COLLATERAL SCORE ON CT ANGIOGRAPHY IN PATIENTS WITH ACUTE ISCHEMIC STROKE: A RETROSPECTIVE STUDY

Mathan Raj[1], Shahizon Azura Mukari[1], Wan Asyraf Wan Zaidi[2], Ahmad Sobri Muda[3*]

[1]Radiology Department, Faculty of Medicine, Universiti Kebangsaan Malaysia, 56000 Cheras, Kuala Lumpur, Malaysia.
[2]Department of Medicine, Faculty Medicine, Universiti Kebangsaan Malaysia Medical Centre, 56000 Cheras, Kuala Lumpur, Malaysia.
[3]Department of Radiology and Imaging, Faculty of Medicine, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia.

***Corresponding author:**
Dr. Ahmad Sobri Muda, Radiology Department, Hospital Pengajar Universiti Putra Malaysia (HPUPM), 43400 Serdang, Selangor, Malaysia. Tel: +603-9145 8289. Fax: +603-9145 6682. E-mail: asobri@upm.edu.my

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ABSTRACT
Objective: Clinically assessing the status of cerebral collaterals is thought to provide invaluable diagnostic and prognostic data in managing acute ischemic stroke (AIS) patients. In this study we present a report, based on commonly used collateral grading system, assessing the correlation between the collateral status seen on CT angiography and patients' functional outcome at Day 90 in our institution.
Method: Patients presenting to the Emergency Department within 6 hours of onset of stroke from January 2010 until December 2014 were chosen for the study. CT angiography source images were retrospectively reviewed and given a "collateral score" (CS) by a radiologist who was blinded to the patient's clinical information on presentation, as well as the clinical outcomes at 90 days. Patients' mRS score at 90 days was obtained retrospectively and compared against the "collateral score".
Results: 87 patients were enrolled into this study, of which 60 (69%) were male and 27 (31%) were female with a mean age of 60.3 years. In this study, 56 (64.4%) patients had a collateral score (CS) ≥ 2 and 31 (35.6%) patients had a CS < 2. Out of 56 patients who had a CS ≥ 2, 51 of them (91%) had good clinical outcome with a mRS ≤ 2. All the patients who had CS < 2 showed poor clinical outcome with a mRS > 2. The collateral score predicts accurately the clinical outcome with an area under the curve (ROC) of 0.75 (95% CI, 0.675-0.871, P=0.001). There is significant Spearman correlation between CS and the clinical outcome at Day 90, in patients with AIS during CTA analysis.
Conclusion: Our data supports the potential use of CS analysis in predicting clinical outcome of patients with AIS. Nevertheless, further study on a larger scale is strongly suggested to verify the reliability and reproducibility of CS assessment in CTA analysis prior to reperfusion in AIS patients.

Keywords: CTA brain, collateral score, clinical outcome, acute ischemic stroke, modified Rankin scale

1. INTRODUCTION

Cerebral collateral circulation is a vital alternative for temporary restoration of blood flow to ischemic areas due to obstruction within the principal arterial vessels supplying the brain. Collaterals are recruited primarily because of the restriction of blood flow as seen in acute ischemic stroke (AIS)[1]. An effective intrinsic reperfusion to the ischemic area is achieved by having an overall net flow between residual anterograde flow across the obstructive lesion and the circumventing contra-flow of blood around the lesion via collateral routes. The three major collateral pathways within the cerebrum that could potentially be recruited during arterial insufficiency events are the Circle of Willis, leptomeningeal collaterals, and extracranial–intracranial anastomosis[2].

Different imaging modalities have been employed to assess cerebral collateral flow in patients with ischemic stroke, namely digital subtraction angiography (DSA), computed tomography angiography (CTA) and magnetic resonance angiography (MRA)[3,4]. The degrees of utilization amongst these modalities, however, are varied. Although conventional DSA remains to be the most effective method to measure the degree of collateral extension and number, CTA is still considerably more favorable for grading collateral flow in a larger patient population, and has demonstrated good inter-observer reliability and correlation with patients' clinical outcome[5]. As any other technological innovation, the availability of advanced imaging modalities has increased, and is becoming cheaper and more accessible, as time goes by. CTA is frequently performed and supersedes conventional angiography for the assessment of patients with acute ischemic stroke in many hospitals, as CTA is more widely available and provides a rapid assessment of vascular anatomy and site of occlusion[6].

