EVALUATION OF THE CLOT BURDEN SCORE (CBS) FOR ACUTE ISCHEMIC STROKE (AIS) IN INTENT-TO-TREAT PATIENTS

Sarah Yaziz[1], Ahmad Sobri Muda[2,*], Wan Asyraf Wan Zaidi[3], Nik Azuan Nik Ismail[4],

[1]*Department of Radiology, Hospital Kuala Lumpur, 50586 Jalan Pahang, Kuala Lumpur, Malaysia*
[2]*Department of Imaging, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia.*
[3]*Department of Medicine, Universiti Kebangsaan Malaysia Medical Centre, 56000 Cheras, Kuala Lumpur, Malaysia.*
[4]*Department of Radiology, Universiti Kebangsaan Malaysia Medical Centre, 56000 Cheras, Kuala Lumpur, 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

Background : The clot burden score (CBS) is a scoring system used in acute ischemic stroke (AIS) to predict patient outcome and guide treatment decision. However, CBS is not routinely_practiced in many institutions. This study aimed to investigate the feasibility of CBS as a relevant predictor of good clinical outcome in AIS cases.

Methods: A retrospective data collection and review of AIS patients in a teaching hospital was done from June 2010 until June 2015. Patients were selected following the inclusion and exclusion criteria. These patients were followed up after 90 days of discharge. The Modified Rankin scale (mRS) was used to assess their outcome (functional status). Linear regression Spearman Rank correlation was performed between the CBS and mRS. The quality performance of the correlations was evaluated using Receiver operating characteristic (ROC) curves.

Results: A total of 89 patients with AIS were analysed, 67.4% (n=60) male and 32.6% (n=29) female. Twenty-nine (29) patients (33.7%) had a CBS ≥6, 6 patients (6.7%) had CBS <6, while 53 patients (59.6%) were deemed clot free. Ninety (90) days post insult, clinical assessment showed that 57 (67.6%) patients were functionally independent, 27 (30.3%) patients functionally dependent, and 5 (5.6%) patients were deceased. Data analysis reported a significant negative correlation (r= -0.611, p<0.001). ROC curves analysis showed an area under the curve of 0.81 at the cut-off point of 6.5. This showed that a CBS of more than 6 predicted a good mRS clinical outcome in AIS patients; with sensitivity of 98.2%, specificity of 53.1%, positive predictive value (PPV) of 76%, and negative predictive value (NPV) of 21%.

Conclusion: CBS is a useful additional variable for the management of AIS cases, and should be incorporated into the routine radiological reporting for acute ischemic stroke (AIS) cases.

Keywords: Acute ischemic stroke (AIS); Thrombus; Clot burden score (CBS); Modified Rankin scale (mRS); Receiver operating characteristics (ROC)

1. INTRODUCTION

Acute ischemic stroke (AIS) is defined as a rapid brain injury secondary to the disruption of blood flow to the brain tissue from a vascular luminal blockage[1]. It can be divided into two main types, i.e. thrombotic and embolic[2]. Thrombotic strokes occur due to thrombus that develops in the arteries that supply blood to the brain. On the other hand, an embolic stroke happens when a blood clot or plaque debris that developed elsewhere in the body travels and gets lodged into the cerebral vessels[3]. The occlusion deprives blood flow to the brain, i.e. impedes the oxygen and glucose supply to brain cells, which subsequently causes cellular necrosis and finally loss of normal bodily functions. Stroke, regardless of its origin, is one of the leading causes of death and the most frequent cause of disability in Malaysia[4]. Early revascularization to the ischemic brain regions has become a primary goal in the management of stroke patients, for minimizing brain injury[5].

