Original Paper

2D Parametric Parenchymal Blood Flow as a Predictor of the Hemorrhagic Events after Endovascular Treatment of Acute Ischemic Stroke: A Single-Center Retrospective Study

Nada Elsaid^a Ahmed Saied^a Krishna Joshi^a Jessica Nelson^b
John Baumgart^b Demetrius Lopes^a

^aDepartment of Neurosurgery, Rush University Medical Center, Chicago, IL, USA;

^bSiemens Medical Solutions, Malvern, PA, USA

Keywords

Parenchymal blood flow · Endovascular treatment · Ischemic stroke · Hemorrhagic events · Predictors

Abstract

Background and Purpose: Intracranial hemorrhage (ICH) is one of the major adverse events related to the endovascular management of acute ischemic stroke. It is important to evaluate the risk of ICH as it may result in clinical deterioration of the patients. Development of tools which can predict the risk of ICH after thrombectomy can reduce the procedure-related morbidity and mortality. 2D parenchymal blood flow could potentially act as an indicator for ICH. **Methods:** 2D parenchymal blood flow was used to evaluate pre- and postthrombectomy digital subtraction angiography series of patients with acute ischemic stroke in the anterior circulation. A recently developed software allows the separation of the vascular filling and parenchymal blush signals using band-pass and band-reject filtering to allow for greater visibility of the parenchyma offering a better visual indicator of the effect of treatment. The “wash-in rate” was selected as the parameter of interest to predict ICH. **Results:** According to the presence or absence of signs of intracranial parenchymal hemorrhage in the follow-up dual-energy CT brain scans, the patients were classified into a hemorrhagic and nonhemorrhagic group (15 patients each). The only significant difference between the groups is the calculated wash-in rate after thrombectomy ($p = 0.024$). The cutoff value of the wash-in rate after thrombectomy was suggested to be 11,925.0, with 60% sensitivity to predict the hemorrhage and 93.3% specificity. **Conclusions:** Elevated parametric parenchymal blood flow wash-in rates after thrombectomy may be associated with increased risk of hemorrhagic events.

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Nada Elsaid
Department of Neurosurgery, Rush University Medical Center
1725 W Harrison St
Chicago, IL 60613 (USA)
E-Mail Nada.neurology@gmail.com

Introduction

Intracranial hemorrhage (ICH) is one of the major adverse events related to the endovascular management of acute ischemic stroke. It is very important to evaluate the risk of ICH as it may result in clinical deterioration of the patients. Hemorrhagic transformation of acute ischemic stroke is a complex and multifactorial phenomenon. Within minutes after the onset of ischemia, there is a reduction in ATP and a subsequent cessation of Na^+/K^+ -ATPase activity leading to a variety of cellular and metabolic derangements, which collectively lead to a disruption of the blood-brain barrier. Furthermore, ischemia results in a robust inflammatory response, which further disrupts normal cerebrovascular anatomy and physiology. The resulting disruption of the blood-brain barrier along with the impairment of the autoregulatory capacity of the cerebral vasculature predisposes to hemorrhagic transformation when the ischemic tissue is reperfused. Catheter manipulation of the tortuous intracranial blood vessels may also cause postthrombectomy hemorrhages [1–3].

Multiple recent randomized clinical trials and meta-analyses reported that the hemorrhagic event risk is higher with endovascular treatment than thrombolytic therapy [4]. The incidence of parenchymal ICH related to the endovascular treatment was recently reported to be 6.0% [5].

Multiple risk factors have been suggested to increase the risk of ICH after thrombectomy such as: cardioembolic stroke, poor collateral circulation, delayed endovascular treatment, multiple passes with stent retriever device, and lower pretreatment Alberta Stroke Program Early Computed Tomography (ASPECT) score [4, 6].

The 2D parametric parenchymal blood flow analysis software was developed by Siemens. 2D parametric parenchymal blood flow could potentially act as an indicator for post-thrombectomy ICH. Digital subtraction angiography (DSA) images contain information pertaining to both the vascular filling and parenchymal blush. The software allows the separation of these two signals using band-pass and band-reject filtering to allow for greater visibility of the parenchyma. As the goal of vascular treatment is to enhance the tissue perfusion, the suppression of the vascular signal and enhancement of the parenchymal signal offers a better visual indicator of the effect of treatment. Contrast transit curves for the tissue can be analyzed in the same manner as those for the vessels, including showing time to peak contrast, “wash-in” rate of contrast, and volume of contrast over a time interval. Without the presence of the strong signal from the vessels, both the qualitative and the quantitative analyses of the contrast portrayed in the tissue are more meaningful.

