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ORIGINAL RESEARCH

Association of Pretreatment Perfusion Imaging Parameters With 90-Day Excellent Functional Outcomes in Anterior Circulation Distal Medium Vessel Occlusion Stroke

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ABSTRACT

BACKGROUND AND PURPOSE: Acute ischemic strokes caused by distal medium vessel occlusions (DMVO) represent a significant proportion of all stroke cases, yet the predictors of excellent functional outcomes in these patients remain poorly understood. This study aims to identify pretreatment computed tomography perfusion (CTP) parameters associated with excellent functional outcomes, defined as a modified Rankin Scale (mRS) score of 0-1 at 90 days, in patients with anterior circulation DMVO.

MATERIALS AND METHODS: We conducted a retrospective multicenter study involving patients with anterior DMVO, from three stroke centers within the Johns Hopkins Medical Enterprise. Baseline demographic, clinical, and imaging data were collected, with CTP parameters analyzed using RAPIDAI software. Univariable and multivariable logistic regression models were used to identify predictors of excellent outcomes. Receiver operating characteristic (ROC) curves were constructed to assess the predictive accuracy of CTP parameters.

RESULTS: Among the 82 patients (median age, 71 years; 57% female), occlusions were located in the M2 segment in 89%, M3 in 8.5%, and A2 in 2.4%. IVT was administered to 37% of patients, and EVT was attempted in 59%. Excellent outcomes at 90 days were achieved in 45% of patients. In univariate analysis, white race (OR, 4.14; 95% CI, 1.66–10.9; P=0.003), higher CBV index (OR per 0.1-unit change, 1.45; 95% CI, 1.08–2.05; P=0.022), and lower relative cerebral blood flow (rCBF < 20%) volumes (OR, 0.91; 95% CI, 0.81–0.98; P=0.038) were significantly associated with excellent outcomes. In multivariate analysis adjusting for age, sex, race, IVT administration, EVT attempted, dyslipidemia, and premorbid mRS, higher CBV index remained a significant independent predictor (OR per 0.1-unit change, 1.72; 95% CI, 1.14–2.81; P=0.017), and lower rCBF < 20% volume was associated with better outcomes (OR, 0.91; 95% CI, 0.80–0.98; P=0.05). The multivariate model demonstrated good predictive performance (area under the ROC curve, 80%; 95% CI, 70%–90%; P < 0.001).

CONCLUSIONS: In patients with anterior circulation DMVO, a higher CBV index on pretreatment CTP is an independent predictor of excellent functional outcomes at 90 days. These findings suggest that CTP parameters, particularly the CBV index, may be useful in prognostic assessment for this stroke population. Further studies are needed to validate these results and optimize therapeutic approaches.

ABBREVIATIONS: ABC = definition; XYZ = definition.

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INTRODUCTION

Acute ischemic strokes resulting from occlusions in medium-sized vessels or distal vessels, collectively known as Distal Medium Vessel Occlusion (DMVO) strokes, account for a significant proportion of 25-40% of all acute stroke cases.[1,2] According to the consensus definition from Saver et al., DMVOs include occlusions in arteries with diameters between 0.75 and 2.0 mm, such as the M2-M4 segments of the middle cerebral artery (MCA), A2-A5 segments of the anterior cerebral artery (ACA).[3] These vessels supply superficial cortical and subcortical areas, making their occlusion often resulting in disabling but heterogeneous syndromes depending on the specific vascular territory involved. However, the clinical management and prognostic evaluation of these DMVO strokes pose substantial challenges.[2,4–16]

While Ospel et al. focused on the natural course of medium-vessel occlusion stroke in untreated patients, our study included a real-world patient population where various treatments were administered.[17] The role of endovascular therapy (EVT) in DMVO stroke treatment remains an evolving field of research. Although EVT has been shown to be beneficial in large vessel occlusions (LVO), its utility in DMVO is less well-established. The smaller caliber and distal location of these vessels increase the risk of hemorrhagic complications, as noted in several studies by Salim et al.[2,18,19] Additionally, the clinical management of DMVO is complicated by diagnostic limitations. Although computed tomography angiography (CTA) is commonly used, it can miss up to one-third of DMVO cases and is less sensitive than CT perfusion (CTP).[20–22]

CTP, on the other hand, is gaining traction as a promising tool for diagnosis, but its ability to predict outcomes specifically for DMVO patients remains underexplored.[23,24] More and more, CTP is being used to assess the extent of brain ischemia and the status of collateral circulation in DMVO strokes. Key perfusion metrics such as, cerebral blood volume (CBV), cerebral blood flow (CBF), and time to maximum (Tmax), offer important insights into the viability of brain tissue, which might help predicting functional outcomes.[13,25–27] Collateral flow, in particular, plays a critical role in determining infarct size and recovery potential, with well-collateralized tissue being more resistant to ischemic damage.[13]

Despite use of CTP for decision making in LVO, there remains a large gap between our understanding of the relationship between perfusion imaging parameters and functional outcome in patients with DMVO strokes.[28] Large-scale studies, such as the study by Yedavalli et al., which analyzed 1,568 patients, have provided valuable insights into pretreatment factors associated with DMVO outcomes.[6,9,29] In addition, a study by Nome et al. demonstrated the importance of clinical and technical factors in predicting DMVO outcomes post-MT, highlighting the role of procedural variables and patient age.[30] However, the association between specific perfusion parameters and clinical outcomes in DMVO patients has not been thoroughly characterized and requires further investigation.

