Cerebral vessel anatomy as a predictor of first-pass effect in mechanical thrombectomy for emergent large-vessel occlusion

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OBJECTIVE Mechanical thrombectomy is effective in acute ischemic stroke secondary to emergent large-vessel occlusion, but optimal efficacy is contingent on fast and complete recanalization. First-pass recanalization does not occur in the majority of patients. The authors undertook this study to determine if anatomical parameters of the intracranial vessels impact the likelihood of first-pass complete recanalization.

METHODS The authors retrospectively evaluated data obtained in 230 patients who underwent mechanical thrombectomy for acute ischemic stroke secondary to large-vessel occlusion at their institution from 2016 to 2018. Eighty-six patients were identified as having pure M₁ occlusions, and 76 were included in the final analysis. The authors recorded and measured clinical and anatomical parameters and evaluated their relationships to the first-pass effect.

RESULTS The first-pass effect was achieved in 46% of the patients. When a single device was employed, aspiration thrombectomy was more effective than stent retriever thrombectomy. A larger M₁ diameter ($p = 0.001$), decreased vessel diameter tapering between the petrous segment of the internal carotid artery (ICA) and M₁ ($p < 0.001$), and distal collateral grading ($p = 0.044$) were associated with first-pass recanalization. LASSO (least absolute shrinkage and selection operator) was used to generate a predictive model for recanalization using anatomical variables.

CONCLUSIONS The authors demonstrated that a larger M₁ vessel diameter, low rate of vessel diameter tapering along the course of the intracranial ICA, and distal collateral status are associated with first-pass recanalization for patients with M₁ occlusions.

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KEYWORDS first-pass effect; mechanical thrombectomy; vessel tapering; vascular disorders

ACUTE ischemic stroke is a leading cause of morbidity and mortality in the United States. The efficacy of endovascular mechanical thrombectomy over medical care in select patients with acute ischemic stroke caused by large-vessel occlusion in the anterior circulation has been confirmed.^{4,10} However, for this technique to be optimally effective, fast and complete recanalization is of paramount importance.¹⁷ First-pass recanalization only occurs in approximately 1 in 4 patients who undergo mechanical thrombectomy, and additional retrieval attempts in the remaining 75% of patients are associated with procedural complications and worse clinical outcomes.² Anatomical predictors of a first-pass effect are lacking in the neurointerventional literature but could be crucial in guid-

ing the development of improved retrieval devices and techniques that are individualized to each patient's unique anatomy. Upstream vessel morphology and anatomical parameters have previously been demonstrated to be associated with downstream hemodynamic consequences, but such relationships have not been explored in the context of stroke intervention for large-vessel occlusion.^{5,7} The purpose of our study was to explore and evaluate relationships between anatomical parameters of intracranial vessels and first-pass recanalization. We hypothesized that internal carotid and middle cerebral arterial diameters and the rate of diameter tapering along the intracranial internal carotid artery (ICA) impact the likelihood of first-pass recanalization and may be predictive of the first-pass effect. In this

ABBREVIATIONS ASPECTS = Alberta Stroke Program Early Computed Tomography Score; GLM = generalized linear model; ICA = internal carotid artery; LASSO = least absolute shrinkage and selection operator; MCA = middle cerebral artery; NIHSS = NIH Stroke Scale; ROC = receiver operating characteristic; TIC1 = thrombolysis in cerebral infarction.

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FIG. 1. Example of manual segmentation length measurements of the intracranial ICA: posterior-anterior (A) and lateral (B) views.

study, we compared the vascular anatomy of patients with middle cerebral artery (MCA) M_1 segment occlusions who underwent mechanical thrombectomy with first-pass recanalization versus non-first-pass recanalization.

Methods

Data Collection

Using an institutional review board–approved retrospective case-control study design, we evaluated all patients who underwent mechanical thrombectomy for acute ischemic stroke secondary to large-vessel occlusion at University Hospitals Cleveland Medical Center from 2016 to 2018. Of the 230 patients identified in our thrombectomy database, 86 patients were identified as having pure M_1 occlusions without associated tandem ICA occlusion. Ten patients were further excluded due to incomplete imaging or clinical outcome information availability.

Medical records were reviewed to obtain the following demographic variables for the final 76 patients included in our analysis: age, sex, history of hypertension, diabetes mellitus type 2, coronary artery disease, smoking, admission NIH Stroke Scale (NIHSS) score, intravenous tissue plasminogen activator status, preintervention Alberta Stroke Program Early Computed Tomography Score (ASPECTS), and occlusion location.