Patients and Methods

In this retrospective study, we selected patients with acute ischemic anterior circulation stroke, admitted to the neurosurgical department at our institute.

The inclusion criterion was the following: patients with acute ischemic stroke in the anterior circulation, who underwent mechanical thrombectomy within 6 h of the onset, with or without postendovascular parenchymal hemorrhagic events. The hemorrhagic transformation was defined based on the follow-up CT finding using the ECASS II classification [7].

Exclusion criteria were as follows: patients with ischemic stroke along the posterior circulation territories; postintervention subarachnoid hemorrhage (SAH); and low frame rate processed data (less than 4.5 frames/s) or angiographic images with motion-induced artifacts.

The following data were collected: (1) detailed history, (2) evaluation of the severity of neurologic deficits by using the National Institutes of Health Stroke Scale (NIHSS) at the time of admission, (3) laboratory investigations (platelet count and INR), (4) ASPECT score of prethrombectomy CT brain scans, (5) pre- and postthrombectomy angiographic data, and (6) follow-up dual-energy CT brain scans to discriminate between contrast extravasation and intracerebral hemorrhage.

Pre- and postthrombectomy DSA series (lateral view) were processed on the appropriate workstation (Leonardo Workstation; Siemens AG, Forchheim, Germany) using Prototype (syngo 2D parenchymal blood flow; Siemens AG).

The color-coding algorithm visualizes a complete 2D-DSA run into a colored single image, which shows the time-dependent intensity of contrast medium within the tissues, quantifying the time between contrast medium injection and maximum opacification for each pixel. This time delay is then converted into a specific color ranging from red (early maximum density) to blue (late maximum density). The wash-in rate (the rate at which contrast increases from arrival to peak intensity) was selected as the parameter of interest. Interactive tools allow us to generate a numerical value of the wash-in rate in a user-placed region of interest (ROI). While the wash-in rate would ideally be expressed in terms of a specific volume over time, a 2D projection image does not convey volumetric information in a meaningful manner. The intensity of contrast in the projection image can serve as a surrogate for this. We can then use the change in projected contrast intensity of one pixel over time to represent the wash-in rate for that pixel. For a ROI comprising many pixels, the rate would be an average of the change in intensity over time for all pixels within the region. While still dimensionless, the ratio of the projection-based wash-in rate calculated for one area to that of the reference area is expected to correlate to the ratio of the wash-in rates were it possible to calculate them on the volumetric data. In this study, a standardized circular ROI with a surface area of 2,021 mm², placed around the middle cerebral artery territory just above the internal carotid artery bifurcation (not including the parenchymal areas supplied by the anterior cerebral artery), was used (Fig. 1). The users who placed the ROI were blinded to the identity of the patients as a member of the hemorrhagic or the nonhemorrhagic groups.

We did not need an IRB approval as this was a retrospective observational study.

Statistical Analysis of the Data

Data were fed to the computer and analyzed using the IBM SPSS software package version 20.0. Qualitative data were described using number and percent. Quantitative data were described using median (minimum and maximum) for nonparametric data and mean after testing normality using the Kolmogorov-Smirnov test. Significance of the obtained results was judged at the 5% level. All tests were 2-tailed.

The χ^2 test was used for categorical variables to compare between two groups. The Fisher exact and Monte Carlo tests were used as correction for the χ^2 test when more than 25% of the cells counts less than 5. The Student *t* test was used to compare parametric continuous variables between 2 studied groups. The Mann-Whitney U test was used to compare nonparametric continuous variables between 2 studied groups. The receiver operating characteristic curve (ROC curve) was used to reveal the validity of the wash-in rate in the detection of hemorrhagic status with calculation of the area under curve, sensitivity and specificity of the best cutoff point that had the highest sensitivity and specificity; cross-tabulation was used to calculate positive and negative predictive values and accuracy. Binary logistic regression was used to discover significant predictors with the calculation of odds ratio (95.0% CI) and overall percent predicted using the forward Wald technique after the application of bivariate analysis to detect significance between hemorrhagic and nonhemorrhagic cases.

Results

This study was conducted on 30 patients with acute ischemic anterior circulation stroke, treated by mechanical thrombectomy within 6 h of onset.