For the DMVO stroke population, the selection of functional outcomes needs to be tailored. While a favorable functional outcome, such as a modified Rankin Scale (mRS) score of 0 to 2, is an acceptable primary endpoint for LVO strokes, this maybe a suboptimal primary outcome for DMVO.[2,14] Some studies have suggested that it may be appropriate to use more stringent outcome measures for this patient population, such as mRS 0-1.[31] This stricter outcome measure could better reflect the expected course of DMVO and ensures that outcome measures are sensitive enough to detect meaningful clinical improvements in this population.[6]

The objective of this study is to identify which pretreatment CTP parameters that are associated with excellent functional outcomes, defined as a 90-day mRS score of 0 to 1, in patients with anterior DMVO strokes.

MATERIALS AND METHODS

Study Design

In this retrospective cohort multicenter analysis, we identified patients with anterior circulation DMVOs from three stroke centers within the Johns Hopkins Medical Enterprise. The study was approved through the Johns Hopkins institutional review board (IRB #00269637).[13,25–27,32,33] The Health Insurance Portability and Accountability Act (HIPAA) and the Declaration of Helsinki were followed in the conduct of the study. The institutional review boards waived informed consent due to the retrospective method of research. We have followed the STROBE checklist guidelines as an observational study.[34]

Consecutive patients who met our inclusion criteria were chosen from the dates 29 July 2019 to 1 October 2023. Inclusion criteria included: (1) Diagnostically adequate multimodal pretreatment CT imaging, including non-contrast head CT, CT angiography and CT perfusion. (2 Anterior circulation DMVO, as defined by Saver et al., encompassing occlusions in the M2, M3 and M4 segments of the middle cerebral artery (MCA) and the A2, A3, A4 and A5 segments of the anterior cerebral artery (ACA)[3,35,36]. While, (3), Availability of 90-day mRS score. Patients were excluded if they had: (1) posterior circulation occlusions, which were excluded to ensure the homogeneity of the study population; or (2) poor-quality or non-diagnostic CT perfusion imaging; or (3) presence of multiple simultaneous infarcts or infarcts outside the territory of the occluded vessel.

Data Collection

We collected a specific set of baseline demographic and clinical data for each patient through the stroke center database. Baseline data included age, sex, race, date of admission. Clinical data included past medical history data such as hyperlipidemia, coronary artery disease (CAD), hypertension, diabetes, alcohol, smoking, atrial fibrillation, and other, as these serve as AIS risk factors. Admission data included admission glucose, NIH stroke scale (NIHSS), and the Alberta Stroke Program Early CT Score (ASPECTS), with the ASPECTS score applied specifically to patients with middle cerebral artery (MCA) strokes. Time data included well to door time, door to needle time in patients who received intravenous thrombolysis (IVT), and door to groin puncture times.

Imaging markers obtained from CT scans included the occlusion site, laterality of the occlusion, CT perfusion parameters, and the modified Thrombolysis in Cerebral Infarction (mTICI) score, which is a grading system used to assess the degree of blood flow restoration.[12] The mTICI score was assessed using digital subtraction angiography (DSA) by board-certified neuroradiologists for patients who underwent EVT. Successful recanalization was defined as mTICI grades of 2b-3, while excellent recanalization was defined as mTICI grades of 2c-3. Recanalization success was not evaluated in patients treated with only medical management. Additionally, we recorded any hemorrhagic transformation of infarctions using the ECASS-2 criteria to classify hemorrhagic changes.[37] Individual choices on the use of EVT and/or IVT were based on consensus assessments by the stroke team in accordance with institutional standards.

Non-Contrast CT (NCCT)

NCCT scans in our study were conducted using helical scanning technique. The scans were performed with each slice having a thickness of 5 mm and a reconstruction resolution of 0.75 mm. The kilovoltage peak (kVp) was set at 120, and the milliampere-seconds (mAs) were set at 365. The rotation time of the CT scanner was maintained at 1 second, and the total acquisition time for each scan ranged between 6 to 8 seconds. The collimation of the scans was 128 x 0.6 mm, and a pitch value of 0.55 was used. All scans were performed in a craniocaudal direction.

Pretreatment CTA

The CTA of the head and neck in our study was carried out as a single-phase CTA, with administration of non-ionic iodinated contrast material in the volume range of 50-70 ml, injected at a flow rate of 5-6 ml per second. The contrast was introduced from the aortic arch through to the vertex of the head, employing a bolus-triggered technique. The scanning process was conducted with a slice thickness of 3 mm and further refined with 0.75 mm reconstructions. The CTA scanning parameters were: the kVp was adjusted to a range of 90/150 with the utilization of an Sn filter. The Quality Reference mAs was set to 180. The rotation time was 0.25 seconds, with an average acquisition time ranging from 3 to 5 seconds for efficient imaging. The collimation was set at 128 x 0.6 mm, and a pitch value of 0.7 was used. The scans were conducted in a craniocaudal direction.[13]

Pretreatment CTP

Only the CT perfusion images that were judged sufficiently diagnostic were included in the study. All images were evaluated for diagnostic adequacy by board-certified neuroradiologists with ten years of practical experience.

