Large Vessel Occlusion Score: A Screening Tool to Detect Large Vessel Occlusion in the Acute Stroke Setting

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Background: The results of recent trials of mechanical thrombectomy for acute ischemic stroke have increased the demand for identification of patients with large vessel occlusion (LVO) at the primary stroke center, where a prompt detection may expedite transfer to a comprehensive stroke center for endovascular treatment. However, in developing countries, a noncontrast computed tomography (NCCT) may be the only neuroimaging modality available at the primary stroke center scenario, what calls for a screening strategy accurate enough to avoid unnecessary transfers of noneligible patients for endovascular therapy. Algorithms based on National Institute of Health Stroke Scale (NIHSS) and NCCT findings can be used to screen for LVO in patients with anterior circulation stroke (ACS). *Objective:* To test the accuracy of a score based on NIHSS and NCCT to detect LVO in patients with ACS. *Methods:* We evaluated 178 patients from a prospective stroke registry of patients admitted to an academic tertiary emergency unit. NIHSS and vessel attenuation values of the middle cerebral artery on NCCT absolute vessel attenuation (VA) were collected by 2 investigators that were blind to CT angiography (CTA) findings. We used receiver operating characteristics curve analysis and C-statistics to predict LVO on CTA. *Results:* NIHSS and vessel attenuation were highly associated with LVO with an area under the curve (AUC) of .86 and .77. The LVO score, built by logistic regression coefficients of the NIHSS and VA, showed the highest accuracy for the presence of LVO on CTA (AUC of .91). *Conclusion:* The LVO score may be a useful screening approach to identify LVO in patients with ACS.

Key Words: Ischemic stroke—endovascular treatment—large vessel occlusion—thrombectomy

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Introduction

Patients with ischemic stroke related to large vessel occlusion (LVO) have the highest morbidity and mortality and the lowest chance of arterial recanalization with intravenous thrombolysis.[1-3] The robust results of recent trials of mechanical thrombectomy for acute ischemic stroke

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(AIS) have increased the demand for identification of patients with LVO at the primary stroke center level, since quick detection of LVO may expedite transfer to a comprehensive stroke center for endovascular treatment.[4-8]

Nevertheless, in developing countries, a noncontrast computed tomography (NCCT) may be the only neuroimaging modality available at the primary stroke center. In this context of limited resources, any screening strategy for LVO needs to be accurate enough to identify potential candidates for mechanical thrombectomy but also to avoid a large number of unnecessary transfers of noneligible patients to packed emergency units.

Different cut-offs of the National Institute of Health Stroke Scale (NIHSS) have been used for LVO screening with controversial results,[9-12] and scales based on specific items have been adapted for LVO screening in the prehospital scenario.[13-15]

Nowadays, with the development of mobile stroke units and the improvement of telemedicine, the combination of NCCT data and clinical evaluation through the NIHSS could potentially be used to improve the accuracy of LVO screening in a patient with AIS at the primary stroke center level.

Subjects and Methods

We retrospectively evaluated consecutive patients with anterior circulation stroke from a prospective stroke registry of patients in an academic tertiary emergency unit during 2014 that had NCCT and CT angiography at admission. Our Institutional Review Board approved this study.

We defined LVO as an occlusion of extracranial, intracranial internal carotid artery, or M1 segment of the middle cerebral artery (MCA). Age, admission NIHSS, stroke side, sex, absolute vessel attenuation (VA), and relative vessel attenuation (rVA) of MCA on NCCT, hyperdense middle cerebral artery sign (HMCAS), and clinical outcome (modified Rankin scale—mRS in 90 days) were gathered by 2 investigators blinded to angiography CT findings.

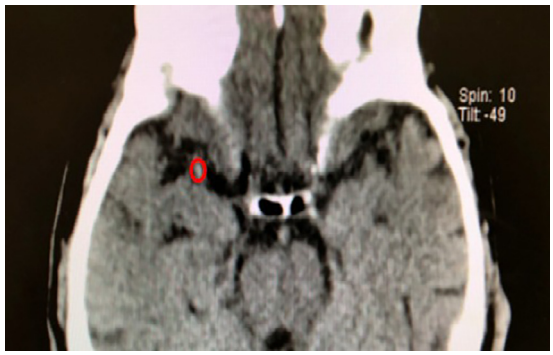


Figure 1. *Evaluation of MCA attenuation from an ROI drawn on NCCT blinded to CTA on the region of highest vessel attenuation ipsilateral to the involved hemisphere. Abbreviations: CTA, computed tomography angiography; MCA, middle cerebral artery; NCCT, noncontrast computed tomography; ROI, regions of interest. (Color version of figure is available online.)*