In clinical practice, there are two types of reperfusion treatment approved for AIS, i.e. intravenous thrombolysis (IVT), and endovascular mechanical thrombectomy (MT)[6]. IVT is indicated for lysis of thrombus with the administration of intravenous recombinant tissue plasminogen activator (IV-rtPA). On the other hand, MT is an image guided minimally invasive procedure utilizing thrombectomy devices; such as stent retrievers and/or aspiration devices to trap and remove clots in the occluded artery[7]. Increasingly evidence shows greater recanalization rates with MT from 2015 onwards, especially cases with large vessel occlusions (LVOs) of the anterior circulation[8-10]. Nevertheless, the clot burden must be objectively quantified prior to initiating any form of reperfusion therapy. Thus, the stroke severity, and salvageability of the ischemic brain tissue can be determined, allowing appropriate treatment to be given promptly to patients[11].

The clot burden score (CBS) is a form of stroke assessment scale, which is developed to evaluate the degree of intracranial thrombus burden in patients with anterior circulation acute ischemic stroke[12]. It is a semi-quantitative based-scale, in which scores range from 0 to 10, based on the contrast opacification on computed tomography (CT) angiography[13]. A higher score implies the absence of a visible large vessel occlusion, while a lower score denotes visible clot; lower scores being worse. However, CBS scoring is not routinely practised in the clinical setting of AIS, and its value in the prediction of clinical outcome in stroke patients remains to be validated. Therefore, the present study aims to evaluate the reliability of CBS in predicting the clinical prognosis in intent-to-treat AIS patients.

2. SUBJECTS AND METHODS

Patients: This retrospective study was conducted on intent-to-treat AIS patients with CT Brain Perfusion (CTP) and subsequent CTA including MRA brain or cerebral angiography at the teaching hospital in Malaysia, between June 2010 and June 2015. Patients included in this study should not be diagnosed to have intracranial haemorrhage or mass effect during initial non-contrasted computed tomography (NCCT) brain examination.

Patients were excluded if they did not undergo brain CTA with either MRA or cerebral angiography assessment. Their demographic data, clinical presentation, and CBS scores were documented. Patients were grouped arbitrarily into CBS <6 and CBS≥6, i.e. high clot burden and low clot burden, respectively. The clinical outcome after 3 months (90 days) of initial presentation was assessed on follow up at the outpatient Neurology Clinic, in the teaching hospital.

Image acquisition: Computed Tomography (CT)

The CT imaging for stroke was performed using a 64-slice CT scanner (Sensation, Siemens). A plain CT brain, with contrasted CTA/CTP protocols were performed during the analysis. Vascular access was obtained via an 18G cannula at the antecubital fossa. Topogram was placed to include the C3 vertebral level cranially until the vertex; with acquisition parameters as follows: kV=80, mA=50, 0.2 s scan time, 0.6 mm slice thickness, 256 mm tomogram length, lateral view tube position. Non-contrasted brain plain sequential scan was proceeded from the base of skull area until the vertex with the following parameters: kV=120 mA=380, 51.05 mGy dose volumes, 1.0 s scan time, 2.4 mm slice thickness.

The images were reconstructed to image Kernel=H31s smooth with cerebrum windowing. Perfusion scan was performed at the level of the basal ganglia with 40 ml of low osmolar contrast media (LOCM Omnipaque 350 mg I/ml) with flow rate of 5 ml/s, kV= 80 mA=240, 434.70 mGy dose volumes, 40.15 s scan time, 5 s delay scan time after contrast insertion, 9.6 mm slice thickness, caudo-cranial image order at the area of the basal ganglia (axial view) using helical scanning. The images were then reconstructed to image Kernel=H31s smooth with cerebrum windowing. CTA brain proceeded with ROI placed at either internal carotid arteries (ICAs).

Image acquisition: Magnetic resonance imaging / angiography (MRI/MRA)

The MRI sequences included T2 FLAIR, GRE/SWI, DWI and MRA TOF. The acquisition parameters for **T2 FLAIR Coronal** sequence were as follows: TE=8100 ms, TE=107.0 ms, phase over sampling=0. **GRE** TE=26.0 ms, TR=800 ms, phase oversampling=0. **SWI** TR=27 ms, TE=20.0 ms phase oversampling=0, slice oversampling=12.5. **DWI/ADC** TE=97 ms, TR 3300 ms, phase over sampling=0. **MRA TOF** TR=25, TE=7.0.