Coronal and sagittal reconstructions of preintervention thin-cut CT angiogram of the head in addition to interventional cerebral angiograms were used to obtain the following radiographic metrics: petrous ICA diameter, M_1 origin diameter, length along the ICA between the petrous ICA and M_1 origin, degree of diameter tapering between the petrous ICA and M_1 origin (measured by dividing the difference between the petrous ICA diameter and the M_1 origin diameter by the length along the ICA between the

petrous ICA and M_1 origin), angle between the ICA/MCA in the coronal plane, presence of an anterior communicating artery, presence of a posterior communicating artery, and degree of distal collateral grading (Tan collateral grading: 4-point grading scale ranging from 0 = absent collaterals to 3 = collaterals filling 100% of the occluded territory).¹⁵ All measurements were recorded manually and lengths were manually segmented according to a standardized study protocol (Fig. 1A and B). Our standard study protocol for manual segmentation is summarized as follows: posteroanterior (Fig. 1A) and lateral (Fig. 1B) angiographic views were retrospectively reviewed for each patient. Vessel length was measured in the posteroanterior view from the origin of the petrous segment to the first cavernous segment genu. Vessel length was then measured in the lateral view from the first cavernous segment genu up to the ICA terminus. These two vessel lengths were then added together to obtain the total vessel length of the intracranial ICA. A convenience sample was used to test intraclass correlation between 3 authors (Y.D., J.P., S.P.).

Procedural reports were reviewed to obtain the following procedure variables: use of general anesthesia, onset to puncture time, puncture to revascularization time, use of aspiration thrombectomy, use of stent retriever thrombectomy, number of passes, pretreatment thrombolysis in cerebral infarction (TICI) grade, and posttreatment TICI grade. Medical records were further reviewed to obtain the following outcome variables: hemorrhagic transformation, in-hospital mortality, postintervention NIHSS score, discharge location, and 90-day modified Rankin Scale score. Our primary outcome measure or dependent variable was first-pass complete recanalization defined as achievement of a TICI score of 3 after a single mechanical thrombectomy pass.

Statistical Analysis

Patient demographic variables were tabulated for all patients and presented as means, standard deviations, or percentages with Clopper-Pearson confidence intervals in the case of dichotomous variables. For continuous variables, patient subgroup comparison tests were conducted using nonparametric Mann-Whitney U-tests to control for any potential normality violations given the limited sample size. Dichotomous variables were compared between subgroups using Fisher exact tests. Next, bivariate tests were performed to compare individual demographic and anatomical patient variables to thrombectomy outcome measures. Pearson's correlations were used for continuous-continuous variable pairs, point-biserial comparisons for dichotomous-continuous variable pairs, ANOVA for categorical-continuous variable pairs, Fisher exact tests with odds ratio estimation for dichotomous-dichotomous variable pairs, and logistic regression for continuous-dichotomous variable pairs, for evaluation of potential predictor-outcome variable associations, respectively. All statistical analysis was performed using R (version 3.6.0).

Multivariate logistic regression was used to evaluate potential multivariate linear models incorporating multiple demographic and anatomical variables to predict complete first-pass recanalization (TICI grade 3), our primary outcome. Multivariate generalized linear models (GLMs) were defined in the form $Z_R = \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_N x_N$, where $x_1 \dots x_N$ represent the set of predictor variables, $\beta_1 \dots \beta_N$ indicate the fitted regression coefficients, and the GLM output variable Z_R indicates the logit (i.e., log-odds) of p_R , the estimated probability of successful recanalization, such that $Z_R = \log_e(p_R) - \log_e(1 - p_R)$. Conversely, p_R is obtained by transforming Z_R through a logistic function: $p_R = 1/(1 + \exp(-Z_R))$. Fitted models were presented both with unstandardized regression coefficients using the raw predictor variables and in the form of standardized regression coefficients fitted on Z-scored predictor variables (i.e., subtracting the mean and dividing by the standard deviation within each input variable column) as described by Menard⁹ and Agresti.¹ Using standardized input data yields an equivalent model of the form $Z_R^* = \beta_1^*[(x_1 - \bar{x}_1)/s_1] + \beta_2^*[(x_2 - \bar{x}_2)/s_2] + \dots + \beta_N^*[(x_N - \bar{x}_N)/s_N]$, where $\bar{x}_i$ and s_i are the mean and standard deviation for input variable i , and $\beta_1^* \dots \beta_N^*$ are the standardized regression coefficients. Standardizing the input variables in this fashion allows for more meaningful interpretation of the relative magnitude of the resulting standardized regression coefficients with respect to their importance for outcome prediction.