The patients were classified into 2 groups according to the presence or absence of signs of intracranial parenchymal hemorrhage in the follow-up CT scans of the brain.

1. Hemorrhagic group (15 patients): the parenchymal hemorrhagic transformation was defined based on the CT finding using the ECASS II classification. Out of 34 patients in our institute stroke registry who suffered hemorrhagic events in the period between 2012 and 2017, only 15 patients were eligible after the application of the inclusion and exclusion criteria; 8 patients were excluded due to the presence of SAH, 7 were excluded due to a low frame rate or motion-induced artifacts, and 4 patients had ischemic stroke along the posterior circulation territories.

Fig. 1. Position of regions of interest during parametric blood flow wash-in rate measurement. **a–d** Samples of the nonhemorrhagic group. **e–h** Samples of the hemorrhagic group. **a, c, e, g** Pretherapeutic parametric blood flow wash-in rate color-coded images showing restricted diffusion in the middle cerebral artery territory. **b, d, f, h** Posttherapeutic parametric blood flow wash-in rate color-coded images showing middle cerebral artery recanalization after treatment.

2. Nonhemorrhagic group: 15 patients were randomly selected and matched with the hemorrhagic group.

There was no statistically significant difference between the 2 groups with regard to age and gender: the mean age in the hemorrhagic group was 65.73 ± 13.8 years, while in the nonhemorrhagic group it was 70.53 ± 9.4 years. The total number of male patients was 16; 10 (62.5%) in the hemorrhagic group and 6 (37.5%) in the nonhemorrhagic group. The total number of female patients was 14 patients; 5 (35.7%) in the hemorrhagic group and 9 (64.3%) in the nonhemorrhagic group (Table 1).

There was no statistically significant difference between the 2 groups regarding the past medical history including hypertension, diabetes mellitus, hyperlipidemia, ischemic heart disease, atrial fibrillation, and smoking status. The prevalence of hypertension was slightly higher in the hemorrhagic group (53.8%) than in the nonhemorrhagic group (46.2%). The majority of the diabetic patients were in the hemorrhagic group (61.5%), yet this was statistically nonsignificant ($p = 0.27$). The total hyperlipidemic patients were 24 patients; 11 (45.8%) in the hemorrhagic group and 13 (54.5%) in the nonhemorrhagic group. The total number of smokers were relatively small (12) and slightly higher in the hemorrhagic group (Table 1). According to the TOAST classification, most of the cases were due to large-vessel atherosclerosis while only 11 cases were cardioembolic with no statistical difference between the 2 groups.

Most of the study participants had ischemic stroke along the middle cerebral artery territory. Only 4 of the study participants had ischemic stroke in the internal carotid artery territory, 3 of which were in the hemorrhagic group and 1 in the nonhemorrhagic group (Table 1).

On admission, there was no significant difference between the 2 groups regarding the ASPECT score or the NIHSS score. The median ASPECT score was 7 for both groups, while the median NIHSS score was 20 in the hemorrhagic group and 22 in the nonhemorrhagic group (Table 1).

The initial mean systolic blood pressure (SBP) on admission was higher in the hemorrhagic group (135.86 ± 10.73 mm Hg) than in the nonhemorrhagic group (129.46 ± 10.14 mm Hg), but this was not statistically significant. Also, there was a nonsignificant rise in the SBP in the hemorrhagic group at the time of the hemorrhage diagnosis (142.8 ± 13.21 mm Hg) compared to the initial SBP on admission ($p = 0.06$). As regards the random blood sugar at the time of admission, there was no statistically significant difference between the 2 groups (Table 1).

The mean platelet count was $229.07 \pm 54.6/\mu\text{L}$ of blood in the hemorrhagic group and $211.33 \pm 51.63/\mu\text{L}$ in the nonhemorrhagic group, while the median INR values was 1.14 in the hemorrhagic group and 1.12 in the nonhemorrhagic group. There was no statistically significant difference between the 2 groups (Table 1).

As regards the past history of prophylactic antiplatelet or anticoagulant intake, there was no significant difference between the 2 groups. The patients varied between either no history of medication intake (9 patients), history of single prophylactic antiplatelet (aspirin in 4 patients in each group, clopidogrel in only 1 patient in the hemorrhagic group, and GPIIb-IIIa inhibitor in only 1 patient in the nonhemorrhagic group), history of dual prophylactic antiplatelet (aspirin and clopidogrel only in 1 patient in the nonhemorrhagic group), history of prophylactic anticoagulation with warfarin in 4 (66.7%) patients in the hemorrhagic group and 3 (33.3%) in the nonhemorrhagic group, rivaroxaban (1 patient in each group), and dabigatran (only 1 patient in the hemorrhagic group).