Assessment of clot burden: The score for each individual patient was done retrospectively using a standard DICOM viewer software. The vascular images of the intracerebral CT angiography were viewed using OSIRIX Software approved by the Food and Drug Administration (FDA) for regular reporting. The scoring was done by a single reader, whom referred to an acknowledged CBS scheme, as well as correlated with the verified reports.

A score of 2 points is subtracted for thrombus found on CTA in the (a) supraclinoid ICA and each of the (b) proximal and (c) distal halves of the MCA trunk (Figure 1). A score of 1 point is subtracted for thrombus found in the (d) infraclinoid ICA and (e) A1 segment and for each affected M2 branch. A score of 10 indicates the absence of occlusion, while a score of 0 signified occlusion in all major intracranial anterior circulation arteries (Figure 2). In cases where the CT angiography/CBS was contradictory to that of the verified reports, the images were reviewed again by a staff neuro-radiologist.

Assessment of patient prognosis: The ability of patients to function independently was reassessed after 3 months of their initial presentation to UKMMC using the modified Rankin scale (mRS). The degree of disability was measured with a scale of 0 to 6. Functional independence were given scores of 0-2, while functional dependence with mRS scores of 3-6.

Statistical analysis: Data was reported using standard descriptive statistics, and analysed using IBM SPSS Statistical Software, version 22.0 (IBM Corp., USA). Receiver operating characteristic (ROC) curves analysis was performed on the CBS to evaluate its potential to serve as a tool to predict good clinical outcome in AIS patients. The area under the curve (AUC) was measured during the analysis. The correlation between the CBS and patient outcome, based on mRS, was analysed using the Spearman Rank correlation coefficient. Both the odds ratio (OR) and 95% CI were obtained. A p value of <0.05 was considered to be statistically significant.

3. RESULTS

Baseline data: A total of 105 patients who had AIS were identified during the study period. Among these, 89 were eligible to be enrolled into the study, in which the majority (60 patients, 67.4%) were male. A total of 23 patients had a median age of 61 ± 12.2 years old. The youngest and oldest patients were 28 and 86 years old, respectively. Forty-five of the included patients (50.6%) presented with unilateral left sided weakness, and 41 patients (46.1%) had unilateral weakness on the right side.

Clinical outcome: After 3 months of initial presentation, 57 patients (67.6%) were functionally independent, 27 patients (30.3%) were functionally dependent, and 5 patients (5.6%) were deceased. Fifty-three patients (59.6%) scored a CBS of 10. Six patients (6.7%) had a high clot burden (CBS <6), while 29 patients (33.7%) had a low clot burden (CBS ≥6).

Correlation between CBS and mRS (clinical outcome): ROC analysis demonstrated an AUC of 0.81 (95% CI, 0.70-0.92; P = .000). CBS of ≥6 predicted good clinical outcome with a sensitivity of 98.2%, specificity of 53.1%, positive predictive value (PPV) of 76%, and negative predictive value (NPV) of 21% (Figure 3). The odds ratio (OR) and likelihood ratio (LR) of the analysis were 11.7 (95% CI 3.4-40.0) and 19.1, respectively. The Spearman Rank correlation indicated a significant negative association between CBS and mRS (r= -0.611, p<0.001). Patients who presented with a high CBS (CBS>6) had a better prognosis or mRS, in comparison to that of those with CBS ≤6 (Figure 4).

4. DISCUSSION

Currently, the assessment of the clot burden in institutions in the country is done by a rough estimation of clot presence and extension with no standard evaluation followed. This method is prone to inter-reader variability; and reduces homogeneity of the group of patients treated, particularly when the evaluation of treatment outcome is of concern. The current assessment using CBS is fast and easy, however, is limited to the anterior circulation. This scoring system allots a total of 10 points for presence of contrast opacification in the major arteries on CTA; 2 points each are deducted for clot presence in the proximal M1, distal M1, and supraclinoid ICA, while 1 point each if it involves the infraclinoid ICA, M2 branches, and the A1 segment (Figure 1 and 2).

