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Original Research

Excellent Recanalization and Small Core Volumes Are Associated With Favorable AM-PAC Score in Patients With Acute Ischemic Stroke Secondary to Large Vessel Occlusion

Vivek Yedavalli, MD, MS [a], Manisha Koneru, MS [b], Meisam Hoseinyazdi, MD [a], Karen Copeland, PhD [c], Risheng Xu, MD, PhD [d], Licia Luna, MD, PhD [a], Justin Caplan, MD [d], Adam Dmytriw, MD, MPH, MSc [e], Adrien Guenego, MD, PhD [f], Jeremy Heit, MD, PhD [g], Gregory Albers, MD [h], Max Wintermark, MD, MS, MBA [i], Fernando Gonzalez, MD [d], Victor Urrutia, MD [j], Judy Huang, MD [d], Richard Leigh, MD [j], Elisabeth Marsh, MD [j], Rafael Llinas, MD [j], Marlis Gonzalez Hernandez, MD, PhD [j], Argye Hillis, MD [j]

[a] *Department of Radiology and Radiological Sciences, Johns Hopkins School of Medicine, Baltimore, MD*
[b] *Cooper Medical School of Rowan University, Camden, NJ*
[c] *Boulder Statistics, Boulder, CO*
[d] *Department of Neurosurgery, Johns Hopkins School of Medicine, Baltimore, MD*
[e] *Department of Neuroradiology, Massachusetts General Hospital & Harvard Medical School, Cambridge, MA*
[f] *Department of Radiology, Université Libre De Bruxelles Hospital Erasme, Brussels, BE*

List of Abbreviations: AIS, acute ischemic stroke; AIS-LVO, acute ischemic stroke caused by large vessel occlusion; AM-PAC, Activity Measure for Post-Acute Care; AUC, area under the curve; CS, collateral status; CT, computed tomography; CTA, computed tomography angiography; CTP, computed tomography profusion; IQR, interquartile range; IV, intravenous; IV tPA, intravenous thrombolysis; LVO, large vessel occlusion; MT, mechanical thrombectomy; mTICI, modified thrombolysis in cerebral infarction; NIHSS, National Institutes of Health Stroke Scale; rCBF, relative cerebral blood flow; Tmax, time to maximum.

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[g] Department of Radiology, Stanford University School of Medicine, Palo Alto, CA
[h] Department of Neurology, Stanford University School of Medicine, Baltimore, MD
[i] Department of Radiology, University of Texas MD Anderson Center, Houston, TX
[j] Department of Neurology, Johns Hopkins School of Medicine, Baltimore, MD

KEYWORDS
Acute ischemic stroke;
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Abstract *Objective:* To assess pretreatment and interventional parameters as predictors of favorable Activity Measure for Post-Acute Care (AM-PAC) scores for optimal discharge planning.
Design: In this prospectively collected, retrospectively reviewed multicenter study from 9/1/2017 to 9/22/2022, patients were dichotomized into favorable and unfavorable AM-PAC. Multivariate logistic regression and receiver operator characteristics analyses were performed for the identified significant variables. A *P* value of ≤.05 was significant.
Setting: Hospitalized care.
Participants: In total, 229 patients (mean ±SD 70.65 ±15.2 [55.9% women]) met our inclusion criteria. Inclusion criteria were (a) computed tomography (CT) angiography confirmed LVO from 9/1/2017 to 9/22/2022; (b) diagnostic CT perfusion; and (c) available AM-PAC scores.
Interventions: None.
Main Outcome Measures: Favorable AM-PAC, defined as a daily activity score ≥19 and basic mobility score of ≥17.
Results: Patients with favorable AM-PAC were younger (61.3 vs 70.7, *P*<.001), had lower admission glucose (mean, 124 vs 136, *P*=.042), lower blood urea nitrogen (mean, 15.59 vs 19.11, *P*<.001), and lower admission National Institutes of Health Stroke Scale (NIHSS) (mean, 10.58 vs 16.15, *P*<.001). No differences in sex were noted. Multivariate regression analyses revealed age, admission NIHSS, relative cerebral blood flow (rCBF) <30% volume, and modified thrombolysis in cerebral infarction (mTICI) score to be independent predictors of favorable AM-PAC (*P*<.047 for all predictors). The combined model revealed an area under the curve (AUC) of 0.83 (IQR 0.75-0.86).
Conclusion: Excellent recanalization, smaller core volumes, younger age, and lower stroke severity independently predict favorable outcomes as measured by AM-PAC.