Only 19 patients were candidates for thrombolytic therapy (IV tPA) with no significant difference in their distribution among the 2 groups. Among those who were not legible for IV rtPA, only 1 patient in each group was given intraarterial thrombolytic therapy. All the study

Table 1. Characteristics of patients with and without ICH

Parameters	Hemorrhagic (n = 15), n (%)	Nonhemorrhagic (n = 15), n (%)	Test of significance
<i>Characteristics</i>			
Age (mean ± SD), years	65.73±13.8	70.53±9.4	t = 1.12 p = 0.27
Gender			
Male (n = 16)	10 (62.5)	6 (37.5)	χ ² = 2.14
Female (n = 14)	5 (35.7)	9 (64.3)	p = 0.14
Hypertension (n = 26)	14 (53.8)	12 (46.2)	FET p = 0.59
Diabetes (n = 13)	8 (61.5)	5 (38.5)	χ ² = 1.22 p = 0.27
HLD (n = 24)	11 (45.8)	13 (54.2)	FET p = 0.65
Heart disease			
IHD (n = 14)	7 (50.0)	7 (50.0)	χ ² = 0.29
AF (n = 11)	6 (54.5)	5 (45.5)	p = 0.86
Smoking (n = 12)	7 (58.3)	5 (41.7)	χ ² = 0.56 p = 0.46
<i>Occlusion site</i>			
CA (n = 26)	12 (46.2)	14 (53.8)	
CA (n = 4)	3 (75.0)	1 (50.0)	
<i>Baseline measurements</i>			
ASPECTS score			
6 (n = 11)	6 (54.5)	5 (45.5)	MC
7 (n = 9)	5 (55.6)	4 (44.4)	p = 0.67
8 (n = 5)	1 (20.0)	4 (80.0)	
9 (n = 5)	3 (60.0)	2 (40.0)	
Median (min–max)	7 (6–9)	7 (6–9)	
NIHSS score on admission, median (min–max)	20 (14–28)	22 (15–28)	t = 1.4 p = 0.17
SBP at admission (mean ± SD)	135.86±10.73	129.46±10.14	t = 1.67 p = 0.52
RBS at admission (mean ± SD)	186.6±84.6	185±86.6	t = 0.05 p = 0.47
Platelet count (mean ± SD)	229.07±54.6	211.33±51.63	t = 0.91 p = 0.37
INR, median (min–max)	1.14 (0.98–3.49)	1.12 (1.03–1.2)	Z = 0.31 p = 0.75
<i>Procedure process and results</i>			
IV rtPA (n = 19)	10 (52.6)	9 (47.4)	χ ² = 0.144 p = 0.71
Thrombectomy method			
Aspiration (n = 7)	4 (57.1)	3 (42.9)	MC
Stent retriever (n = 5)			p = 1.0
Both (n = 18)	2 (40.0)	3 (60.0)	
mTICI score			NA
≤2A	2 (13.3)	0 (0.0)	
>2A	13 (86.7)	15 (100)	
<i>Clinical outcome and mortality</i>			
NIHSS score at discharge, median (min–max)	11 (6–32)	10 (4–30)	t = 0.26 p = 0.39

Figures are n (%) unless indicated otherwise. HLD, hyperlipidemia; IHD, ischemic heart disease; AF, atrial fibrillation; MCA, middle cerebral artery; ICA, internal carotid artery; SBP, systolic blood pressure; RBS, random blood sugar; p, probability; FET, Fisher exact test; MC, Monte Carlo test; t, Student t test; Z, Mann-Whitney U test; NA, not applicable because one cell contain zero.