We have shown that in our clinical setting, a CBS <6 predicted a poor outcome, while those scoring 6 and above predicted a good outcome, using the mRS at 90 days. The analysis reported a smooth ROC curve with the AUC of 0.810 (95% CI 0.703-0.917), representing a good quality test. Our findings are similar to that of the study by Tan et al.[14], evaluating CBS and patient outcome. Since then, there have been a few studies, which corroborate these, findings[15-16]. Additionally, the utilization of CBS in routine radiological reporting may assist in identification of tandem lesions. Tsivgoulis et al., in their meta-analysis, found that those with a higher clot burden tend to also have tandem lesions, which render pre-treatment with IVT futile, making endovascular reperfusion with MT necessary[17].

Due to the retrospective nature of the study, our analysis is limited by heterogeneity in treatment, follow up technique, and time to treatment; common limitations in a clinically managed cohort of patients. A standardized algorithm in the management of future AIS cases may be invaluable to further validate the results of this study.

The decision on patient treatment pathway, and possible outcome may not only be based solely on CBS scores. Although it does seem ideal, proven to have a strong significant correlation, and is a good predictor of patient outcome, it is not without limitations. One study found that CTA regularly overestimates thrombus length[18]. The authors, in their study, showed that the distal end of the thrombus is overestimated due to non-opacification of the vessel and poor collateral supply. They proposed a role for delayed contrast enhanced CT to overcome this limitation. Additionally, the roles of NIHSS and ASPECT scores are relevant in our clinical setting, especially in situations where accessibility to CTA, MRA or cerebral angiography is limited.

5. CONCLUSION

The current study shows that CBS is a good predictor of patient outcome. It is a relatively easy and simple method in quantifying clot burden, apart from being systematic. This reduces heterogeneity in patient selection, assists in selection of treatment strategies, and prognosticates patient outcome; and should be incorporated in routine radiological reporting of AIS cases.

Figure

***Figure 1**. An image of T-carotid with segmental values for CBS, adopted from Puetz et. al.[13]*

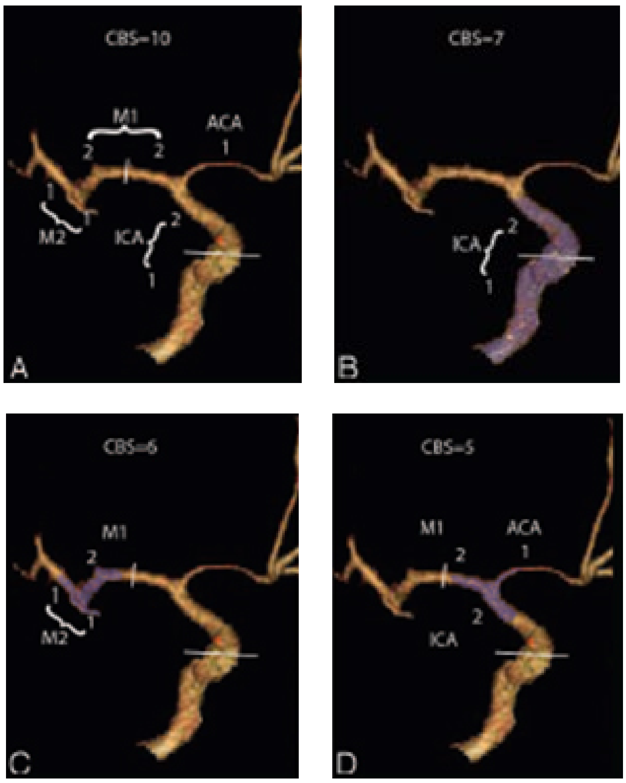

***Figure 2**. An example of substraction evalution of CBS, with presence of clot in the particular segments adopted from Tan et.al.[14]*