Large vessel occlusions (LVOs) cause acute ischemic stroke (AIS) in up to 46% of patients[1] and are a leading cause of morbidity across the world.[2] Patients presenting with AIS caused by LVO (AIS-LVO) have disproportionately increased functional limitations compared with patients with non-LVO AIS,[3] underscoring the importance of timely treatment in these patients. Functional limitations, as a result of the hospital stay of a patient with AIS, is an important determinant of discharge location.[4-6] Although functional limitations are an important factor, there are several other factors that affect the patient's discharge disposition after acute hospital admission.[4] The challenges with the discharge location decision making process emphasize the importance of investigating the utility of predictive biomarkers as additional supportive data points for consideration.

The Activity Measure for Post-Acute Care (AM-PAC) score is a reliable and easy to perform validated metric that measures daily activity and basic mobility.[7,8] AM-PAC scores are predictive of not only discharge location[4] but 30-day hospital readmission[7] and functional outcomes[9] in poststroke care assessments. Furthermore, AM-PAC scores are used to determine the most appropriate type of discharge facility[4] and minimize hospital readmission when preventable.[7] For the aforementioned reasons, AM-PAC is now increasingly used to patients with stroke (inclusive of patients with AIS-LVO) as a unique assessment of in-hospital activity for discharge status determination.[10-12]

For patients with AIS-LVO, baseline neuroimaging with CT is an important component within the overall workup. Pretreatment comprehensive CT imaging consisting of noncontrast CT, CT angiography, and CT perfusion (CTP) provides information on the ischemic core, salvageable tissue or penumbra, and collateral status (CS).[13] The valuable information given by the CT evaluation aids in the decision-making process with administering reperfusion therapies — namely, intravenous thrombolysis (IV tPA), mechanical thrombectomy (MT), or both. Prior landmark trials have validated the use of perfusion imaging in determining MT eligibility, demonstrating improved outcomes for up to 24 hours after symptom onset.[14,15] Nevertheless, the potential utility of pretreatment comprehensive CT imaging, in conjunction with clinical and demographic factors, in determining post-acute care discharge needs for patients with AIS-LVO has not been explored to date.

The purpose of our study is to determine which pretreatment and interventional parameters are predictive of favorable AM-PAC scores in patients presenting with AIS-LVO with a focus on pretreatment CT imaging. We hypothesize that patients with smaller baseline ischemic cores and robust CS are associated with favorable AM-PAC daily activity and basic mobility scores.

Methods

Population

We identified patients with confirmed anterior circulation LVOs on CT angiography (CTA) from 9/1/2017 to 9/22/2022 using baseline comprehensive CT evaluation (which includes noncontrast CT, CTA, CTP) from 3 centers within the Johns Hopkins Medical Enterprise (Johns Hopkins Hospital - East Baltimore, Bayview Medical Campus, and Suburban Hospital). The Johns Hopkins East Baltimore and Bayview campuses are accredited comprehensive stroke centers. This study was approved through the Johns Hopkins School of Medicine institutional review board (JHU-IRB00269637). Informed consent was not applicable. Inclusion criteria were as follows: (a) CTA confirmed LVO; (b) diagnostic CT perfusion; and (c) available AM-PAC scores.

Data collection

Baseline and clinical data collected for each patient included demographics, risk factors for AIS (including diabetes mellitus, hypertension, coronary artery disease, atrial fibrillation), admission glucose, admission National Institutes of Health stroke scale (NIHSS), admission blood urea nitrogen, admission creatinine, admission hemoglobin, Alberta Stroke Program Early CT Score (Barber et al, [16]) scores, site of occlusion, and laterality of occlusion. Additional collected parameters include number of passes, recanalization time, modified thrombolysis in cerebral infarction (mTICI) score; presence of complication such as hemorrhagic transformation of subtype only as defined by the European Cooperative Acute Stroke Study 2 trial.[17] Alberta Stroke Program Early CT Score scores were calculated and baseline CTAs were reviewed for presence and site of LVO by an experienced neuroradiologist (VSY, 6 years of experience). Treatment type including IV tPA, MT, or both were noted. Patients were then dichotomized into favorable (defined as a daily activity score ≥19 and basic mobility score of ≥17)[7] and unfavorable AM-PAC (defined as a daily activity score <19 and basic mobility score of <17)[7] for analysis. Patients who have favorable AM-PAC scores in daily activity or basic mobility assessments, but not in both, were categorized as unfavorable.