Clinically gauging the status of these cerebral collaterals is thought to provide invaluable diagnostic and prognostic data, in managing acute ischemic stroke patients. It has been considered as the only radiological predictor of clinical outcome in AIS despite its simplistic binary categorization[7]. According to Menon BK et all, a higher collateral score correlates with grade 2 or lower grading in modified Rankin Scale (mRS) 3 months after a stroke[8]. In the same study, good clinical outcomes were seen in 52% of patients, with good regional leptomeningeal collateral

(rLMC) score (17-20), 34 % with medium rLMC score (11-16), and 7% with poor rLMC score (0-10)[8].

In this article, we present a report, based on a commonly used collateral grading system[6], assessing the correlation between the collateral status seen on CT angiography and patients' functional outcome at Day 90, in our institution. We also present evidence showing the reliability of the collateral score in predicting favorable clinical outcome in acute ischemic stroke patients.

2. SUBJECTS AND METHODS

Patients: This 5-year, single-center, retrospective study was performed at one of the teaching hospitals in Kuala Lumpur, from January 2010 to December 2014. Patients presenting to the Emergency Department of the said teaching hospital within 6 hours of onset of stroke were chosen for the study. Patients with intracranial bleed, or upon radiological assessment revealed very poor image quality, incomplete coverage, or poor contrast opacification of the vessels on the normal side were excluded from this study.

The patients' collateral circulation from the CTA source images upon admission were retrospectively reviewed by a radiologist with 5-years of experience, and were scored based on locally developed guidelines. Patients' mRS ratings at Day 90 post-admission from acute ischemic stroke were gathered from their clinical case notes separately, and were compared against the "collateral scores" given. Patients' clinical information on presentation, as well as their mRS at Day 90 was withheld from the reviewing radiologist.

"Collateral score": The commonly used collateral grading system was used to predict tissue fate in the setting of acute ischemic stroke. This scoring system, termed "collateral score" (CS) consists of a grade of 0 to 3 (Table 1 & Figure 1). Grade 0 is defined as an absence of collateral vessels compared to the contralateral normal hemisphere. Grade 1 is defined as less than 50% of collateral vessels compared to the contralateral normal hemisphere. Grade 2 is defined as collaterals more than 50%, but less than 100% of collateral vessels compared to the contralateral normal hemisphere. Grade 3 is defined as those having 100% collateral vessels compared to the contralateral normal hemisphere.

Imaging analysis: Patients were scanned using a Siemens multi-section 64 detectors CT scanner. Non-contrast enhanced CT (NCCT) of the head with slice thickness of 5 mm followed by CTA with a helical scan technique were employed. The coverage for CTA brain was set to extend from the aortic arch, to the vertex of the skull with continuous axial sections.

CTA acquisition using bolus tracking was obtained after a single, 100 ml non-ionic intravenous bolus contrast media injection (Iopamiro) at 5 mls/sec via an 18G venous access cannulation at the antecubital fossa. Region of Interest (ROI) was placed at the ascending aorta. An image processing software designed for multiplanar reconstruction and volume rendering was used to reconstruct 2D multiplanar reconstruction images in axial, coronal and sagittal planes. The collateral scores were graded from these images.

Clinical assessment: Patients' clinical conditions at the 90th day after the onset of AIS, assessed by neurologists or neurology specialist trainees in the stroke clinic, were obtained from their clinical notes. The mRS scores, ranging from 0-6 were given. For the purpose of this report, the mRS scores were classified into two main groups: good functional outcome (scale of 0-2) and poor functional outcome (scale of 3-5; with 3 being partially dependent and 5 fully dependent).

3. RESULTS

A total of 87 patients who fulfilled all the inclusion and exclusion criteria were chosen for this study, of which 60 (69%) were male, and 27 (31%) were female (Figure 2). The mean age is 60.3 years, with the youngest being 35 years old and the oldest patient being 91 years old (Figure 3).

In this study, 56 (64.4%) patients had a CS $\geq$ 2 and 31 (35.6%) patients had a CS < 2 (Table 2), based on the blinded assessment carried out by the radiologist. 51 (91%) out of 56 patients who scored 2 or more on the CS showed a good clinical outcome, with mRS $\leq$ 2. Interestingly, all patients who had CS of less than 2 were reported to have poor clinical outcome, with a mRS > 2. The Spearman correlation analysis between the collateral score and modified Rankin scale showed a significant negative correlation ($r = -0.877$; $p = 0.01$; Table 3).

The collateral score (CS) has accurately predicted the clinical outcome of these patients, with an area under the Receiver-Operating Characteristic (ROC) curve of 0.77 (95.0% CI, 0.675-0.871; p=0.001) (Figure 4). From this analysis, the calculated specificity (true positive rate) is 72.2%, and its false positive rate 26.1%, with 1.5 as its cut off point.