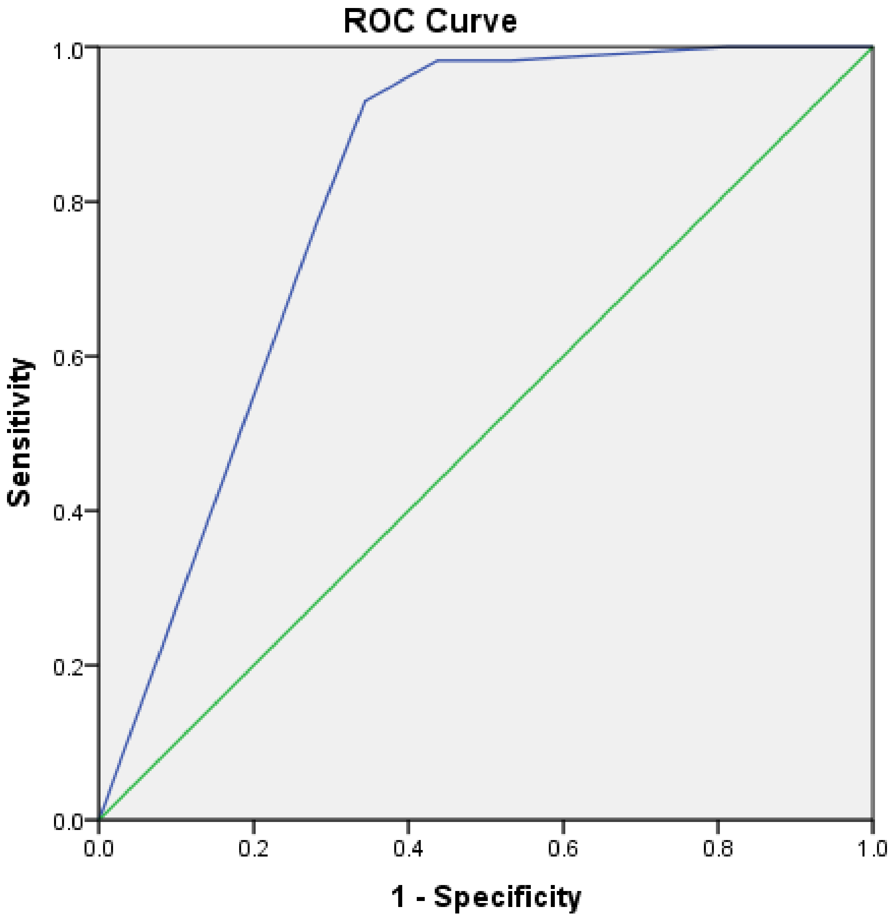

***Figure 3.** ROC curve on CBS versus patient outcome (mRS) showing good quality of test.*

[a]CBS	Patients n (%)	[b]mRS ≤ 2 n (%)	mRS ≥ 3 n (%)
Number of cases	89		
≥ 6	83 (93.3)	57	26
≤ 6	6 (6.7)	0	6

[a]CBS;clot burden score ≥ 6 (low clot burden) ≤ 6 (high clot burden)
[b]mRS;modified Rankin Score ≤ 2 (good outcome) ≥ 3 (poor outcome)

***Figure 4**. Patient outcome; CBS and mRS in 90 days*

REFERENCES

1. Catanese L, Tarsia J, Fisher M. Acute ischemic stroke therapy overview. Circ Res. 2017;120(3):541–558. doi:10.1161/CIRCRESAHA.116.309278.
2. Rink C, Khanna S. Significance of brain tissue oxygenation and the arachidonic acid cascade in stroke. Antioxid redox signal. 2011;14(10):1889–1903. doi:10.1089/ars.2010.3474.
3. Hinkle JL, Guanci MM. Acute ischemic stroke review. J Neurosci Nurs. 2007;39(5):285–293. doi:10.1097/01376517-200710000-00005.
4. Aziz ZA, Lee YYL, Ngah BA, Sidek NN, Looi I, Hanip MR, et al. Acute stroke registry Malaysia, 2010-2014: results from the National Neurology Registry. J Stroke Cerebrovasc Dis. 2015;24(12):2701–2709. doi:10.1016/j.jstrokecerebrovasdis.2015.07.025.