Imaging analysis

Whole brain pretreatment CTP was performed on the Siemens Somatom Force[a] with the following parameters: 70 kVP, 200 Effective mAs, Rotation Time 0.25 s, Average Acquisition Time 60 s, Collimation 48 × 1.2 mm, Pitch Value 0.7, 4D Range 114 mm × 1.5 seconds. CTP images are then post-processed using RAPID commercial software[b] for generating quantitative relative cerebral blood flow (rCBF) and time to maximum (Tmax) volumes as well as qualitative Tmax maps. Hypoperfusion index ratio (HIR) was calculated as the ratio of the Tmax >10 seconds and Tmax >6 seconds volumes.[18] An HIR of 0.4 and below is deemed robust CS.[19]

Clinical outcomes assessment

AM-PAC scores were determined by the certified physical and occupational therapists providing clinical care at discharge.

Outcome measures

The primary outcomes were favorable AM-PAC, defined as a daily activity score ≥19 and basic mobility score of ≥17.[7]

Statistical analysis

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics software version 28.0.[c] Quantitative data were tested for normality using Shapiro-Wilk test, described as mean and SD, and compared using the 2-sided Student *t* test. If data were not normally distributed, they were described as median with interquartile ranges (IQRs), and compared using the Mann Whitney test. Categorical variables were reported as frequencies and compared using the likelihood ratio test. Univariate and multivariate regression analyses for predicting favorable AM-PAC scores were performed. A multivariate logistic regression was built using statistically significant univariate predictors and pre-specified clinical factors. The multivariate model was refined with elimination of non-significant parameters with the lowest effect size, yielding a model with 4 clinical parameters and 3 imaging parameters. Receiver operating characteristics curve with area under the curve (AUC) was used to evaluate model performance. A P value ≤.05 was significant.

Results

In total, 229 patients (mean ±SD 70.65 ±15.2 [55.9% women]) met our inclusion criteria with 79 (79/229, 34.5%) in the favorable and 150 (150/229, 65.5%) in the unfavorable groups, respectively.

Patients with favorable AM-PAC score were younger (61.3 vs 70.7, P<.001), had lower admission glucose (mean, 124.19 vs 136.83, P=.042), lower blood urea nitrogen (mean, 15.59 vs 19.11, P<.001), and lower admission NIHSS (mean, 10.58 vs 16.15, P<.001; table 1).

On pretreatment imaging, patients with favorable AM-PAC had significantly lower rCBF and Tmax volumes (P<.049 for all parameters; table 2).

Multivariate logistic regression analyses revealed age (P<.001), admission NIHSS (P<.001), mTICI score (P=.038), and rCBF <30% volume (P=.047), to be independent predictors of favorable AM-PAC (table 3). Admission glucose (P=.062) and women sex (P=.310) approached significance in favorable AM-PAC prediction. The receiver operator characteristics curve for the combined model revealed an AUC of 0.83 (95% confidence interval 0.75-0.86; fig 1).

Discussion

Our study demonstrates that excellent recanalization, smaller core volumes, lower age, and decreased initial stroke severity are all independent predictors of favorable

Table 1 Baseline demographic and clinical characteristics for patients with either favorable or unfavorable AMPAC scores