4. DISCUSSION

The current treatment strategy for acute stroke focuses on early recanalization to prevent patients from suffering irreversible neurological deficits due to an ischemic event of the affected brain region. However, the success of revascularization depends not only on the restoration of the primary arterial occlusion, but also on the presence of reperfusion at the distal vascular bed, supplied by the collateral vessels. Prior to recanalization, it is a widely held view that the degree of collateral flow should be evaluated to predict the final infarct volume and to determine the clinical outcome of AIS patients.

Based on our results, we found a strong negative correlation between these two parameters; the higher the CS given at presentation, the lower the mRS obtained approximately 3 months after. In other words, the more collateral vessels present at the ischemic area within 6 hours of symptom presentation corresponds to a better functional outcome in patients with acute ischemic stroke at the end of the 90th day from the onset of stroke. Our findings broadly support, and are consistent with, the work of other studies that look into the correlation of collateral assessment in predicting patients' functional outcomes with an acute ischemic stroke, albeit of the varying imaging methods and grading systems [2, 5-6, 8-11]. These results also beg a further question; as to whether it is about time for collateral vessels assessment to be incorporated into stroke management guidelines and

algorithm, given the benefits it has in providing diagnostic value, as well as prognostication, for the clinicians.

In a more recent study conducted by[12], the collateral flow has been shown to play a more substantial role in infarct growth and penumbral salvage as opposed to the time of onset of stroke symptoms. Hence, the "collateral clock" should be considered and prioritized as one of the key factors to a successful reperfusion, which is objectively made possible with collateral assessment grading, as opposed to the the 6-hour window period requirement in re-establishing the arterial flow. Furthermore, latest evidence from the DAWN Trial study has advocated the extension of the window period for reperfusion for acute stroke of up to 24 hours with endovascular thrombectomy for patients with clinical-infarct mismatch[13].

Collateral vessel assessment is only made possible with the availability of advanced imaging tools, such as CTA, a non-invasive diagnostic tool, which is widely available in many secondary care hospitals. It provides a rapid assessment of the vascular anatomy and the site of occlusion in AIS. In comparison to MRA, CTA has a faster scanning time and allows more accurate morphological assessment of the vascular anatomy, which further facilitates the decision for interventional therapy, and prognostication[8]. A recent monograph has also shown that CTA collaterals and CT perfusion can predict similar tissue sustenance[14].

Conflict of Interest
None declared.

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Other than providing physicians with insights on the prognosis of AIS patients, the assessment of CS via CTA imaging may be a practical instrument for decision-making in providing the appropriate treatment, i.e. intravenous thrombolysis versus endovascular thrombectomy. The National Institutes of Health Stroke Scale (NIHSS) alone is insufficient to predict the probability of ischemic or hemorrhagic stroke, let alone in deciding a comprehensive treatment strategy for AIS patients. The findings of the CS could very well be, and serve as a useful diagnostic tool in the clinical setting of AIS. Further work is required to look at the usefulness of collateral grading towards the decision-making process, in terms of the recanalization treatment approach. We also propose a larger prospective study in the future to verify the reliability and reproducibility of the CS assessment on patients' outcome.

5. CONCLUSION

This study has demonstrated a significant correlation between the CS and clinical outcome at the 90th day, in patients with AIS during CTA analysis. Our data supports the potential of CS analysis from CTA to be used as a predictor for physicians to establish the prognosis of AIS. Nevertheless, further studies on a larger scale are strongly suggested to verify the reliability and reproducibility of the CS assessment in CTA analysis prior to reperfusion therapy in AIS patients.

Figure Legends
Figure 1. Examples of CT brain images with corresponding collateral scoring written at the left upper corner.
Figure 2. ROC for collateral score (CS) prediction of clinical outcome. A threshold of >1.5 was found with an AUC of 0.77 (95.0% CI, 0.675-0.871, P=0.000).
Figure 3. Non-enhanced CT (NECT) brain (a) shows acute left MCA infarct and CTA brain (b) demonstrates a CS of 1 at left fronto-parietal region.

Figure 4. Non-enhanced CT (NECT) brain (c) shows acute right MCA infarct and CTA brain (d) demonstrates a CS of 3 at right fronto-parietal region.