The CTP imaging was conducted using a pre-specific protocol. Initially, patients received an injection of 50 ml of non-ionic iodinated contrast material followed by a 30 ml saline chaser, delivered at a rate of 5-6 ml per second. The anatomical coverage for this scan ranged from 70 to 100 mm with each slice having a thickness of 5 mm. The scanning parameters were set to 70 kVP, 200 mAs, with a rotation time of 0.25 seconds and an average acquisition time of 60 seconds. The collimation used was 48 x 1.2 mm, with a pitch value of 0.7, and a 4D coverage range of 114 mm at an interval of 1.5 seconds, scanning in a craniocaudal direction.[32]

Using commercial RAPIDAI perfusion software, version 5.2.2 (iSchemaView, Menlo Park, CA, USA), CT perfusion source images were post-processed to yield automated measures of different thresholds of relative cerebral blood flow (rCBF), which measures the blood flow in a specific brain region relative to normal tissue, with thresholds of < 20%, 30%, 34%, 38%; relative cerebral blood volume (CBV) < 34%, 38%, 42% and, time to maximum (Tmax) volumes of > 4 seconds, > 6 seconds, > 8 seconds, > 10 seconds. We also calculated the CTP parameters of tissue collateral including CBV index (defined as the mean relative CBV obtained by dividing the average of all CBV values from the Tmax > 6 s region within the ischemic hemisphere by the average of all CBV values from all tissues with Tmax ≤ 4 s) and HIR (defined as the ratio of the Tmax > 10 s lesion volume divided by the Tmax > 6 s lesion volume).

Outcome measure

The primary outcome measure of our study was 90-day mRS of 0-1. The 90-day mRS were determined by a stroke neurologist or certified nurse practitioner by either telephone interviews or during the patients' follow-up visits.

Statistical Analysis

Descriptive statistics were used to summarize patient data. Categorical variables are presented as frequencies and percentages, while continuous variables are summarized using medians and interquartile ranges (IQRs).

Univariable logistic regression was performed to examine the association between pre-stroke clinical factors, imaging parameters, including CTP, and treatment factors with excellent outcomes (90-day mRS score of 0-1). Variables with a p-value less than 0.10 in the univariable analysis were included in a multivariable logistic regression model. The results are reported as odds ratios (ORs) with 95% confidence intervals (CIs).

Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the predictive performance of CTP imaging parameters for a 90-day mRS score of 0-1, with the area under the curve (AUC) calculated to assess discrimination. No imputations have been done, analyses were performed using complete case analysis as the number of missing data was negligible as documented in supplementary figure-1. All statistical tests were two-sided, and p-values less than 0.05 were considered statistically significant. Analyses were conducted using R software (version 4.2.2).

Power Calculation

We performed a retrospective power analysis to evaluate the adequacy of the sample size for comparing the CBV index between two groups using a two-sample t-test. With a two-sided alpha level of 0.05, the analysis determined that the study had a 73.71% probability of detecting a statistically significant difference between the groups.

RESULTS

Baseline Characteristics

A total of 82 consecutive patients met our inclusion criteria. The baseline demographics of the study population reveal a median age of 71 years (IQR 62-79), with a higher proportion of females (57%) compared to males (43%). Racial composition includes 45% Black, 54% White, and 1.2% Asian. The majority of occlusions were located in the M2 segment (89%), followed by M3 (8.5%) and A2 (2.4%). Significant comorbidities included hypertension (82%), dyslipidemia (66%), heart disease (49%), and atrial fibrillation (39%). The median NIHSS score on admission was 8 (IQR 5-13), with a median ASPECTS score of 9 (IQR 8-10). Hemorrhagic transformation occurred in 23% of cases with a predominant hemorrhagic infarction (H1) type 2 category. Notably, 59% of patients underwent EVT, and 37% received IVT. Detailed demographics are shown in Supplementary Table 1.

Univariable and Multivariable Regression

In the univariable analysis, several factors were significantly associated with excellent outcomes (mRS 0-1) at 90 days. White race was a strong predictor (OR 4.14, 95% CI 1.66-10.9, p=0.003), while dyslipidemia showed a trend towards significance (OR 2.25, 95% CI 0.89-5.93, p=0.091). Lower volumes of regions rCBF <20% were associated with better outcomes (OR 0.91, 95% CI 0.81-0.98, p=0.038). Premorbid mRS of 0 compared to 1 showed a non-significant trend towards predicting favorable outcomes (OR 0.35, 95% CI 0.11-1.00, p=0.059). The CBV index (per 0.1 change) was higher in patients with 90-day mRS 0-1 as compared to 90-day mRS 2-6, (OR 1.45, 95% CI 1.08 to 2.05, p=0.022). Detailed univariable regression between prestroke, perfusion parameters, treatment factors and 90-day mRS is characterized in Supplementary Table 2.

Multivariable logistic regression analysis further confirmed the predictors of excellent outcomes. After adjustment for age, sex, race, IVT administration, MT attempt, dyslipidemia, and premorbid mRS, lower mismatch volume was independently associated with excellent outcomes (OR 0.98, 95% CI 0.96-1.00; p=0.048). The CBV Index was a particularly strong predictor with an OR of 1.45 per 0.1-unit change (95% CI 1.08-2.05, p=0.017). The rCBF <20% volume (OR 0.91, 95% CI 0.80-0.98, p=0.05) approached statistical significance. (Table-1)

Table 1: Multivariable logistic regression model for perfusion parameters after adjusting for related prestroke and treatment factors