We used the least absolute shrinkage and selection operator (LASSO) regression approach, a well-described, well-validated, and widely implemented approach for defining predictive linear models.⁸ Of note, the LASSO technique is independent of the order in which variables are included in the model, in contrast to other techniques for model selection, such as stepwise regression. LASSO regression was used to determine multivariate models incorporating only the preinterventional clinical and anatomical variables most predictive of thrombectomy outcome on a patient-wise basis.

All multivariate models were fit on the basis of cross-

validated data, using an N-fold “leave-one-out” cross-validation approach. In this fashion, LASSO regression was performed on N (i.e., 76) subsets of the patient data, each with a single patient left out of the predictor data and used as the “test” data from which mean model misclassification error was determined. The mean misclassification error was defined as the mean absolute error between the true recanalization status (0 for failure, 1 for success) and the model's estimated probability of successful recanalization p_R , which lies on a continuous distribution between 0 and 1.

LASSO regularization was then carried out, with predictor variables penalized and excluded across a range of λ values affecting the stringency of the model in excluding less predictive variables. Model misclassification error was compared across the range of possible models to first identify “lenient” models achieving the lowest misclassification error possible (i.e., fewest predictor variables). The value of λ at which minimum mean misclassification error was achieved was defined as $\lambda_{\min}$. Following standard practice, more stringent models were subsequently defined by increasing λ beyond $\lambda_{\min}$ such that the surviving regression coefficients would be further penalized and potentially discarded. This process resulted in a second “stringent” model fit demarcated by λ_{1se} , which we define as the λ value for which the mean model misclassification error would exceed the minimum achieved model error by one standard error if λ were increased any further beyond $\lambda_{\min}$.¹² Stringent and lenient model fits were then compared to ascertain whether the additional variable penalization and elimination were negligible in their effects on model prediction or whether they resulted in meaningful decreases in model performance.

Finally, we determined receiver operating characteristic (ROC) curves to evaluate the sensitivity, specificity, and overall accuracy of thrombectomy outcome prediction for all fitted models. This was done by adjusting the binary threshold used to classify the logit model output Z_R^* as a predicted recanalization “failure” or “success.” For example, a classifier threshold of 0 would make a binary prediction of recanalization success when $Z_R^* > 0$, or equivalently, when $p_R > 0.5$. The classifier threshold was adjusted through the full range of possible values to compute the resulting pairs of model sensitivity and specificity, generating the ROC curve.

As an additional quantifier of model performance, we determined the Youden index for each ROC curve, defined as the optimal classifier threshold for the model output (Z_R^*) that yields the maximum binary classifier accuracy (percent correct predictions). We then tabulated the corresponding Youden accuracy, sensitivity, and specificity achieved at this cut-point.¹³ Multivariate models and ROC statistics were determined using the *glmnet* and *ROCR* packages for R, respectively.^{3,13,14}

Results

Clinical and anatomical characteristics were recorded and analyzed for 76 patients with M₁ occlusions. Thirty-five patients experienced first-pass complete recanalization, whereas 41 patients required more than one mechani-