Image Protocol and Review

All images were reviewed by a stroke neurologist using the WEASIS Medical Viewer version 3.0.2 (Weasis team. Geneva, Switzerland) for studies with 5 mm-slice features. We used a ratio between 2 regions of interest (rVA) that were drawn on NCCT: (1) on the region of highest MCA attenuation (measured in units of Hounsfield, HU) ipsilateral to the involved hemisphere, and (2) mirror regions of interest on the corresponding vessel segment of the contralateral hemisphere (Fig 1). In order to simplify the analysis, we classified LVO as present or absent.

To study the intraobserver variability, the same investigator reviewed the images 4 months later. A second investigator (stroke neurologist) performed a blind review of the images and calculated the interobserver variability.

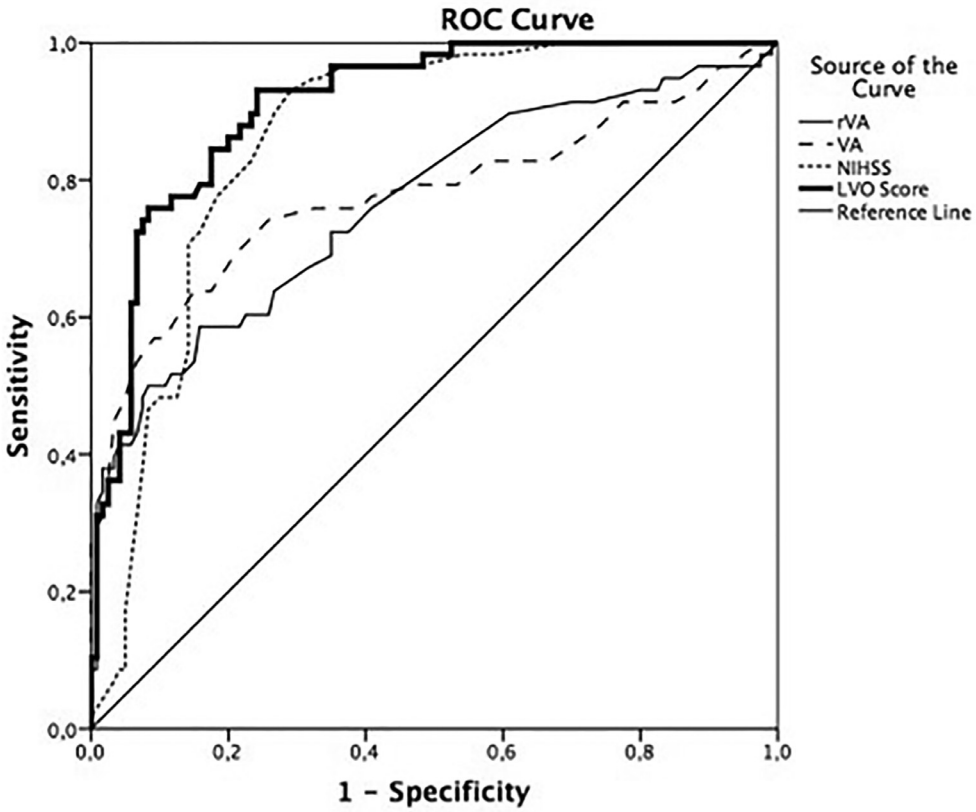
Inclusion and Exclusion Criteria

We included patients with AIS of anterior circulation that had NCCT brain and CT angiography in the first 24 hours. We excluded patients with a transient

Table 1. *Characteristics of patients with acute ischemic stroke of the anterior circulation in our sample*

Variables	Total (n = 1 78)	Large vessel occlusion		*P* value
		Yes (n = 58)	No (n = 120)	
Age	65.5 (57-74.2)	63.5 (54.7-73)	67 (58.2-76)	.15
Male	98 (55.1%)	32 (55.1%)	66 (55%)	.55
NIHSS	12.5 (5-20)	21.1 (19.4-22.7)	7 (4-14)	<.01
HMCAS	38 (21.3%)	36 (62%)	02 (1.6%)	<.01
MCA (VA)	40 (± 10.5)	50 (± 12.5)	37 (± 6.7)	<.01
MCA ratio (rVA)	1.02 (0.97-1.17)	1.19 (1.01-1.53)	1.0 (.94-1.08)	<.01
mRS >2-90 d	101 (56.7%)	45 (80.4%)	56 (46.7%)	<.01
mRS 90 d	3.0 (2.0-5.0)	5.0 (3.0-6.0)	2.0 (1.0-4.0)	<.01