Characteristics	All (n=229)	Favorable AMPAC Score (n=79)	Unfavorable AMPAC Score (n=150)	*P* Value
Demographic				
Age (years), mean ± SD	67.43 (15.50)	61.32 (14.42)	70.65 (15.12)	**<.0001**
Sex, no. (%)				
Women	128 (55.90%)	45 (56.96%)	83 (55.33%)	.8134
Men	101 (44.10%)	34 (43.04%)	67 (44.67%)	
Race, no. (%)				
Black/African American	97 (42.36%)	31 (39.24%)	66 (44.00%)	.7419
Caucasian	120 (52.40%)	44 (55.70%)	76 (50.67%)	
Asian	5 (2.18%)	1 (1.27%)	4 (2.67%)	
Other	7 (3.06%)	3 (3.80%)	4 (2.67%)	
Tobacco use, no. (%)	100 (43.67%)	34 (43.04%)	66 (44.00%)	.8890
Hypertension, no. (%)	179 (78.17%)	57 (72.15%)	122 (81.33%)	.1134
Dyslipidemia, no. (%)	118 (51.53%)	39 (49.37%)	79 (52.67%)	.6349
Diabetes mellitus, no. (%)	59 (25.76%)	16 (20.25%)	43 (28.67%)	.1608
Heart disease, no. (%)	117 (51.09%)	34 (43.04%)	83 (55.33%)	.0765
Atrial fibrillation, no. (%)	89 (38.86%)	25 (31.65%)	64 (42.67%)	.1014
Prior stroke/transient ischemic attack, no. (%)	42 (18.34%)	14 (17.72%)	28 (18.67%)	.8602
BMI (kg/m^2), mean ± SD	29.38 (7.91)	29.82 (7.70)	29.15 (8.04)	.5438
SBP (mmHg), mean ± SD	152.28 (29.11)	149.92 (28.51)	153.52 (29.43)	.3710
DBP (mmHg), mean ± SD	87.62 (20.30)	87.01 (20.02)	87.93 (20.51)	.7443
HR (bpm), mean ± SD	85.10 (20.62)	82.78 (16.07)	86.31 (22.61)	.1736
Glucose (mg/dL), mean ± SD	132.47 (52.54)	124.19 (33.59)	136.83 (59.82)	**.0418**
BUN (mg/dL), mean ± SD	17.90 (9.02)	15.59 (5.69)	19.11 (10.17)	**.0009**
Cr (mg/dL), mean ± SD	1.09 (0.61)	1.01 (0.32)	1.13 (0.72)	.0812
Hemoglobin (g/L), mean ± SD	12.97 (1.94)	12.80 (1.85)	13.05 (1.99)	.3462
Stroke characteristics				
Admission NIHSS, mean ± SD	14.22 (6.86)	10.58 (6.61)	16.15 (6.20)	**<.0001**
Premorbid mRS, no. (%)	n=228	n=79	n=150	
0	87 (38.16%)	49 (67.12%)	87 (58.00%)	.1483
1	19 (8.33%)	14 (19.18%)	19 (12.67%)	
2	7 (3.07%)	4 (5.48%)	7 (4.67%)	
3	24 (10.53%)	4 (5.48%)	24 (16.00%)	
4	0 (0.00%)	0 (0.00%)	0 (0.00%)	
5	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Stroke Etiology (TOAST Criteria), no. (%)				
Larger artery atherosclerosis	39 (17.18%)	12 (15.38%)	27 (18.12%)	.2693
Cardioembolism	117 (51.54%)	35 (44.87%)	82 (55.03%)	
Small-vessel occlusion	0 (0.00%)	0 (0.00%)	0 (0.00%)	
Stroke of other determined etiology	12 (5.29%)	5 (6.41%)	7 (4.70%)	
Stroke of undetermined etiology	59 (25.99%)	26 (33.33%)	33 (22.15%)	
Laterality, no. (%)				
Left	108 (47.16%)	35 (44.30%)	73 (48.67%)	.2962
Right	120 (52.40%)	43 (54.43%)	77 (51.33%)	
Bilateral	1 (0.44%)	1 (1.27%)	0 (0.00%)	
Occlusion site, no. (%)				
ICA	8 (2.64%)	2 (2.60%)	6 (2.67%)	.9943
M1	163 (71.81%)	55 (71.43%)	108 (72.00%)	
M2	58 (25.55%)	20 (25.97%)	38 (25.33%)	
IV tPA, no. (%)	62 (27.07%)	24 (30.38%)	38 (25.33%)	.4165
MT not attempted, no. (%)	48 (20.96%)	20 (25.32%)	28 (18.67%)	.0773
mTICI, no. (%)	n=181	n=59	n=122	
0	8 (4.42%)	1 (1.69%)	7 (5.74%)	
1	4 (2.21%)	1 (1.69%)	3 (2.46%)	
2A	7 (3.87%)	1 (1.69%)	6 (4.92%)	
2B	42 (23.20%)	9 (15.25%)	33 (27.05%)	
2C	28 (15.47%)	8 (13.56%)	20 (16.39%)	
3	92 (50.83%)	39 (66.10%)	53 (43.44%)	