Perfusion Parameter	Adjusted Model*	
	OR (95% CI)1	p-value
rCBF <20% volume (mL)	0.91 (0.80 to 0.98)	0.05
rCBF <30% volume (mL)	0.97 (0.92 to 1.00)	0.089
rCBF <34% volume (mL)	0.97 (0.93 to 1.00)	0.061
rCBF <38% volume (mL)	0.97 (0.94 to 1.00)	0.053
Tmax >4s volume (mL)	1.00 (0.99 to 1.00)	0.64
Tmax >6s volume (mL)	0.99 (0.98 to 1.00)	0.15
Tmax >8s volume (mL)	0.98 (0.96 to 1.00)	0.12
Tmax >10s volume (mL)	0.98 (0.96 to 1.00)	0.12
Mismatch Volume (mL)	0.98 (0.96 to 1.00)	0.048
Mismatch Ratio	1.04 (1.00 to NA)	0.42
HIR (per 0.1 change)	0.83 (0.67 to 1.01)	0.071
CBV <34 mL	0.97 (0.92 to 1.00)	0.16
CBV <38 mL	0.98 (0.93 to 1.00)	0.15
CBV <42 mL	0.98 (0.94 to 1.00)	0.14
CBV Index (per 0.1 change)	1.72 (1.14 to 2.81)	0.017

ROC Analysis of Perfusion Parameters

Table 2 presents the predictive accuracy of various perfusion parameters in determining excellent stroke outcomes at 90 days. The rCBF <20% volume demonstrated moderate predictive power, with an AUC of 61% (95% CI: 53% to 70%) and a statistically significant p-value of 0.01. Notably, the CBV Index exhibited a higher predictive accuracy with an AUC of 64% (95% CI: 52% to 76%) and a significant p-value of 0.02. (Figure-1)

Table 2: Predictive Accuracy of Perfusion Predictors for 90-Day Excellent Stroke Outcomes

Perfusion Parameter	AUC (95% CI)	P-value
rCBF <20% volume (mL)	61% (53% to 70%)	0.01
rCBF <30% volume (mL)	56% (45% to 68%)	0.3
rCBF <34% volume (mL)	59% (47% to 71%)	0.13
rCBF <38% volume (mL)	59% (47% to 71%)	0.15
Tmax >4s volume (mL)	60% (48% to 73%)	0.11
Tmax >6s volume (mL)	62% (50% to 74%)	0.06

Tmax >8s volume (mL)	61% (49% to 73%)	0.09
Tmax >10s volume (mL)	61% (49% to 73%)	0.08
Mismatch Volume (mL)	60% (48% to 73%)	0.11
HIR	60% (47% to 73%)	0.13
CBV <34 mL	58% (47% to 68%)	0.14
CBV <38 mL	57% (46% to 68%)	0.2
CBV <42 mL	59% (48% to 70%)	0.12
CBV Index	64% (52% to 76%)	0.02

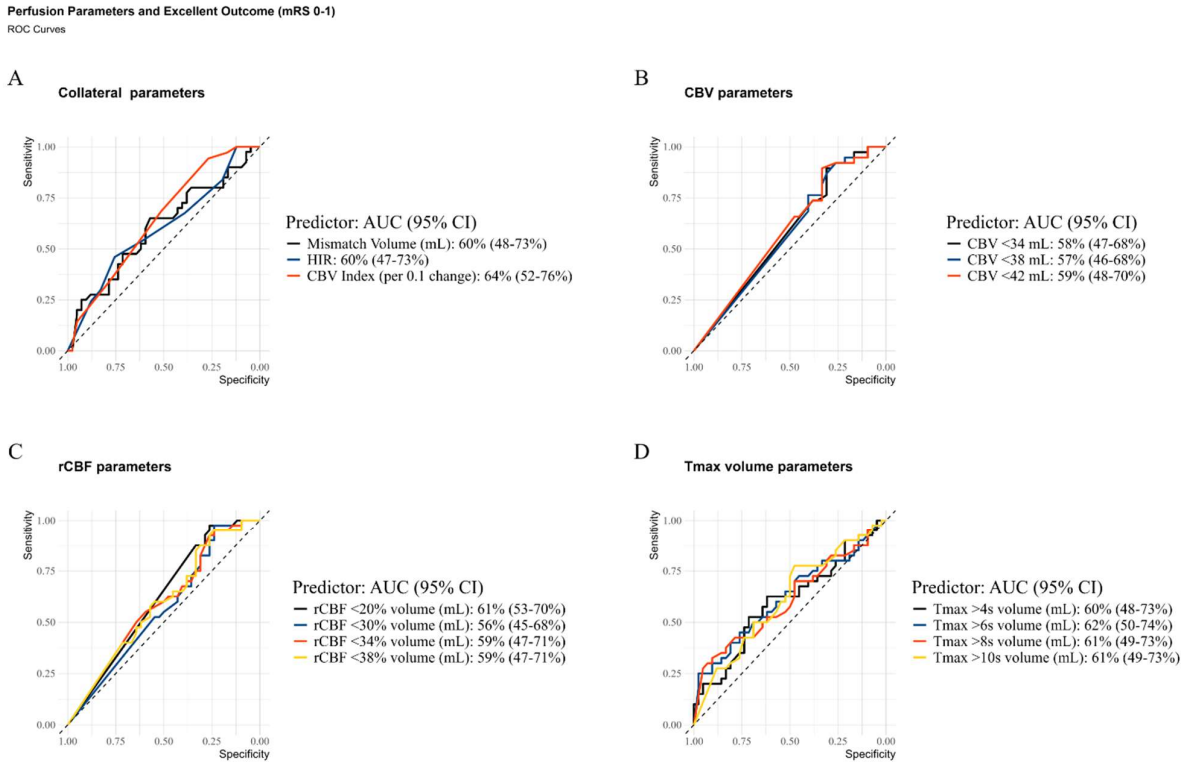

FIG 1. ROC Curves for CT Perfusion Parameters Predicting Excellent Outcome (mRS 0-1). (A) Mismatch volume, HIR, and CBV index. (B) CBV thresholds: <34 mL, <38 mL, <42 mL. (C) rCBF thresholds: <20%, <30%, <34%, <38%. (D) Tmax thresholds: >4s, >6s, >8s, >10s. AUC values with 95% CIs are shown for each parameter.