Table 1. Collateral scoring system

Collateral Score	Collateral grading (compared to contralateral normal hemisphere)
0	Absent
1	0% < collateral < 50%
2	50% < collaterals<100
3	100%

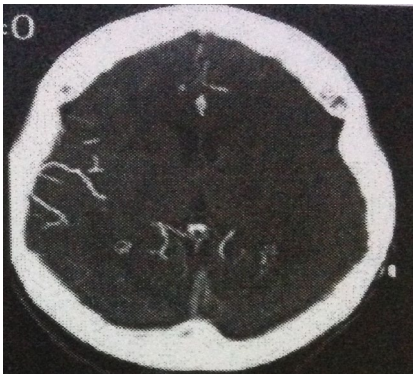
Table 2. *Patient clinical outcome dichotomized into good (mRS≤2) and poor outcome (mRS>2) at 90 days*

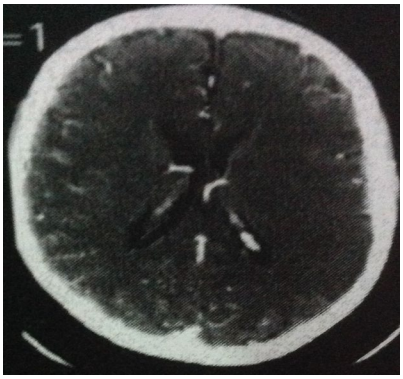
	Number of patients	mRS ≤ 2	mRS >2
Collateral score (CS), ≥2	56	51	5
Collateral score (CS), <2	31	0	31
Total	87	51	36

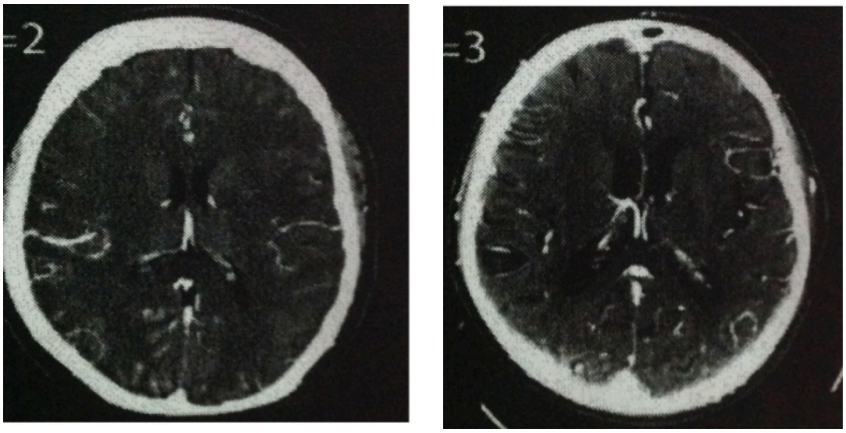
Table 3. *Spearman rank correlation of collateral score on CTA brain and modified rankin score (mRS)*

			Collateral score test person	Modified Rankin score test person
Spearman's rho	**Collateral score test person**	Correlation coefficient	1.000	-.874**
		Sig. (2-tailed)	-	.000
		N	87	87
	Modified rankin score test person	Correlation coefficient	-.874	1.000
		Sig. (2-tailed)	.000	-
		N	87	87

** *Correlation is significant at 0.01 level (2-tailed)*







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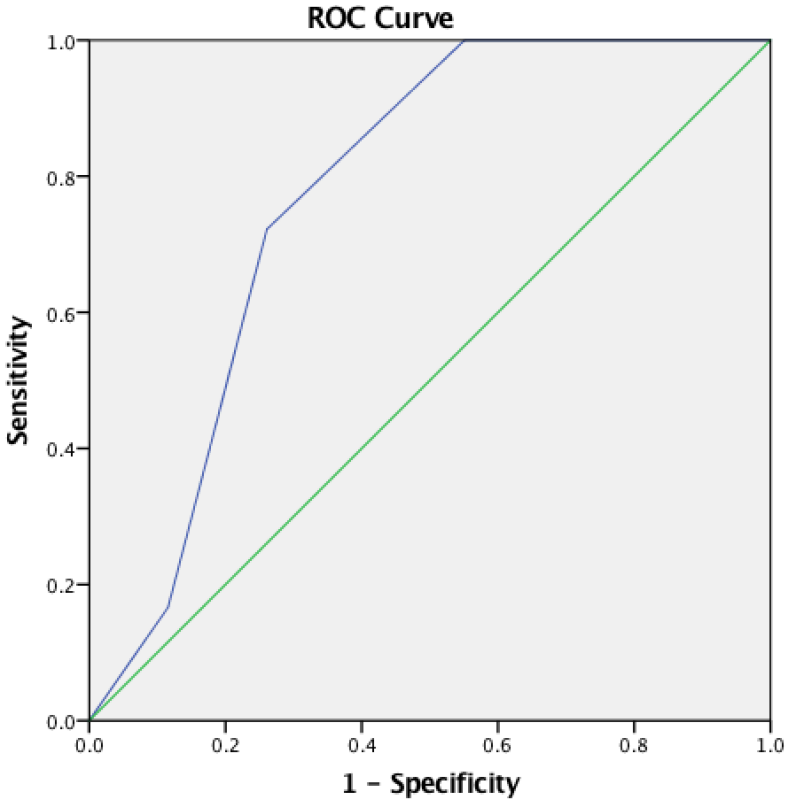