Table 2. Difference between the pre- and postthrombectomy wash-in rates in each group separately

Wash-in rate	Prethrombectomy, median (min–max)	Postthrombectomy, median (min–max)	Test of significance
Hemorrhagic (<i>n</i> = 15)	2,493.0 (0.0–8331.0)	13,138.0 (2,700.0–19,182.0)	<i>Z</i> = 3.4 <i>p</i> = 0.001**
Nonhemorrhagic (<i>n</i> = 15)	1,777.0 (0.0–6163.0)	7,037.0 (966.0–12,296.0)	<i>Z</i> = 3.4 <i>p</i> = 0.001**

Z, Wilcoxon signed rank test; *p*, probability; **, highly statistically significant if *p* < 0.01.

participants underwent mechanical thrombectomy either by aspiration, stent retriever or a combination of both with no statistical difference between the 2 groups. Seven patients had aspiration alone; 4 (57.1%) in the hemorrhagic group and 3 (42.9%) in the nonhemorrhagic group, while 5 patients were treated by stent retrieval only; 2 (40.0%) in the hemorrhagic group and 3 (60.0%) in the nonhemorrhagic group. Most of the patients (9 patients in each group) were treated by combined aspiration and stent retrieval (Table 1).

There was no statistically significant difference among the 2 groups in the degree of post-operative recanalization assessed by the modified Thrombolysis in Cerebral Infarction (mTICI) score. TICI 2a was detected only in 2 patients in the hemorrhagic group (13.3%), while TICI >2a was detected in 13 patients in the hemorrhagic group (86.7%), and the entire nonhemorrhagic group (Table 1).

The median NIHSS score at discharge improved in both groups with no statistical difference. Only 3 patients died; 2 in the hemorrhagic and 1 in the nonhemorrhagic group (Table 1).

Among the hemorrhagic group, 86.6% of the hemorrhages were lobar and 13.3% were basal ganglionic. According to the ECASS II classification, 10 cases were classified as parenchymal hemorrhagic transformation type 2, the other 5 cases were parenchymal hemorrhagic transformation type 1 [7].

2D Parametric Parenchymal Blood Flow Analysis

There was a statistically significant difference between the pre- and postthrombectomy wash-in rates in each group separately indicating recanalization (*p* = 0.001) (Table 2). The median wash-in rate value in the ROI before thrombectomy was calculated as 2,493.0 and 1,777.0 in the hemorrhagic and nonhemorrhagic groups, respectively, and after thrombectomy as 13,138.0 and 7,037.0 in the hemorrhagic and nonhemorrhagic groups, respectively (Table 2).

There was a statistically significant difference between the 2 groups as regards the median value of the wash-in rate in the ROI after thrombectomy (*p* = 0.024), with no statistically significant difference in the wash-in rates before thrombectomy (*p* = 0.13), or in the difference between the wash-in rates before and after thrombectomy (*p* = 0.1), or in the percent of increase in the postthrombectomy wash-in rates relative to the prethrombectomy values (*p* = 0.5) (Table 3).

By means of the ROC curve, the validity of the wash-in rate in the detection of hemorrhagic status was tested, and a cutoff value of 11,925.0 was suggested, above which the sensitivity of the wash-in rate after thrombectomy to predict the hemorrhage is 60.0% and the specificity is 93.3% (Fig. 2) (Table 4).

Table 3. Comparison between the wash-in rates values between the 2 groups

	Hemorrhagic (n = 15)	Nonhemorrhagic (n = 15)	Test of significance
Wash-in rate prethrombectomy	2,493.0 (0.0–8,331.0)	1,777.0 (0.0–6,163.0)	Z = 1.52 p = 0.13
Wash-in rate postthrombectomy	13,138.0 (2,700.0–19,182.0)	7,037.0 (966.0–12,296.0)	Z = 2.26 p = 0.024*
Difference between pre- and postthrombectomy wash-in rate	7,488.0 (757.0–19,182.0)	5,260.0 (161.0–10,165.0)	Z = 1.64 p = 0.1
Percent of increase	192.02 (33.98–19,182.0)	375.59 (5.15–5,199.0)	Z = 0.64 p = 0.5

Figures are medians with ranges in parentheses. Z, Mann-Whitney U test; p, probability; *, statistically significant if $p < 0.05$.

Fig. 2. Receiver operating characteristic (ROC) curve for the wash-in rate after thrombectomy as a predictor of hemorrhagic events.

Discussion

The incidence of ICH after endovascular treatment of ischemic stroke in reality may be higher than in the randomized clinical trial [8]. Our study aimed to find out if the 2D parametric parenchymal blood flow can be used as a predictor of ICH. The participants were classified into a hemorrhagic and nonhemorrhagic group.