Clinical Predictors and Multivariable Model for 90-Day Excellent Stroke Outcomes

Table 3 details the predictive accuracy of clinical predictors and a multivariable model in achieving excellent stroke outcomes at 90 days. The multivariable model demonstrated superior predictive accuracy with an AUC of 80% (95% CI: 70% to 90%) and a highly significant p-value of <0.001. The performance of the reduced model including only variables with significant the discriminatory power is presented in supplementary Figure 2.

Table 3: Predictive Accuracy of Clinical Predictors and Multivariable Model for 90-Day Excellent Stroke Outcomes

Variable	AUC (95% CI)	P-value
Multivariable Model	80% (70% to 90%)	<0.001
CBV Index	64% (52% to 76%)	0.02
Age	50% (37% to 63%)	0.99
Sex	52% (41% to 63%)	0.68
IVT	53% (43% to 64%)	0.54
MT	52% (41% to 63%)	0.69
Dyslipidemia	59% (49% to 69%)	0.09
Premorbid mRS	59% (50% to 68%)	0.05

Race	68% (57% to 78%)	<0.001

Among the individual clinical predictors, the CBV Index emerged as the most significant, with an AUC of 64% (95% CI: 52% to 76%) and a p-value of 0.02. Conversely, age, sex, IVT, and MT showed limited predictive power, with AUC values ranging from 50% to 53% and non-significant p-values. (Figure-2)

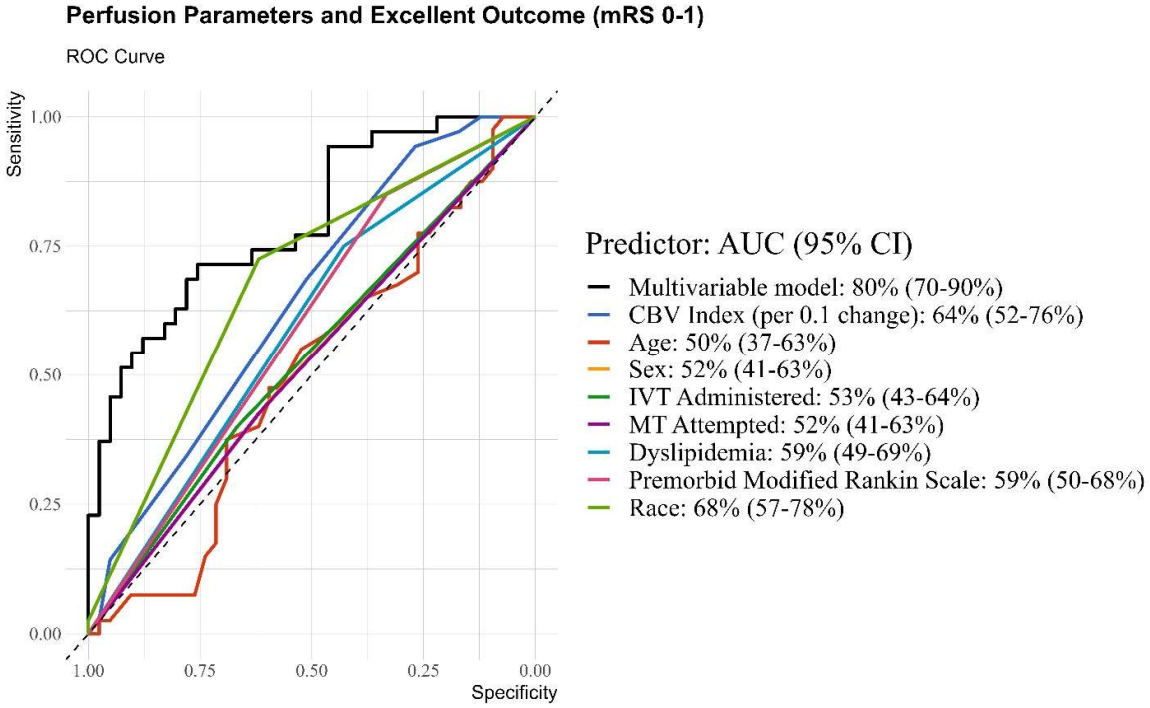

FIG 2. Multivariate Model ROC Curve of CBV index

DISCUSSION

In this retrospective multicenter study involving patients with anterior circulation DMVO, we aimed to identify pretreatment CTP parameters associated with excellent functional outcomes, defined as a mRS score of 0–1 at 90 days. We found that a higher CBV index was significantly associated with excellent functional outcomes at 90 days. Specifically, for every 0.1-unit increase in the CBV index, the odds of achieving an excellent outcome increased by 45% (odds ratio, 1.45; 95% CI, 1.08 to 2.05; $P = 0.017$). Additionally, lower rCBF < 20% were associated with excellent outcomes (odds ratio, 0.91; 95% CI, 0.80 to 0.98; $P = 0.05$). To our knowledge, this is the first study to evaluate CTP parameters as predictors of excellent mRS 0–1 outcomes in anterior circulation DMVO patients.