Figure 2. *ROC for collateral score (CS) prediction of clinical outcome. A threshold of >1.5 was found with an AUC of 0.77 (95.0% CI, 0.675-0.871, P=0.000).*

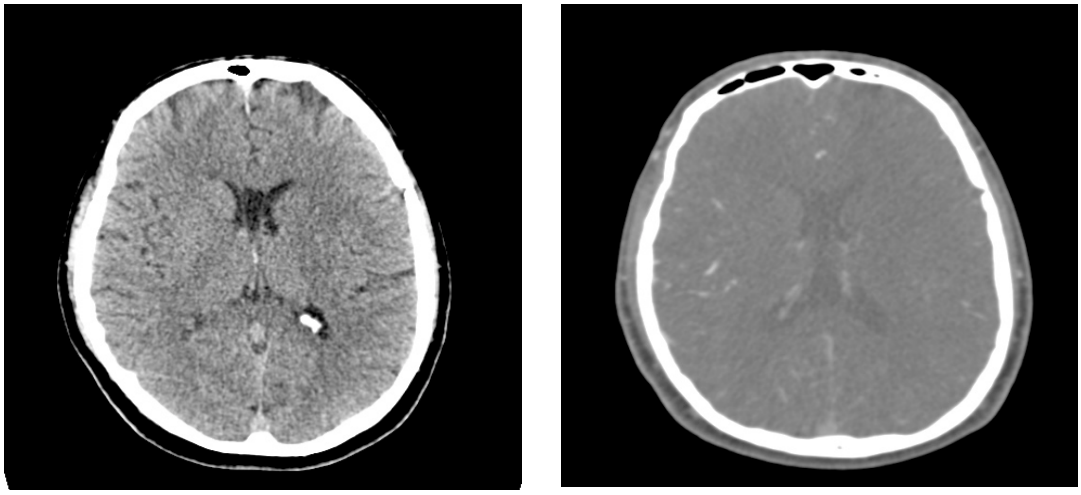

Figure 3. *NECT brain (a) shows acute left MCA infarct and CTA brain (b) demonstrates a CS of 1 at the left fronto-parietal region.*

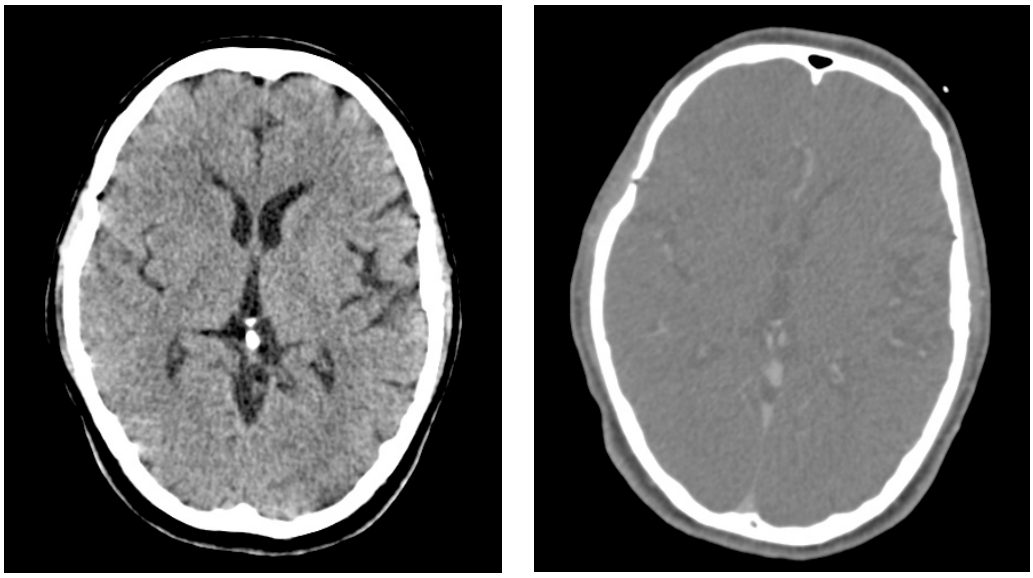

Figure 4. *NECT brain (c) shows acute right MCA infarct and CTA brain (d) demonstrates a CS of 3 at the right fronto-parietal region.*

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