TABLE 1. Patient demographic and clinical characteristics

Characteristic	All Patients (n = 76)	Successful First-Pass Complete (TICI grade 3) Recanalization		p Value
		Yes (n = 35)	No (n = 41)	
Patient demographics				
Age, yrs	66.2 [62.7, 69.6]	65.7 [60.4, 71.0]	66.5 [61.9, 71.2]	0.975
No. of females	48, 63.2% [51.3%, 73.9%]	22, 62.9% [44.9%, 78.5%]	26, 63.4% [46.9%, 77.9%]	>0.999
HTN	48, 63.2% [51.3%, 73.9%]	27, 77.1% [59.9%, 89.6%]	21, 51.2% [35.1%, 67.1%]	0.031
DM2	14, 18.4% [10.5%, 29%]	6, 17.1% [6.6%, 33.6%]	8, 19.5% [8.8%, 34.9%]	>0.999
CAD	25, 32.9% [22.5%, 44.6%]	9, 25.7% [12.5%, 43.3%]	16, 39% [24.2%, 55.5%]	0.23
Smoker	21, 27.6% [18%, 39.1%]	11, 31.4% [16.9%, 49.3%]	10, 24.4% [12.4%, 40.3%]	0.61
Stroke characteristics				
NIHSS score (preintervention)	16 (2–28)	16 (2–28)	16 (3–26)	0.79
IV tPA	44, 57.9% [46%, 69.1%]	22, 62.9% [44.9%, 78.5%]	22, 53.7% [37.4%, 69.3%]	0.49
ASPECTS	10 (6–10)	10 (7–10)	10 (6–10)	0.72
Occlusion location				0.029
Right M ₁	33 (43.4%)	10 (28.6%)	23 (56.1%)	
Left M ₁	43 (56.6%)	25 (71.4%)	18 (43.9%)	
Anatomical characteristics				
Petrous ICA diameter	3.9 [3.8, 4]	3.8 [3.7, 4]	4 [3.8, 4.2]	0.33
M ₁ origin diameter	2.3 [2.2, 2.4]	2.5 [2.4, 2.6]	2.2 [2, 2.3]	0.001
Distance btwn petrous ICA & clot face	57.8 [55.8, 59.7]	58.4 [55.8, 61]	57.2 [54.3, 60.1]	0.62
Tapering btwn ICA & M ₁	0.0284 [0.0264, 0.0305]	0.0235 [0.0211, 0.0259]	0.0326 [0.03, 0.0352]	1.05E-06
Branching angle of MCA off ICA	138.9 [135.8, 142.1]	140.5 [135.5, 145.4]	137.6 [133.6, 141.6]	0.66
Ipsilat AComA present	53, 69.7% [58.1%, 79.8%]	24, 68.6% [50.7%, 83.1%]	29, 70.7% [54.5%, 83.9%]	>0.999
Ipsilat PComA present	57, 75% [63.7%, 84.2%]	28, 80% [63.1%, 91.6%]	29, 70.7% [54.5%, 83.9%]	0.43
Ipsilat AComA & PComA both present	42, 55.3% [43.4%, 66.7%]	20, 57.1% [39.4%, 73.7%]	22, 53.7% [37.4%, 69.3%]	0.82
Distal collateral grading (Tan score)				0.044
0	11 (14.5%)	4 (11.4%)	7 (17.1%)	
1	27 (35.5%)	8 (22.9%)	19 (46.3%)	
2	18 (23.7%)	9 (25.7%)	9 (22%)	
3	20 (26.3%)	14 (40%)	6 (14.6%)	
Procedure characteristics				
General anesthesia	2, 2.6% [0.3%, 9.2%]	1, 2.9% [0.1%, 14.9%]	1, 2.4% [0.1%, 12.9%]	>0.999
Hours to puncture	6.6 [4.9, 8.3]	7.5 [4.1, 10.8]	5.9 [4.5, 7.2]	0.46
Aspiration used	61, 80.3% [69.5%, 88.5%]	29, 82.9% [66.4%, 93.4%]	32, 78% [62.4%, 89.4%]	0.77
Aspiration only	30, 39.5% [28.4%, 51.4%]	24, 68.6% [50.7%, 83.1%]	6, 14.6% [5.6%, 29.2%]	1.75E-06
Stent retriever used	43, 56.6% [44.7%, 67.9%]	11, 31.4% [16.9%, 49.3%]	32, 78% [62.4%, 89.4%]	6.37E-05
Stent retriever only	15, 19.7% [11.5%, 30.5%]	6, 17.1% [6.6%, 33.6%]	9, 22% [10.6%, 37.6%]	0.77
Aspiration & stent retriever both used	28, 36.8% [26.1%, 48.7%]	5, 14.3% [4.8%, 30.3%]	23, 56.1% [39.7%, 71.5%]	0.00027
No. of passes	1.8 [1.5, 2]	1 [1, 1]	2.4 [2, 2.8]	4.78E-10

AComA = anterior communicating artery; CAD = coronary artery disease; DM2 = diabetes mellitus type 2; HTN = hypertension; IV tPA = intravenous tissue plasminogen activator; PComA = posterior communicating artery.

Unless otherwise noted, values are reported as the number, percentage [95% confidence interval]. Median and range are reported for preprocedural NIHSS score and ASPECTS. p values reflect group differences determined by Mann-Whitney U-tests. Boldface type indicates statistical significance.

cal thrombectomy attempt in order to achieve recanalization.

Table 1 summarizes comparisons between patients in whom the first-pass effect (i.e., TICI grade 3 complete recanalization on the first catheter pass) was achieved or was not achieved. Clinical factors including age, sex, and history of medical comorbidities were not significantly dif-

ferent between patients achieving or failing to achieve the first-pass effect. Additionally, stroke severity represented by preintervention NIHSS score and ASPECTS and frequencies of intravenous thrombolytic administration were not significantly different between the two groups.

When comparing anatomical characteristics, patients who experienced the first-pass effect were more likely

FIG. 2. Examples of rapid diameter taper along a relatively short, nontortuous intracranial ICA (A) and a gentle diameter taper along a relatively long, tortuous intracranial ICA (B).

to harbor left-sided M_1 occlusions. Most notably, patients who experienced the first-pass effect had significantly larger M_1 origin diameters, a significantly lower degree of vessel tapering from the petrous ICA to the M_1 origin, and more robust distal collaterals (Table 1 and Fig. 2).