The CBV index is an important surrogate of tissue collateral circulation and indicator of the relative blood volume within critically hypoperfused tissue and represents an indirect compensatory response to acute occlusion through collateralization.[38] A higher CBV index indicates improved collateral blood flow and is associated with smaller infarct volumes, better functional outcomes, and increased likelihood of favorable response to EVT.[39] Conversely, a lower CBV index suggests poor collateral status, increased risk of infarct growth, and worse clinical outcomes.[39] The CBV index has been shown to be an independent predictor of functional independence at 90 days in patients treated with MT, even in extended time in patients with LVO.[39] In our previous paper, a recent analysis of DMVO, the CBV Index was independently associated with final infarct volumes demonstrating the role of collateral blood flow.[13] Importantly, the predictive accuracy of the CBV index, was moderate (AUC 64%, 95% CI 52% to 76%). Clinically, this means that the CBV index should not be used in isolation to guide treatment decisions. Instead, it should be incorporated into a broader clinical assessment that includes other important factors (supplementary figure-2), and that is evident in our multivariable model, in which the predictive accuracy improved significantly (AUC 80%, 95% CI 70% to 90%, p<0.001).

Our study adds to the growing evidence of CBV index as a strong biomarker for collateral assessment and outcomes in DMVO. A recent study showed that a CBV index ≤ 0.7 was independently associated with HT in patients with medium-vessel occlusion, although HT occurred in 23% of patients, we chose not to include it in the multivariable analysis because it is a post-treatment event that may act as a mediator between treatment and outcomes rather than as a confounder.[40] Another recent study demonstrated that a CBV index ≥ 0.7 may be independently associated with good clinical outcomes caused by MCA-DMVO who were successfully treated with EVT.[38] Furthermore, a recent study also showed that an HIR < 0.3 is also associated with functional independence.[38] Interestingly, in our study, HIR approached significance (P = 0.071) but was not a significant predictor of excellent outcomes, which aligns with another study where HIR did not correlate with clinical outcomes after successful endovascular recanalization in DMVO patients.[41] The lack of concordance between CBV index and HIR could be related to the pathophysiology of how these parameters are calculated in post processing of CT perfusion. The

HIR is predicated on the hypothesis that tissue with comparatively lower perfusion will exhibit prolonged transit times, which is indicative of microvascular perfusion. This concept is grounded in the understanding that mean transit time and Tmax are critical parameters in assessing tissue perfusion.[42] Moreover, our smaller sample size and the resultant limited statistical power may have contributed to the lack of statistical significance.

Our findings also highlight the limitations of using ASPECTS alone in predicting outcomes for DMVO patients. Although ASPECTS has been widely shown to predict outcomes in LVO, it did not reach statistical significance in our cohort of DMVO patients (odds ratio, 1.19; 95% CI, 0.88 to 1.65; $P = 0.28$). This may be attributed to the relatively small infarct volumes typically seen in DMVO, which may not be adequately captured by the semi-quantitative nature of ASPECTS scoring.[13] In contrast, quantitative perfusion metrics, such as rCBF < 20% volume, provided significant predictive value in our study. rCBF < 20% volume offers a more precise measure of the ischemic core, whereas ASPECTS may lack the sensitivity needed to detect smaller infarcts commonly seen in DMVO.[27,32]

White race emerged as a strong predictor of excellent functional outcomes at 90 days. This finding aligns with previous research indicating racial disparities in stroke outcomes. Several factors may contribute to this observation. Socioeconomic factors and access to healthcare services play crucial roles; Black patients often face barriers to timely and high-quality acute stroke care, including delays in hospital arrival and lower rates of reperfusion therapies.[43,44] Additionally, differences in the prevalence of comorbidities may impact recovery, as Black patients have higher rates of hypertension, which is associated with more severe strokes and poorer outcomes.[45(pp1976-1978)]

While our study offers important insights into the predictors of excellent functional outcomes in patients with anterior DMVO, several limitations must be considered. First, the relatively small sample size limits the ability to perform meaningful subgroup analyses across different treatment modalities. Furthermore, the limited sample size also results in reduced statistical power. Second, the retrospective design of the study inherently introduces selection bias, which may limit the generalizability of the findings. Third, although CTP is widely implemented in comprehensive stroke centers, our results may not be broadly applicable, particularly given that automated CTP calculations were derived from a single commercial software platform. Fourth, our inclusion criteria did not restrict variables such as time to admission, treatment allocation, or treatment success, potentially introducing heterogeneity into our patient cohort. However, univariable logistic regression analyses showed that these variables were not significantly associated with excellent functional outcomes (90-day mRS 0-1), as shown in Table 2, suggesting that their exclusion from the inclusion criteria is unlikely to have affected the results of our study. Lastly, the study cohort predominantly consisted of patients with M2 segment occlusions (89%), which are more proximal compared to occlusions in more distal DMVO locations, such as the M3 or A2 segments. As a result, the generalizability of our findings to patients with more distal occlusions is limited, and further studies are warranted to validate these findings in these subgroups.

Nonetheless, the study's multicenter design, incorporating data from two comprehensive stroke centers, enhances the diversity and generalizability of the sample compared to single-center studies. Future larger-scale, prospective multicenter studies are needed to validate and extend these findings.

CONCLUSIONS

In conclusion, we found that the CT perfusion parameter of CBV index is an independent predictor of excellent outcomes in patients with anterior circulation DMVO. Determining the optimal CTP parameters could facilitate more targeted research, potentially leading to improved treatment strategies and outcomes for this specific stroke population. Larger studies are needed in the future to confirm and expand upon our findings.

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Conflict of interest:

None

Funding

N/A

Informed Consent and Ethical Approval

The study protocol was approved by the institutional review boards of both centers. Patient informed consent was waived by our review boards for this retrospective study.