5. Balami JS, Hadley G, Sutherland BA, Karbalai H, Buchan AM. The exact science of stroke thrombolysis and the quiet art of patient selection. Brain. 2013;136(Pt 12):3528–3553. doi:10.1093/brain/awt201.
6. Bhaskar S, Stanwell P, Cordato D, Attia J, Levi C. Reperfusion therapy in acute ischemic stroke: dawn of a new era? BMC Neurol. 2018;18(8):1–26. doi:10.1186/s12883-017-1007-y.
7. Leung V, Sastry A, Srivastava S, Wilcock D, Parrott A, Nayak S. Mechanical thrombectomy in acute ischaemic stroke: a review of the different techniques. Clin Radiol. 2018;73(5):428–438. doi:10.1016/j.crad.2017.10.022.
8. Bracard S, Ducrocq X, Mas JL, Soudant M, Oppenheim C, Moulin T, et al. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial. Lancet Neurol. 2016;15(11):1138–1147. doi:10.1016/S1474-4422(16)30177-6.
9. Fischer U, Kaesmacher J, Mendes Pereira V, Chapot R, Siddiqui AH, Froehler MT, et al. Direct mechanical thrombectomy versus combined intravenous and mechanical thrombectomy in large-artery anterior circulation stroke: a topical review. Stroke. 2017;48(10):2912–2918. doi:10.1161/STROKEAHA.117.017208.
10. Saver JL, Goyal M, Bonafe A, Diener H-C, Levy EI, Pereira VM, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med. 2015;372(24):2285–2295. doi:10.1056/NEJMoa1415061.
11. Morgan CD, Stephens M, Zuckerman SL, Waitara MS, Morone PJ, Dewan MC, et al. Physiologic imaging in acute stroke: patient selection. Interv Neuroradiol. 2015;21(4):499–510. doi:10.1177/1591019915587227.
12. Mokin M, Levy EI, Siddiqui AH, Goyal M, Nogueira RG, Yavagal DiR, et al. Association of clot burden score with radiographic and clinical outcomes following Solitaire stent retriever thrombectomy: analysis of the SWIFT PRIME trial. J Neurointerv Surg. 2017;9(10):929–932. doi:10.1136/neurintsurg-2016-012631.
13. Puetz V, Dzialowski I, Hill MD, Subramaniam S, Sylaja PN, Krol A, et al. Intracranial thrombus extent predicts clinical outcome, final infarct size and hemorrhagic transformation in ischemic stroke: the clot burden score. Int J Stroke. 2008;3(4):230–236. doi:10.1111/j.1747-4949.2008.00221.x.
14. Tan I, Demchuk A, 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. Am J Neuroradiol. 2009;30(3):525–531. doi:10.3174/ajnr.A1408.
15. Legrand L, Naggara O, Turc G, Mellerio C, Roca P, Calvet D, et al. Clot burden score on admission T2*-MRI predicts recanalization in acute stroke. Stroke. 2013;44(7):1878–1884. doi:10.1161/STROKEAHA.113.001026.
16. Sillanpaa N, Saarinen JT, Rusanen H, Hakomaki J, Lahteela A, Numminen H, et al. The clot burden score, the Boston acute stroke imaging Scale, the cerebral blood volume ASPECTS, and two novel imaging parameters in the prediction of clinical outcome of ischemic stroke patients receiving intravenous thrombolytic therapy. Neuroradiology. 2012;54(7):663–672. doi:10.1007/s00234-011-0954-z.
17. Tsivgoulis G, Katsanos AH, Schellinger PD, Köhrmann M, Varelas P, Magoufis G, et al. Successful reperfusion with intravenous thrombolysis preceding mechanical thrombectomy in large-vessel occlusions. Stroke. 2018;49(1):232–235. doi:10.1161/STROKEAHA.117.019261.
18. Mortimer AM, Little DH, Minhas KS, Walton ERJ, Renowden SA, Bradley MD. Thrombus length estimation in acute ischemic stroke: a potential role for delayed contrast enhanced CT. J Neurointerv Surg. 2014;6(3):244–248. doi:10.1136/neurintsurg-2013-010769.