For the hemorrhagic group, SAH was excluded from our study as the mechanism of postintervention SAH differs from that of parenchymal hemorrhage. Subsequently, the SAH predictors differed from those of parenchymal hemorrhage [9]. The mechanism of postintervention SAH was mainly attributed to vessel perforation or endothelial damage of arterioles or capillaries in subarachnoid space by the endovascular devices, especially with multiple passes (>3 passes) with the stent retriever device leading to arterial microdissections [9, 10].

Fig. 3. The wash-in rate on the time intensity curve.

Table 4. Validity of wash-in rate before and after thrombectomy in diagnosing hemorrhage

	AUC (95% CI)	p value	Cutoff value	Sensitivity	Specificity
Wash-in rate after treatment	0.74 (0.55–0.93)	0.024*	≥11,925.0	60.0%	93.3%

AUC, area under curve; *, statistically significant if $p < 0.05$.

For parenchymal hemorrhage, low ASPECTS score, high NIHSS score, stroke of the cardioembolic type, prior antiplatelet therapy, and hemorrhagic tendency related to anticoagulation or thrombolysis agents were associated with ICH after endovascular treatment [4, 5, 11, 12].

For our study participants, the absence of a statistically significant difference between the 2 groups as regards the previously mentioned predictors suggests homogeneity between the 2 groups, giving us a chance to exclude these risk factors as the cause of the hemorrhage in these cases as follows:

The median ASPECT score in both groups was 7, while the published data reported that an ASPECT score <6 is the cutoff associated with increased ICH risk (OR, 2.27; 95% CI, 1.24–4.14) [6]. An NIHSS score ≥ 19 was reported to be a risk factor of ICH with OR of 7.78 (95% CI: 1.63–59.44) [11]. The median NIHSS of our patients was 20 and 22 for the hemorrhagic and nonhemorrhagic group, respectively, but with no statistical significance.

For cardioembolic stroke, atrial fibrillation doubles the risk of ICH (OR, 1.61; 95% CI, 1.01–2.55, $p < 0.045$) due to the rapid rate of recanalization and the concurrent anticoagulation therapy, but in our series the number of atrial fibrillation patients was small, and they were almost equally distributed in both groups with no statistical difference [12]. Also, there was no statistically significant difference as regards the prior anticoagulation or antiplatelet use. Prior antiplatelet therapy was reported to increase the risk of the ICH about 8 times (OR, 8.03; 95% CI, 1.83–41.70) [11].

Thrombolytic therapy is also associated with a higher risk of ICH (OR, 1.43; 95% CI, 1.03–2.08, $p < 0.037$) [8]. In our study, IV tPA was given to 10 patients of the hemorrhagic group and 9 in the nonhemorrhagic group with no significant difference in their distribution among the 2 groups ($p = 0.71$). Poor recanalization defined as mTICI $\leq 2a$ was not identified as independent predictor of ICH in multivariate analysis [6, 13].

The only significant difference between the 2 groups to which hemorrhage can be attributed is the wash-in rate after thrombectomy. Wash-in rate was selected as the parameter of interest as it represents the maximum slope between the time of onset of contrast inflow and the time of peak enhancement on the time intensity curve (Fig. 3). Any change in the slope of the density curves provides information about flow alteration after treatment [14]. Our results found a significant difference between the wash-in rate values before and after treatment in each group separately ($p = 0.001$); this indicates increased peak intensity of the contrast media (i.e., amount of blood) and/or decreased the time needed by the contrast to reach the peak (i.e., increased blood velocity) after the endovascular induced recanalization and reperfusion.

There was a significant difference between the 2 groups as regards the value of the wash-in rate after thrombectomy ($p = 0.024$) in absence of a significant difference in the value of the rise of the wash-in rate (i.e., wash-in rate after thrombectomy – wash-in rate before thrombectomy) or the percent of rise relative to the initial value (i.e., (wash-in rate after thrombectomy – wash-in rate before thrombectomy)/wash-in rate before thrombectomy).

This excluded the principle of relativity, or in other words, it is not about the relative increase in the contrast intensity or velocity compared to the initial values, but it is about the absolute value of the wash-in rate after thrombectomy. Based on this, ROC analysis was applied with an area under curve of 0.74. A cutoff value of the wash-in rate after thrombectomy was selected as 11,925.0, above which the sensitivity of the wash-in rate to predict the hemorrhage is 60.0 and the specificity is 93.3%.

Since our study is a retrospective study, we faced some limitations that we tried to minimize as much as possible by the strict inclusion and exclusion criteria. These limitations include the nonstandardized examination protocols and rate of contrast injection, low frame rate of the processed angiographic data, and motion-induced artifacts.