Abbreviations: BUN, blood urea nitrogen, mRS, modified Rankin score

Table 2 Imaging characteristics for patients with either favorable or unfavorable AMPAC scores

Characteristics	All (n=229)	Favorable AMPAC Score (n=79)	Unfavorable AMPAC Score (n=150)	*P* Value
Calculated Tmax >4s volume (mL), median (IQR)	214 (139.75-323.25)	190 (123-247)	214 (139.75-323.25)	**.0406**
Calculated Tmax >6s volume (mL), median (IQR)	117 (65.25-164.75)	97 (51.5-141)	117 (65.25-164.75)	**.0343**
Calculated Tmax >8s volume (mL), median (IQR)	69.5 (36-116.75)	54 (20.5-96)	69.5 (36-116.75)	**.0279**
Calculated Tmax >10s volume (mL), median (IQR)	40 (13.5-95.75)	34 (6.5,-69.5)	40 (13.5-95.75)	**.0257**
Calculated rCBF <20% (mL), median (IQR)	0 (0-13.75)	0 (0-6)	0 (0-13.75)	**.0205**
Calculated rCBF <30% (mL), median (IQR)	8.5 (0-41)	0 (0-16.5)	8.5 (0-41)	**.0010**
Calculated rCBF <34% (mL), median (IQR)	14.5 (0-53.75)	0 (0-23.5)	14.5 (0-53.75)	**<.0001**
Calculated rCBF <38% (mL), median (IQR)	22.5 (5-62)	5 (0-29.5)	22.5 (5-62)	**.0004**
Hypoperfusion Intensity Ratio, median (IQR)	0.4 (0.2-0.55)	0.3 (0.15-0.5)	0.4 (0.2-0.6)	**.0449**
CBV Index, median (IQR)	0.8 (0.7-0.9)	0.8 (0.7-1.0)	0.8 (0.7-0.9)	**.0044**

Table 3 Odds ratio for predictors included in multivariate logistic regression model for predicting favorable over unfavorable AMPAC scores

Characteristic	Odds Ratio (95% CI)	*P* Value
Age (per year)	0.94 (0.92-0.96)	**<.0001**
Admission NIHSS (per unit)	0.88 (0.83-0.93)	**<.0001**
Admission Glucose (per mg/dL)	0.99 (0.98-1.00)	.0618
Sex		
Men	Reference	.3103
Women	1.43 (0.72-2.83)	
rCBF <30% Volume (per mL)	0.99 (0.97-0.99)	**.0465**
mTICI		
0/1/2A/2B	Reference	**.0382**
2C/3	3.06 (1.24-7.52)	

outcomes as measured by AM-PAC. Our combined model with the aforementioned factors demonstrated strong performance (AUC 0.83 [95% CI 0.75-0.86]). To our knowledge, this the first study to investigate the potential of pretreatment imaging parameters in predicting favorable AM-PAC scores.

Standard of care guidelines have prioritized the identification of optimal post-acute care for patients with stroke.[8,20,21] Early discharge planning is essential for patients with AIS-LVO in order to optimally use the finite resources within the hospital and subsequent rehabilitation settings.[8] Furthermore, predicting whether patients can be discharged home instead of a post-acute care setting (acute rehabilitation, subacute, rehabilitation, etc) has important ramifications for the patients' psychosocial profile including cognition, stroke recurrence prevention, insurance status, availability, and treatment of comorbid conditions.[4,5,8,20] This complex and nuanced decision-making process can therefore be aided by pretreatment predictors of discharge status for early planning in patients with AIS-LVO.

Our study suggests that pretreatment comprehensive CT imaging may also be useful adjunct tools in this challenging discharge planning process. Although ischemic core volume in AIS-LVO as a predictive biomarker is well established with widely used functional outcome measures such as modified

