty patients with acute anterior circulation ischemic stroke showed good correlation between rLMC score and 3-monthly clinical outcome. Furthermore, this scoring system gives a comprehensive idea regarding the regional distribution of pial collaterals on an individual-to-individual basis. We hope that with further research in this field, the rLMC score will help in better prediction of the outcome of stroke patients and enable further application of the scoring system as a strong and reliable imaging parameter on multi-phase CTA. Consequently, the rLMC score may in future become an indispensable tool in the hands of the clinicians as well as the radiologists while planning various stroke interventions.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Brozici M, van der Zwan A, Hillen B. Anatomy and functionality of leptomeningeal anastomoses: A review. *Stroke* 2003;34:2750-62.
2. Liebeskind DS. Collateral circulation. *Stroke* 2003;34:2279-84.
3. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. *Alberta Stroke Programme Early CT Score*. *Lancet* 2000;355:1670-4.
4. Menon BK, Smith EE, Modi J, Patel SK, Bhatia R, Watson TW, *et al.* Regional leptomeningeal score on CT angiography predicts clinical and imaging outcomes in patients with acute anterior circulation occlusions. *AJNR Am J Neuroradiol* 2011;32:1640-5.
5. Menon BK, O'Brien B, Bivard A, Spratt NJ, Demchuk AM, Miteff F, *et al.* Assessment of leptomeningeal collaterals using dynamic CT angiography in patients with acute ischemic stroke. *J Cereb Blood Flow Metab* 2013;33:365-71.
6. Shah S, Vanclay F, Cooper B. Improving the sensitivity of

- the Barthel Index for stroke rehabilitation. *J Clin Epidemiol* 1989;42:703-9.
7. Tariq N, Khatri R. Leptomeningeal collaterals in acute ischemic stroke. *J Vasc Interv Neurol* 2008;1:91-5.
 8. Moody DM, Bell MA, Challa VR. Features of the cerebral vascular pattern that predict vulnerability to perfusion or oxygenation deficiency: An anatomic study. *AJNR Am J Neuroradiol* 1990;11:431-9.
 9. Vander Eecken HM, Adams RD. The anatomy and functional significance of the meningeal arterial anastomoses of the human brain. *J Neuropathol Exp Neurol* 1953;12:132-57.
 10. Mohammad Y, Xavier AR, Christoforidis G, Bourekas E, Slivka A. Qureshi grading scheme for angiographic occlusions strongly correlates with the initial severity and in-hospital outcome of acute ischemic stroke. *J Neuroimaging* 2004;14:235-41.
 11. Saito I, Segawa H, Shiokawa Y, Taniguchi M, Tsutsumi K. Middle cerebral artery occlusion: Correlation of computed tomography and angiography with clinical outcome. *Stroke* 1987;18:863-8.
 12. Qureshi AI. New grading system for angiographic evaluation of arterial occlusions and recanalization response to intra-arterial thrombolysis in acute ischemic stroke. *Neurosurgery* 2002;50:1405-14.
 13. Higashida RT, Furlan AJ, Roberts H, Tomsick T, Connors B, Barr J, *et al.* Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. *Stroke* 2003;34:e109-37.
 14. Kim JJ, Fischbein NJ, Lu Y, Pham D, Dillon WP. Regional angiographic grading system for collateral flow: Correlation with cerebral infarction in patients with middle cerebral artery occlusion. *Stroke* 2004;35:1340-4.
 15. Christoforidis GA, Mohammad Y, Kehagias D, Avutu B, Slivka AP. Angiographic assessment of pial collaterals as a prognostic indicator following intra-arterial thrombolysis for acute ischemic stroke. *AJNR Am J Neuroradiol* 2005;26:1789-97.
 16. Miteff F, Levi CR, Bateman GA, Spratt N, McElduff P, Parsons MW. The independent predictive utility of computed tomography angiographic collateral status in acute ischemic stroke. *Brain* 2009;132(Pt 8):2231-8.
 17. Maas MB, Lev MH, Ay H, Singhal AB, Greer DM, Smith WS, *et al.* Collateral vessels on CT angiography predict outcome in acute ischemic stroke. *Stroke* 2009;40:3001-5.
 18. Tan IY, Demchuk AM, Hopyan J, Zhang L, Gladstone D, Wong K, *et al.* CT angiography clot burden score and collateral score: Correlation with clinical and radiologic outcomes in acute middle cerebral artery infarct. *AJNR Am J Neuroradiol* 2009;30:525-31.
 19. Leng X, Fang H, Leung TW, Mao C, Miao Z, Liu L, *et al.* Impact of collaterals on the efficacy and safety of endovascular treatment in acute ischaemic stroke: A systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry* 2016;87:537-44.
 20. Yeo LL, Paliwal P, Teoh HL, Seet RC, Chan BP, Ting E, *et al.* Assessment of intracranial collaterals on CT angiography in anterior circulation acute ischemic stroke. *AJNR Am J Neuroradiol* 2015;36:289-94.
 21. Ryu CW, Shin HS, Park S, Suh SH, Koh JS, Choi HY. Alberta stroke program early CT score in the prognostication after endovascular treatment for ischemic stroke: A meta-analysis. *Neurointervention* 2017;12:20-30.
 22. van Seeters T, Biessels GJ, Kappelle LJ, van der Graaf Y, Velthuis BK, Dutch acute stroke study (DUST) investigators. Determinants of leptomeningeal collateral flow in stroke patients with a middle cerebral artery occlusion. *Neuroradiology* 2016;58:969-77.
 23. Hong L, Cheng X, Lin L, Bivard A, Ling Y, Butcher K, *et al.* The blood pressure paradox in acute ischemic stroke. *Ann Neurol* 2019;85:331-9.
 24. Acampa M, Romano DG, Lazzerini PE, Leonini S, Guideri F, Tassi R, *et al.* Increased arterial stiffness is associated with poor collaterals in acute ischemic stroke from large vessel occlusion. *Curr Neurovasc Res* 2018;15:34-8.
 25. Zhang X, Zhang M, Ding W, Yan S, Liebeskind DS, Lou M. Distinct predictive role of collateral status on clinical outcome in variant stroke subtypes of acute large arterial occlusion. *Eur J Neurol* 2018;25:293-300. doi: 10.1111/ene.13493.