An aspiration-only first-line strategy was more likely to be attempted in patients who experienced first-pass complete recanalization than was a stent retriever-only strategy. When an aspiration-only first-line strategy was used, 80% of patients experienced a first-pass complete recanalization. In comparison, a stent retriever-only first-line strategy was only effective in generating a first-pass complete recanalization in 40% of the cases.

Differences in clinical outcomes between patients with successful or failed first-pass complete recanalization are summarized in Table 2. By definition, the median number of thrombectomy attempts was higher for patients who did not experience a first-pass effect. In our study group, patients who experienced a first-pass effect had significantly shorter puncture-to-revascularization times; lower postintervention NIHSS scores; significantly different discharge dispositions, with higher rates of home discharge; and significantly lower scores on the 90-day modified Rankin Scale. Rates of acute or subacute symptomatic hemorrhage and mortality were low and comparable between the groups (Table 2).

Multivariate logistic regression analysis performed using LASSO regression, and leave-one-out cross-validation predicted first-pass complete recanalization (TICI 3) status, with a peak classifier accuracy of 80%–82% depending on the initial set of predictor variables allowed into

the model and on the stringency of coefficient penalization (Table 3 and Fig. 3). This approach demonstrated that most of the variance in recanalization outcomes was explained by a small subset of the initial 19 predictor variables. Lenient LASSO resulted in a model with 7 of 19 predictor variables surviving:

$$Z_R^* = 0.544 I_{HTN} - 0.0944 I_{CAD} - 0.321 I_{Right-sided\ occlusion} + 0.183 M_1\ origin\ diameter - 0.911 ICA-to-M_1\ tapering + 0.220 ipsi\ PCOM\ present + 0.205 Tan\ score\ (distal\ collateral\ grading)$$

Increasing the stringency of model coefficient penalization until the mean classification error rose one standard error above the minimum achieved error yielded a stringent LASSO model with 5 of 19 predictor variables surviving:

$$Z_R^* = 0.22 I_{HTN} - 0.149 I_{Right-sided\ occlusion} + 0.0741 M_1\ origin\ diameter - 0.688 ICA-to-M_1\ tapering + 0.0549 Tan\ score\ (distal\ collateral\ grading)$$

Although mean classification error with the stringent LASSO model increased to 0.263 versus 0.237 for the lenient LASSO model, the cross-validated binary classifier performance of these two models was identical, resulting in identical ROC curves with a Youden accuracy of 81.6%.

Finally, when LASSO regression models were fit using only the 9 anatomical predictor variables, we obtained a lenient anatomical-only LASSO model, which retained 6 of 9 coefficients:

TABLE 2. Clinical outcomes

Clinical Outcomes	All Patients (n = 76)	Successful First-Pass Complete (TICI grade 3) Recanalization		p Value
		Yes (n = 35)	No (n = 41)	
Time from arterial puncture to recanalization, mins	38.4 [33, 43.9]	28.9 [25.1, 32.7]	46.8 [37.8, 55.7]	0.002
Preintervention TICI grade	0: 71 (93.4%) 1: 3 (3.9%) 2a: 1 (1.3%) 2b: 1 (1.3%) 3: 0 (0%)	0: 31 (88.6%) 1: 2 (5.7%) 2a: 1 (2.9%) 2b: 1 (2.9%) 3: 0 (0%)	0: 40 (97.6%) 1: 1 (2.4%) 2a: 0 (0%) 2b: 0 (0%) 3: 0 (0%)	0.39
Postintervention TICI grade	0: 5 (6.6%) 1: 4 (5.3%) 2a: 1 (1.3%) 2b: 24 (31.6%) 3: 42 (55.3%)	0: 0 (0%) 1: 0 (0%) 2a: 0 (0%) 2b: 0 (0%) 3: 35 (100%)	0: 5 (12.2%) 1: 4 (9.8%) 2a: 1 (2.4%) 2b: 24 (58.5%) 3: 7 (17.1%)	1.07E-10
Near-complete recanalization (TICI grade 2b or 3)	66, 86.8% [77.1%, 93.5%]	35, 100% [90%, 100%]	31, 75.6% [59.7%, 87.6%]	0.001
Complete recanalization after ≥1 pass (TICI grade 3)	42, 55.3% [43.4%, 66.7%]	35, 100% [90%, 100%]	7, 17.1% [7.2%, 32.1%]	6.13E-15
Hemorrhagic transformation	No: 67 (88.2%) Acute (ICU): 5 (6.6%) Subacute: 4 (5.3%)	No: 31 (88.6%) Acute (ICU): 3 (8.6%) Subacute: 1 (2.9%)	No: 36 (87.8%) Acute (ICU): 2 (4.9%) Subacute: 3 (7.3%)	0.575
Symptomatic intracerebral hemorrhage	4, 5.3% [1.5%, 12.9%]	1, 2.9% [0.1%, 14.9%]	3, 7.3% [1.5%, 19.9%]	0.62
In-hospital mortality	4, 5.3% [1.5%, 12.9%]	2, 5.7% [0.7%, 19.2%]	2, 4.9% [0.6%, 16.5%]	>0.999
NIHSS score (postintervention)	5.5 (0–28)	3 (0–23)	11 (1–28)	3.22E-06
Discharge location	SNF: 11 (14.5%) Rehab: 40 (52.6%) Hospice: 3 (3.9%) Expired: 3 (3.9%) LTACH: 3 (3.9%) Home: 16 (21.1%)	SNF: 4 (11.4%) Rehab: 14 (40%) Hospice: 0 (0%) Expired: 1 (2.9%) LTACH: 2 (5.7%) Home: 14 (40%)	SNF: 7 (17.1%) Rehab: 26 (63.4%) Hospice: 3 (7.3%) Expired: 2 (4.9%) LTACH: 1 (2.4%) Home: 2 (4.9%)	0.005
90-day mRS score	2 (0–6)	1 (0–6)	3 (1–6)	1.26E-05