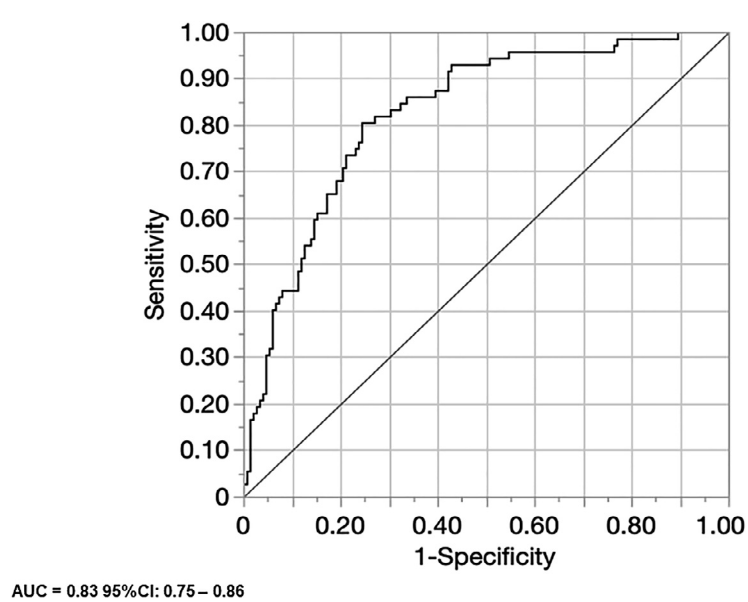

Fig 1 Receiver operator curve analysis of the combined multivariate logistic regression model with age, admission NIHSS, rCBF <30% volume, mTICI score, admission glucose, and sex.

Rankin score,[13,14,22] determining the relation between ischemic core with AM-PAC was yet to be performed. Our findings demonstrate that smaller core volumes based on rCBF <30% volumes independently predict favorable AM-PAC scores. Although the association of smaller ischemic core volumes with better outcomes is an expected finding, it also adds significance to the importance of smaller cores, as this result also affects functional ability and early discharge planning.

Another significant parameter predictive of favorable AM-PAC scores is achieving excellent recanalization by MT (defined as mTICI 2c/3 where unfavorable is considered mTICI 0-2a, successful as mTICI 2b/2c/3, and excellent as mTICI 2c/3).[23] Several landmark trials in 2015 in the early window[24–27] and later in 2018 for the late window[14,22] established MT as the standard of care for AIS-LVO. Additional studies have also demonstrated that achieving excellent recanalization[28–32] further improves outcomes compared with mTICI 2b, despite also being considered successful recanalization. We found a higher likelihood of achieving favorable AM-PAC scores with excellent recanalization (mTICI 2c/3) compared with mTICI 2b or lower (OR 3.06). Our study is concordant with prior trials and subsequent studies, corroborating the efficacy of MT and the need to achieve excellent recanalization to maximize likelihood of favorable functional outcomes. Our work extends these established outcome-related findings by emphasizing the importance of excellent recanalization with discharge planning as well.

Analyses of other baseline characteristics also confirmed some expected findings. Younger patients and patients who presented less severely with AIS were also associated with favorable functional outcomes as measured using AM-PAC. Both of these factors are well known predictors of improved outcomes in patients with AIS-LVO. Younger patients with AIS-LVO, especially those under 50, tend to have fewer post-procedural complications and better outcomes compared with patients 50 years or older.[33] Lower initial stroke severity, similarly, is a well-established independent predictor of better outcomes in AIS-LVO.[33] Our results are therefore concordant with prior studies identifying these factors as long-standing biomarkers of clinical outcomes.

Limitations

We acknowledge some limitations in this study. First, this study is inherently limited by its retrospective approach. Secondly, CTP is not widely available in smaller and rural centers, thus limiting generalizability. Lastly, our time frame includes patients where only IV tPA was administered instead of other newer forms of thrombolysis such as IV tenecteplase. Prospective studies are needed to validate these findings.

Conclusion

Smaller core volumes, younger age, lower initial stroke severity, and excellent recanalization are significantly predictive of favorable functional outcomes as measured using AM-PAC. Our study further emphasizes the significance of minimizing core volume and aiming for excellent recanalization in order to optimize functional outcomes and discharge planning in patients with AIS-LVO.

Suppliers

a. Siemens Somatom Force; Siemens.
b. RAPID commercial software; IschemaView.
c. IBM SPSS statistics software version 28.0; IBM Corp.

Corresponding author

Vivek Yedavalli, MD, MS, Department of Radiology and Radiological Sciences, Johns Hopkins School of Medicine, Phipps B122-D, Baltimore, MD 21287. *E-mail address:* vyedava1@jhmi.edu.

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