Abbreviations: HMCAS, hyperdense middle cerebral artery sign; MCA, middle cerebral artery; mRS, modified Rankin scale; NIHSS, National Institute of Health Stroke Scale; rVA, relative value of MCA attenuation (Hounsfield units); VA, absolute value of MCA attenuation (Hounsfield units).



Abbreviations: NIHSS, national institute of health stroke scale; VA, absolute value attenuation of middle cerebral artery (MCA); rVA, relative value attenuation of MCA; LVO Score, large vessel occlusion score.

	AUC	Std. Error	P value
NIHSS	0.86	0.028	< 0.01
VA	0.77	0.042	< 0.01
rVA	0.76	0.040	< 0.01
LVO Score	0.91	0.022	< 0.01

Figure 2. *Receiver operating characteristic curves comparing the discrimination of National Institutes of Health Stroke Scale (NIHSS), absolute attenuation value of middle cerebral artery (VA), relative attenuation value of middle cerebral artery, and large vessel occlusion score (LVO score).*

ischemic attack and patients that had a previous mRS greater than 2.

Statistical Analysis

Continuous variables were reported as mean ± standard deviation or as median with interquartile range. We reported categorical variables as proportions. Student *t* test, Mann-Whitney *U* test, or Fisher test were used as appropriate to evaluate associations between variables. We entered variables identified at the univariate analyses into a multivariable logistic regression model, in order to establish the independent predictors that could be used to compose a score for LVO screening (LVO score). We

Table 2. *Variables associated with large vessel occlusion in a multivariate analysis*

Variables	Odds ratio	CI	*P* value
NIHSS	1.18	1.11-1.25	<.01
MCA attenuation value (VA)	1.13	1.07-1.20	<.01

Abbreviations: CI, confidence interval; MCA, middle cerebral artery; mRS, modified Rankin scale; NIHSS, National Institute of Health Stroke Scale.

subsequently used receiver operating characteristics analyses and C-statistics to test the discrimination ability of NIHSS, VA, rVA, and the LVO score to predict LVO. A 2-sided *P* value of .05 was used as a threshold for statistical significance. We performed the intra and inter-reliability by calculating the intraclass correlation coefficient. All the analyses were performed by SPSS software version 20.0 (IBM Corp. Armonk, NY).

Results

In total, we studied 178 patients. Among these, 58 had a LVO. These patients had a higher NIHSS median (21.1 [19.4-22.7] versus 7 [4-14]; $P < .01$) and worse clinical outcome (median mRS: 5 [3-6] versus 2 [1-4]; $P < .01$). Regarding the MCA signal attenuation, we observed higher VA values in the LVO group (50 ± 12.5 HU versus 37 ± 6.7 HU; $P <$,01) (Table 1).

The receiver operating characteristics curve analyses demonstrated an area under the curve (AUC) of .86, .77, and .76 when NIHSS, absolute (VA), and relative (rVA) attenuation values were used, respectively, to discriminate LVO (Fig 2).

Using thresholds values derived from these curves, the NIHSS score of greater than or equal to 10 had a sensitivity of 96.5%, specificity of 63.3%, and negative predictive value of 97.4%. An absolute MCA attenuation (VA) value of greater than or equal to50 had a sensitivity of 51.7%, specificity of 94.1%, a positive predictive value of 81%, and negative predictive value of 80.1%. Finally, the