Presentation

N/A

Collaborators

N/A

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SUPPLEMENTAL FILES

Supplementary Table 1: Baseline and demographics

Characteristic	Overall, N = 82
Age, Median (IQR)	71 (62, 79)
Sex, n (%)	
Female	47 (57)
Male	35 (43)
Race, n (%)	
Black	37 (45)
White	44 (54)
Asian	1 (1.2)
Occlusion segment, n (%)	
M2	73 (89)
M3	7 (8.5)
A2	2 (2.4)
Smoking Status, n (%)	39 (48)
Hypertension, n (%)	67 (82)
Dyslipidemia, n (%)	54 (66)
Diabetes, n (%)	16 (20)
Heart Disease, n (%)	40 (49)
Atrial Fibrillation, n (%)	32 (39)
History of Stroke/TIA, n (%)	11 (13)
Admission Glucose Level, Median (IQR)	119 (103, 137)
Admission NIHSS Score, Median (IQR)	8 (5, 13)
Premorbid Modified Rankin Scale, n (%)	
0	62 (76)
1	20 (24)
Occlusion Laterality, n (%)	
left	52 (63)
right	30 (37)
ASPECTS, Median (IQR)	9.00 (8.00, 10.00)
IVT Administered, n (%)	30 (37)
MT Attempted, n (%)	48 (59)
Symptom Onset to Door Time (mins), Median (IQR)	65 (48, 183)
Door to CT Time (minutes), Median (IQR)	26 (15, 42)
Door to Needle Time (minutes), Median (IQR)	64 (49, 85)
Door to Groin Puncture Time (minutes), Median (IQR)	161 (129, 192)
Modified Thrombolysis in Cerebral Infarction (mTICI) Score, n (%)	

0	4 (8.3)
1	3 (6.3)
2b	10 (21)
2c	5 (10)
3	26 (54)
Hemorrhagic Transformation (HT), n (%)	18 (23)
Type of Hemorrhagic Transformation (HT) if Present, n (%)	
HI1	1 (6.7)
HI2	10 (67)
PH1	3 (20)
PH2	1 (6.7)
Modified Rankin Scale at 90 Days, n (%)	
0	19 (23)
1	21 (26)
2	14 (17)
3	7 (8.5)
4	6 (7.3)
5	1 (1.2)
6	14 (17)

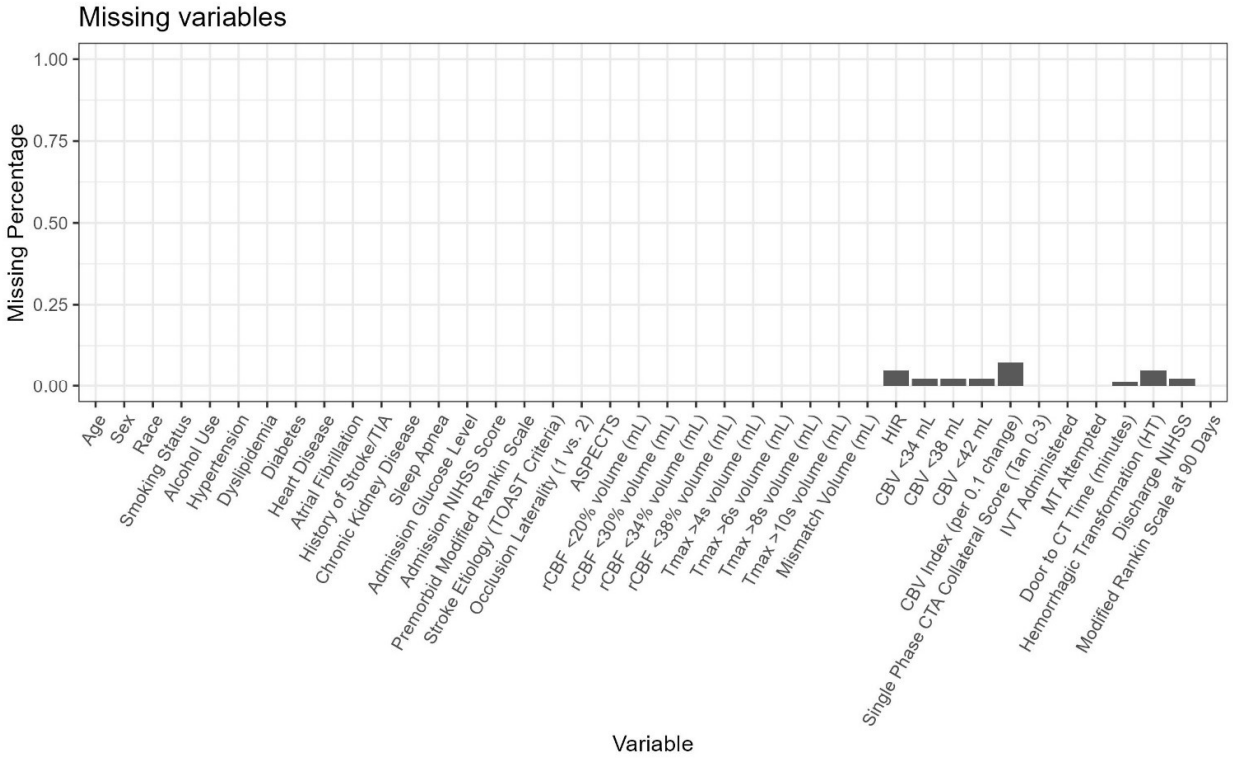
Supplementary Table 2: Univariable logistic regression between prestroke, perfusion parameters, treatment factors and 90-day mRS 0-1