LTACH = long-term acute care hospital; mRS = modified Rankin Scale; SNF = skilled nursing facility.

Unless otherwise noted, values are reported as the number (%) or number, percentage [95% confidence interval]. Median and range are reported for NIHSS and mRS scores. Boldface type indicates statistical significance.

$Z^*_R = 0.451 \text{ M}_1 \text{ origin diameter} - 0.392 \text{ Distance from petrous ICA to clot face} - 1.28 \text{ ICA-to-M}_1 \text{ tapering} - 0.053 \text{ ipsi ACOM present} + 0.389 \text{ ipsi PCOM present} + 0.291 \text{ Tan score (distal collateral grading)}$

The stringent anatomical-only LASSO model retained only 3 of 9 anatomical predictor variables:

$Z^*_R = 0.165 \text{ M}_1 \text{ origin diameter} - 0.760 \text{ ICA-to-M}_1 \text{ tapering} + 0.160 \text{ Tan score (distal collateral grading)}$

The stringent anatomical-only LASSO model achieved a mean misclassification error of 0.276 compared to 0.237 for the lenient anatomical-only LASSO model, but both lenient and stringent models again produced identical ROC curves (Fig. 3) with a Youden accuracy of 80.3% (Table 3). Intra-class correlation among measurements conducted by 3 authors (Y.D., J.P., S.P.) was substantial at 0.972.

In summary, the anatomical predictor variables most significantly correlated with successful first-pass complete recanalization (i.e., largest standardized regression coefficients) were larger M_1 origin diameter, decreased ICA-to- M_1 blood vessel diameter tapering, and better distal collaterals. Stringent model penalization predicted identical thrombectomy outcomes as the lenient models that retained more predictor variables. Thus, the stringent subset of predictor variables was sufficient to achieve the most accurate predictions possible of thrombectomy outcome using this approach.

Discussion

Large-vessel occlusion is present in approximately 30% of all acute ischemic stroke patients and has historically been associated with significant morbidity and mortality.⁴ Significant advancements in catheter technology and neurointerventional techniques have improved the safety

TABLE 3. Multivariate modeling results using logistic LASSO regression and leave-one-out cross-validation for prediction of first-pass complete (TICI grade 3) recanalization