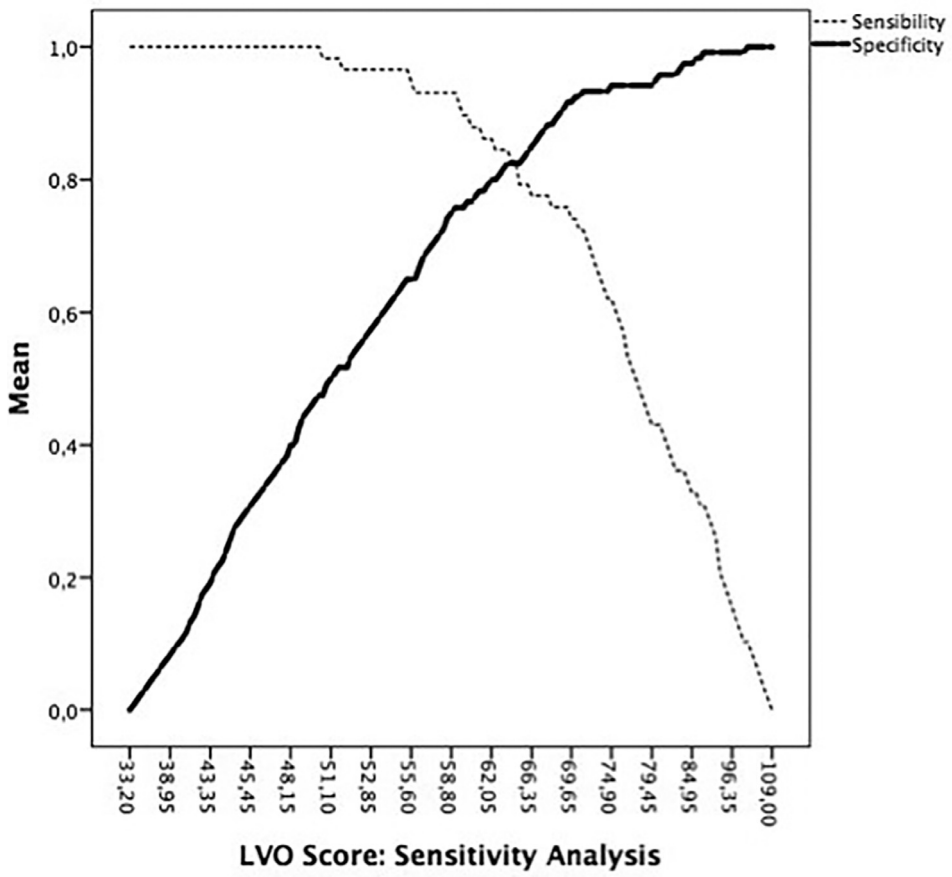


Figure 3. *Sensitivity analysis model for evaluation of LVO score thresholds and its sensitivity and specificity for large vessel occlusion.Abbreviations: LVO, large vessel occlusion.*

Table 3. *Comparison of thresholds of NIHSS, VA, rVA, and LVO score according to sensitivity, specificity, PPV, and NPV (95% confidence interval)*

	NIHSS ≥10	VA ≥50	rVA ≥1.5	LVO score ≥63
Sensitivity	96.5% (88%-99.5%)	51.7% (38.2%-65%)	32.5% (25.7%-40%)	85% (72.5%-92.6%)
Specificity	63.3% (54%-71.9%)	94.1% (88.3%-97.6%)	99.1% (95.4%-99.9%)	81.6% (73.5%-88.1%)
PPV	56% (50%-61.8%)	81% (66.7%-90.1%)	95% (72.2%-99.2%)	69% (60%-76.7%)
NPV	97.4% (90.6%-99.3%)	80.1% (75.4%-s84%)	75.3% (71.8%-78.5%)	91.5% (85.5%-95.2%)

Abbreviations: LVO score, large vessel occlusion score; NIHSS, National Institutes of Health Stroke Scale; NPV, negative predictive value; PPV, positive predictive value; rVA, relative value attenuation of middle cerebral artery; VA, absolute value attenuation of middle cerebral artery.

relative MCA attenuation threshold of (rVA) greater than or equal to 1.5, showed a sensitivity of 32.7%, specificity of 99.1%, a positive predictive value of 95%, and negative predictive value of 75.3% (Table 3). This parameter demonstrated a good intrarater reliability and an excellent inter-rater reliability (intraclass correlation coefficient: .74 (.24-.91) and .90 (.70-.96), respectively.

When entered into a multivariate analysis, the admission NIHSS (OR: 1.18; 95% CI: 1.11-1.25; $P < .01$) and VA (OR: 1.13; 95% CI: 1.07-1.20; $P < .01$) were independent predictors of the presence of LVO (Table 2). We used the odds ratio of those predictors to build a predictive score for this outcome: LVO score = (1.1 × VA) + (1.2 × NIHSS).

The LVO score had an AUC of .91 ($P < .001$) for the presence of LVO (Fig 2). For an LVO score threshold of 63, derived from a sensitivity analysis graph (Fig 3), it showed a sensitivity of 85%, specificity of 81.6%, a positive predictive value of 69%, and a negative predictive value of 91.5% (Table 3; Table 4).