Characteristic	**mRS2-6, N = 42**	**mRS 0-1, N = 40**	**OR (95% CI)[2]**	**p-value**
Pre-stroke factors				
Age, Median (IQR)	70 (62, 81)	71 (63, 78)	1.00 (0.97 to 1.04)	0.97
Sex, n (%)				
Female	25 (60)	22 (55)	—	
Male	17 (40)	18 (45)	1.20 (0.50 to 2.91)	0.68
Race, n (%)				
Black	26 (62)	11 (28)	—	
White	16 (38)	28 (70)	4.14 (1.66 to 10.9)	0.003
Asian	0 (0)	1 (2.5)		
Smoking Status, n (%)	21 (50)	18 (45)	0.82 (0.34 to 1.95)	0.65
Hypertension, n (%)	35 (83)	32 (80)	0.80 (0.25 to 2.47)	0.7
Dyslipidemia, n (%)	24 (57)	30 (75)	2.25 (0.89 to 5.93)	0.09
Diabetes, n (%)	11 (26)	5 (13)	0.40 (0.12 to 1.24)	0.13
Heart Disease, n (%)	19 (45)	21 (53)	1.34 (0.56 to 3.21)	0.51
Atrial Fibrillation, n (%)	13 (31)	19 (48)	2.02 (0.83 to 5.06)	0.13
History of Stroke/TIA, n (%)	7 (17)	4 (10)	0.56 (0.14 to 2.01)	0.38
Chronic Kidney Disease, n (%)	5 (12)	9 (23)	2.15 (0.67 to 7.62)	0.21
Admission Glucose Level, Median (IQR)	120 (103, 144)	119 (104, 127)	1.00 (0.99 to 1.01)	0.72
Premorbid Modified Rankin Scale, n (%)				
0	28 (67)	34 (85)	—	
1	14 (33)	6 (15)	0.35 (0.11 to 1.00)	0.06
Occlusion Laterality, n (%)				
left	27 (64)	25 (63)	—	
right	15 (36)	15 (38)	1.08 (0.44 to 2.67)	0.87
Imaging parameters				
ASPECTS, Median (IQR)	9.00 (8.00, 10.00)	9.50 (8.00, 10.00)	1.19 (0.88 to 1.65)	0.28
rCBF <20% volume (mL), Median (IQR)	0 (0, 9)	0 (0, 0)	0.91 (0.81 to 0.98)	**0.038**

rCBF <30% volume (mL), Median (IQR)	5 (0, 19)	0 (0, 12)	0.97 (0.94 to 1.00)	0.06
rCBF <34% volume (mL), Median (IQR)	9 (0, 29)	3 (0, 17)	0.98 (0.95 to 1.00)	0.055
rCBF <38% volume (mL), Median (IQR)	13 (0, 36)	8 (0, 23)	0.98 (0.95 to 1.00)	0.054
Tmax >4s volume (mL), Median (IQR)	134 (85, 217)	95 (66, 204)	1.00 (0.99 to 1.00)	0.2
Tmax >6s volume (mL), Median (IQR)	56 (37, 84)	42 (16, 69)	0.99 (0.98 to 1.00)	0.15
Tmax >8s volume (mL), Median (IQR)	33 (17, 52)	23 (0, 46)	0.99 (0.97 to 1.00)	0.19
Tmax >10s volume (mL), Median (IQR)	26 (7, 38)	13 (0, 28)	0.99 (0.96 to 1.00)	0.15
Mismatch Volume (mL), Median (IQR)	43 (22, 65)	32 (11, 52)	0.99 (0.98 to 1.00)	0.13
Mismatch Ratio, Median (IQR)	3.4 (2.2, 6.2)	6.4 (3.1, 8.5)	1.15 (1.00 to 1.42)	0.13
Hypoperfusion Intensity Ratio (HIR), Median (IQR)	0.40 (0.30, 0.50)	0.30 (0.10, 0.50)	0.16 (0.02 to 1.15)	0.07
CBV <34 mL, Median (IQR)	0 (0, 11)	0 (0, 3)	0.96 (0.91 to 1.00)	0.09
CBV <38 mL, Median (IQR)	0 (0, 14)	0 (0, 4)	0.97 (0.93 to 1.00)	0.09
CBV <42 mL, Median (IQR)	0 (0, 16)	0 (0, 8)	0.97 (0.93 to 1.00)	0.08
CBV Index (per 0.1 change), Median (IQR)	0.70 (0.60, 0.80)	0.80 (0.70, 0.90)	1.45 (1.08 to 2.05)	0.022
Single Phase CTA Collateral Score (Tan 0-3), Median (IQR)	2.00 (2.00, 3.00)	2.00 (2.00, 3.00)	1.55 (0.85 to 2.94)	0.16
Treatment and procedural factors				
IVT Administered, n (%)	14 (33)	16 (40)	1.33 (0.54 to 3.31)	0.53
MT Attempted, n (%)	26 (62)	23 (58)	0.83 (0.34 to 2.02)	0.68
Symptom Onset to Door Time (mins), Median (IQR)	60 (48, 133)	145 (53, 546)	1.00 (1.00 to 1.00)	0.32
Door to CT Time (minutes), Median (IQR)	27 (15, 42)	26 (15, 39)	1.00 (0.98 to 1.01)	0.62

[2] OR = Odds Ratio, CI = Confidence Interval

Supplementary Figure 1



Supplementary Figure 2

Perfusion Parameters and Excellent Outcome (mRS 0-1)