Initial Predictor Variables	Penalization Extent	Model Specification	Standardized Model Specification	λ	MME	Youden Index	Youden Accuracy	Youden Sensitivity	Youden Specificity
All	Lenient	$Z = 1.12 I_{HTN} - 0.20 I_{CAD} - 0.64 I_{Right-sided\ occlusion} + 0.45 M_1\ origin\ diameter - 99.9\ ICA-to-M_1\ tapering + 0.504\ ipsi\ PCOM\ present + 0.199\ Tan\ score\ (distal\ collateral\ grading)$	$Z = 0.544 I_{HTN} - 0.0944\ I_{CAD} - 0.321 I_{Right-sided\ occlusion} + 0.183 M_1\ origin\ diameter - 0.911\ ICA-to-M_1\ tapering + 0.220\ ipsi\ PCOM\ present + 0.205\ Tan\ score\ (distal\ collateral\ grading)$	0.047	0.237	0.454	81.6%	73.2%	91.4%
All	Stringent	$Z = 0.457 I_{HTN} - 0.299 I_{Right-sided\ occlusion} + 0.182 M_1\ origin\ diameter - 73.2\ ICA-to-M_1\ tapering + 0.053\ Tan\ score\ (distal\ collateral\ grading)$	$Z = 0.222 I_{HTN} - 0.149 I_{Right-sided\ occlusion} + 0.0741 M_1\ origin\ diameter - 0.668\ ICA-to-M_1\ tapering + 0.0549\ Tan\ score\ (distal\ collateral\ grading)$	0.090	0.263	1) 0.454 2) 0.402	1) 81.6% 2) 81.6%	1) 78.0% 2) 73.2%	1) 85.7% 2) 91.4%
Anatomical	Lenient	$Z = 1.11 M_1\ origin\ diameter - 0.0446\ Distance\ from\ petrous\ ICA\ to\ clot\ face - 139.9\ ICA-to-M_1\ tapering - 0.116\ ipsi\ ACOM\ present + 0.893\ ipsi\ PCOM\ present + 0.282\ Tan\ score\ (distal\ collateral\ grading)$	$Z = 0.451 M_1\ origin\ diameter - 0.392\ Distance\ from\ petrous\ ICA\ to\ clot\ face - 1.28\ ICA-to-M_1\ tapering - 0.053\ ipsi\ ACOM\ present + 0.389\ ipsi\ PCOM\ present + 0.291\ Tan\ score\ (distal\ collateral\ grading)$	0.008	0.237	1) 0.449 2) 0.420 3) 0.399	1) 80.3% 2) 80.3% 3) 80.3%	1) 75.6% 2) 70.7% 3) 68.3%	1) 85.7% 2) 91.4% 3) 94.3%
Anatomical	Stringent	$Z = 0.406 M_1\ origin\ diameter - 83.3\ ICA-to-M_1\ tapering + 0.159\ ipsi\ PCOM\ present + 0.155\ Tan\ score\ (distal\ collateral\ grading)$	$Z = 0.165 M_1\ origin\ diameter - 0.760\ ICA-to-M_1\ tapering + 0.0692\ ipsi\ PCOM\ present + 0.160\ Tan\ score\ (distal\ collateral\ grading)$	0.062	0.276	1) 0.449 2) 0.420 3) 0.399	1) 80.3% 2) 80.3% 3) 80.3%	1) 75.6% 2) 70.7% 3) 68.3%	1) 85.7% 2) 91.4% 3) 94.3%

ipsi = ipsilateral; MME = mean misclassification error.

FIG. 3. ROC curves demonstrating model performance at predicting successful first-pass complete recanalization (TICI grade 3) in the patient cohort using leave-one-out cross-validation. The ROC curves are depicted for models fit via LASSO regression using all 19 predictors or the subset of 9 anatomical predictors as the initial input variable set. Lenient and stringent LASSO model fits produced identical ROC curves for both the full and anatomical-only models.

and efficacy profile of mechanical thrombectomy, which has now become standard of care in selected patients with large-vessel occlusion.¹⁰ Multiple studies have compared the safety and efficacy of different mechanical thrombectomy techniques, yet studies examining anatomical predictors of successful recanalization are largely lacking.^{6,16}

To the best of our knowledge, our study is one of the first to describe an association between intracranial ICA vessel caliber tapering and successful recanalization. Specifically, we have found that gentle tapering along the intracranial ICA and larger M_1 diameters is associated with improved likelihood of first-pass complete recanalization, whereas steeper tapering and smaller M_1 diameters are associated with reduced likelihood of first-pass complete recanalization. In our study population, patients who experienced first-pass recanalization had a 30.3% lower degree of vessel tapering from the petrous ICA to the M_1 origin when compared to patients who required multiple passes. Average petrous ICA diameters were comparable between our study groups, but patients with first-pass recanalization had significantly larger M_1 diameters as a result of lower rates of tapering.

Our single-center outcomes are comparable to thrombectomy outcomes described in the current literature. In the previous neurointerventional literature, a recanalization grade greater than or equal to TICI 2b was determined as an acceptable outcome.² We were able to achieve TICI grade 2b or higher recanalization in 86.8% of patients. Recently, however, a call for a higher outcome standard has been made as more up-to-date literature suggests that patients with TICI grade 2b recanalization have inferior outcomes when compared to patients who achieve TICI

grade 2c (defined as near-complete reperfusion except for slow flow in a few distal cortical vessels or the presence of small distal cortical emboli) or TICI grade 3 recanalization. Furthermore, achievement of first-pass TICI grade 3 recanalization not requiring more than one attempt has recently been demonstrated to be associated with significantly higher rates of good clinical outcome but only occurs in approximately 25% of patients.¹⁷ First-pass complete recanalization was achieved in 46% of our patient population, and major hemorrhagic complications occurred in approximately 5% of patients. Over the years of our study, our institution favored aspiration thrombectomy over stent retriever thrombectomy as significantly more first-pass complete recanalizations were achieved when using an aspiration-only strategy versus a stent retriever-only strategy. The anatomical measurement outcomes in our study are also comparable to those described in the literature.¹² Furthermore, our study also supports previous findings that describe the likelihood of first-pass recanalization as dependent on distal collateral status.¹⁵