Conclusion

The development of new tools for the prediction of ICH after thrombectomy can help in increasing its safety and efficacy. Elevated 2D parametric parenchymal blood flow wash-in rates after thrombectomy may be associated with increased risk of hemorrhagic events. Further prospective large sampled studies are needed to validate the 2D parametric parenchymal blood flow as a predictor of ICH after thrombectomy, with standardization of the examination protocols, rates of contrast injections, using higher frame rates, and improving motion correction for unsedated patients.

Disclosure Statement

Demetrius Lopes reports the following conflicts of interest:

- research grant: Penumbra, Stryker, Microvention;
- principal investigator: Dawn, Swift Prime, Therapy;
- consultant/advisory board: Medtronic, Microvention, Asahi, Siemens;
- ownership interest/options: Crowdoptic, Three Rivers, Neurvana, MIVI, Blockade, NDI, Nextgen, Elum, Bendit;
- honoraria: Stryker, Microvention, Medtronic, Penumbra.
- All other authors have no conflicts of interest to disclose.

References

- 1 Sussman E, Connolly E: Hemorrhagic transformation: a review of the rate of hemorrhage in the major clinical trials of acute ischemic stroke. *Front Neurol* 2013;4:69.
- 2 Rossi D, Brady J, Mohr C: Astrocyte metabolism and signaling during brain ischemia. *Nat Neurosci* 2007;10:1377–1386.
- 3 Khatri R, McKinney A, Swenson B, Janardhan V: Blood-brain barrier, reperfusion injury, and hemorrhagic transformation in acute ischemic stroke. *Neurology* 2012;79(suppl 1):S52–S57.
- 4 Berkhemer O, Fransen P, Beumer D, van den Berg L, Lingsma H, Yoo A, et al: A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med* 2015;372:11–20.
- 5 Göllitz P, Struffert T, Lücking H, Rösch J, Knossalla F, Ganslandt O, et al: Parametric color coding of digital subtraction angiography in the evaluation of carotid cavernous fistulas. *Clin Neuroradiol* 2012;23:113–120.
- 6 Goyal M, Menon B, van Zwam W, Dippel D, Mitchell P, Demchuk A, et al: Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* 2016;387:1723–1731.
- 7 Larrue V, von Kummer R, Muller A, Bluhmki E: Risk factors for severe hemorrhagic transformation in ischemic stroke patients treated with recombinant tissue plasminogen activator: a secondary analysis of the European-Australasian Acute Stroke Study (ECASS II). *Stroke* 2001;32:438–441.
- 8 Hao Y, Yang D, Wang H, Zi W, Zhang M, Geng Y, et al: Predictors for symptomatic intracranial hemorrhage after endovascular treatment of acute ischemic stroke. *Stroke* 2017;48:1203–1209.
- 9 Hao Y, Zhang Z, Zhang H, Xu L, Ye Z, Dai Q, et al: Risk of intracranial hemorrhage after endovascular treatment for acute ischemic stroke: systematic review and meta-analysis. *Intervent Neurol* 2017;6:57–64.
- 10 Nogueira R, Gupta R, Jovin T, Levy E, Liebeskind D, Zaidat O, et al: Predictors and clinical relevance of hemorrhagic transformation after endovascular therapy for anterior circulation large vessel occlusion strokes: a multicenter retrospective analysis of 1,122 patients. *J Neurointerv Surg* 2014;7:16–21.
- 11 Qureshi A, Saleem M, Aytac E: Postprocedure subarachnoid hemorrhage after endovascular treatment for acute ischemic stroke. *J Neuroimaging* 2017;27:493–498.
- 12 Shi Z, Liebeskind D, Loh Y, Saver J, Starkman S, Vespa P, et al: Predictors of subarachnoid hemorrhage in acute ischemic stroke with endovascular therapy. *Stroke* 2010;41:2775–2781.
- 13 Sugiura Y, Yamagami H, Sakai N, Yoshimura S: Predictors of symptomatic intracranial hemorrhage after endovascular therapy in acute ischemic stroke with large vessel occlusion. *J Stroke Cerebrovasc Dis* 2017;26:766–771.
- 14 Suh S, Cloft H, Fugate J, Rabinstein A, Liebeskind D, Kallmes D: Clarifying differences among thrombolysis in cerebral infarction scale variants: is the artery half open or half closed? *Stroke* 2013;44:1166–1168.