Discussion

Our results demonstrate an independent association between clinical severity, MCA signal attenuation, and the presence of LVO in patients with AIS of the anterior circulation. The LVO score was a reasonably sensitive tool in the detection of LVO, suitable for screening LVO in the AIS population at the primary stroke center scenario, where clinical assessment and NCCT are the main tools available.

LVO may occur in patients with a low NIHSS, and that is the reason why we believe that the addition of CT findings is helpful to capture those patients. There is great variation among screening scores for LVO, and, assuming that there is no perfect screening tool for this scenario, we believe that the priority should be set to increase sensitivity instead of specificity. Indeed, the LVO score showed higher overall accuracy and sensitivity (AUC: .91; 85% sensitivity and 81.6% specificity for a cut-off of 63) than the FAST ED score published in 2016 by Lima et al (AUC of .81; 61% sensitivity and 89% specificity with a cut-off of 4) for LVO detection.[13-15]

Our study evaluated a larger group of participants in comparison to the initial studies. Besides, we used a definition of LVO that involves lesions located in the proximal segment of MCA and internal carotid artery, in accordance to the recent guidelines for endovascular treatment of acute stroke, where evidence for treatment of more distal lesions of anterior circulation has been uncertain.[16]

Table 4. *C-statistics for large vessel occlusion score (LVO Score)*

LVO Score	Sensibility	Specificity
50	100%	48%
51	98%	51%
52	97%	56%
53	97%	58%
54	97%	62%
55	97%	65%
56	93%	67%
57	93%	71%
58	93%	72%
59	91%	76%
60	90%	77%
61	86%	78%
62	85%	80%
63	85%	81%
64	79%	83%
65	79%	84%
66	78%	85%
67	78%	88%
68	76%	89%
69	76%	92%
70	72%	93%
71	71%	93%
72	67%	93%
73	66%	93%
74	64%	93%
75	60%	94%
76	53%	94%
77	50%	94%
78	47%	94%
79	43%	94%
80	43%	95%
81	40%	96%
82	38%	96%
83	36%	98%

Area under the curve: 0.91; $P < .01$ (95% confidence interval .86%-.95%).

Patients in our series had a higher median NIHSS at admission than the scores observed in previous studies, probably because of the LVO definition used. On the other hand, the incidence of LVO is similar to the data registered by Murphy and Heldner, respectively (32.5% versus 38% and 39%).[1,10]

Our results reinforce the high specificity of the HMCAS for the presence of LVO. These findings were previously reported in a study by Mair et al, where the HMCAS was presented in 47% of LVO cases.[17] In our study, it was present in 62% of patients with LVO. Although widely recognized, the identification of the HMCAS has some limitations related to the subjectivity in its definition, interexaminer, and intraexaminer variability and shows low sensitivity to identify LVO.[17,18] The sign is correctly identified on average in only 50% of LVO cases and, therefore, the evaluation of absolute and relative values of MCA attenuation seems to be an alternative to overcome these setbacks. Previous studies have associated these parameters with the presence of HMCAS to LVO and stroke prognosis, with variable results.[19-21] In the present study, we have found the best thresholds for LVO screening around 50 HU (absolute value) and 1.5 (relative value). By evaluating the vessel attenuation values in conjunction with the NIHSS scores at admission, we were able to improve accuracy for the detection of LVO, allowing a reproducible, feasible, low-cost, and efficient score to screen LVO in the acute stroke setting.

Our study has some limitations. We did not include posterior circulation strokes, limiting the findings to AIS of anterior circulation. Besides, we conducted our study in a single-center (although a comprehensive stroke center, which is the local reference to 26 counties in the state). The implementation of our score as a screening tool for LVO identification at primary stroke centers may increase the number of futile transfers to comprehensive stroke centers. Moreover, our findings need to be applied to an independent multicenter cohort for external validation in order to clarify the additional benefit provided by combining NIHSS to NCCT findings.

Conclusions

In conclusion, we have found that the LVO score, which is based on admission NIHSS and MCA vessel attenuation on NCCT, may be used to detect LVO in patients with AIS of the anterior circulation if validated in an independent multicenter cohort. We believe that the LVO score could be useful to improve the screening process of AIS patients for LVO, thus optimizing and expediting transfer for endovascular treatment.

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