Previous studies have described that upstream vessel tapering and proximal stenosis are associated with downstream flow acceleration and high wall shear stress at downstream vessel bifurcations.^{5,7}

The application of these previous findings in the cerebral aneurysm literature to the conditions surrounding clot retrieval in acute ischemic stroke is speculative, but one may infer the following: a steeper vessel tapering may generate an environment in which a higher retrieval force is required to adequately mobilize an occlusive thrombus due to a higher magnitude of flow acceleration along the intracranial ICA. Current aspiration forces generated by modern aspiration catheter and pump systems may not be enough to overcome forward forces present at the proximal clot interface in vessel systems with significant tapering.

Furthermore, a hypothetical mechanism for loss of stent retriever efficacy in vessel systems with steep tapering could be transient loss of stent retriever wall opposition and downstream embolic showering as the stent retriever is being withdrawn into a vascular system with a progressively increasing diameter in the setting of preserved forward flow.

Despite usage of both modern stent retriever and aspiration technologies, our institutional experience shows that we have had more favorable revascularization results when using aspiration as a first-line technique. Additionally, we do not routinely use balloon guide catheters, and whether or not their use would impact our study findings is unclear.

Nevertheless, our findings provide novel insight into the anatomical factors that impact the success or failure of first-pass clot retrieval in acute ischemic stroke. In the previously described model where the likelihood of thrombus retrieval is determined by competing forward and reverse forces acting at the thrombus,¹¹ vessel tapering may augment the forward force of impaction and hinder effective clot retrieval. Future studies examining the hemodynamic consequences of vessel tapering in large-vessel occlusion may be helpful in supporting a causal relationship between vessel tapering and the first-pass effect. If our findings are supported by future fluid dynamic studies, vessel tapering may become a preintervention variable that guides re-

trieval technique modification, such as theoretical usage of distal protection devices during stent retrieval or usage of relative flow arrest techniques provided by balloon guide catheters.

Limitations

Given the retrospective nature of our study, associations found between vessel tapering and recanalization efficacy suggest single-center correlation but do not represent causation. Computational fluid dynamic simulations beyond the scope of our research may elucidate mechanistic relationships between vessel tapering and hemodynamic forces occurring at the clot-catheter interface. Future multicenter studies with larger sample sizes are required to validate our findings and conclusions in a broader context.

Furthermore, we did not examine associations between large-vessel occlusion etiology and vessel tapering, and whether or not exaggerated vessel tapering is simply a by-product of specific underlying cerebrovascular pathologies such as intracranial atherosclerotic disease remains to be explored. Early in our study design, we wished to investigate large-vessel occlusion etiology as a variable for first-pass effect in our patient population, but we were unable to consistently and reliably determine stroke etiology based on a retrospective review of our medical records. Our results need to be interpreted in the context of omitting this potential confounding variable.

Another limitation to our study is the fact that all measurements were conducted manually on 2D angiograms, which may introduce some degree of error when compared to automated vessel analyses. To the best of our ability, we accounted for this limitation by having all authors involved in vessel measurement follow a reproducible standardized measurement protocol. Interrater agreement was satisfactory, and our methods of measurement are more practical than reliance on automated software measurements until automated segmentation software is made more clinically practical and available.

Conclusions

In this retrospective case-control study, we demonstrated that a larger M_1 diameter and a lower rate of vessel diameter tapering along the course of the intracranial ICA are associated with first-pass recanalization for patients with M_1 occlusions. These findings may guide the development of improved revascularization devices and techniques for acute ischemic stroke secondary to large-vessel occlusion.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Srivatsa, Duan. Acquisition of data: Srivatsa, Duan, Sheppard, Pahwa, Pace, Zhou. Analysis and interpretation of data: Srivatsa, Duan, Sheppard, Pahwa, Pace, Zhou. Drafting the article: Srivatsa, Duan, Sheppard, Pahwa, Pace. Critically revising the article: Bambakidis, Srivatsa, Duan, Pace. Reviewed submitted version of manuscript: Bambakidis, Duan. Approved the final version of the manuscript on behalf of all authors: Bambakidis. Administrative/technical/material support: Srivatsa, Duan. Study supervision: Bambakidis.

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