Stroke

ORIGINAL CONTRIBUTION

Vasospasm During Endovascular Treatment of Ischemic Stroke: Associated Factors, Impact on Outcomes, and the Effect of Intraarterial Nimodipine

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BACKGROUND: Vasospasm occurs in up to 20% of patients with acute ischemic stroke undergoing endovascular treatment, but its clinical impact remains controversial. Intraarterial nimodipine is administered occasionally to treat vasospasm, though its efficacy is uncertain. We aimed to identify factors associated with vasospasm, delineate the impact on clinical outcomes, and assess the effects of intraarterial nimodipine use.

METHODS: We used data from the German Stroke Registry-Endovascular Treatment, an investigator-initiated, prospective, observational, multicenter registry of patients with acute stroke who underwent endovascular treatment at 25 centers between June 2015 and December 2023. Patients with and without vasospasm were analyzed, and among those with vasospasm, we compared outcomes based on intraarterial nimodipine use. The primary outcome was the distribution of modified Rankin Scale scores at 90 days. Secondary outcomes included 90-day mortality, early neurological deterioration, symptomatic intracranial hemorrhage at 24 hours, and successful recanalization (modified Thrombolysis in Cerebral Infarction Score of 2b to 3). Analyses used Inverse Probability of Treatment Weighting adjusted logistic regression; variable selection was performed using Least Absolute Shrinkage and Selection Operator regression.

RESULTS: Seventeen thousand nine hundred eighty-five patients (mean age 73.6 years; 51.2% female) were included in the analysis. Of these, 578 (3.2%) had vasospasm reported, and 300 (58.4%) of those received intraarterial nimodipine. Vasospasm was associated with a shift towards worse modified Rankin Scale outcome (adjusted odds ratio, 1.25 [95% CI, 1.02–1.53]) and higher mortality (36% versus 29.7%; adjusted odds ratio, 1.35 [95% CI, 1.05–1.75]). Intraarterial nimodipine was associated with reduced rates of early neurological deterioration (adjusted odds ratio, 0.54 [95% CI, 0.31–0.91]). Variables associated with vasospasm included younger age, active smoking, M2 occlusion, first-line stent retriever thrombectomy, and multiple recanalization attempts.

CONCLUSIONS: Vasospasm during endovascular treatment is associated with worse outcomes and increased mortality, and should be regarded as a serious procedural complication. Younger patients who are active smokers, presenting with distal occlusions, and require multiple recanalization attempts are at higher risk. Intraarterial nimodipine appears to be a sensible treatment as it may mitigate neurological deterioration without signals of potential harm.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: ischemic stroke ■ middle cerebral artery ■ nimodipine ■ smokers ■ stent

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Nonstandard Abbreviations and Acronyms

aOR	adjusted odds ratio
BA	basilar artery
ECASS	European Cooperative Acute Stroke Study
END	early neurological deterioration
ET	endovascular treatment
IPTW	inverse probability of treatment weighting
MCA	middle cerebral artery
mRS	modified Rankin Scale
NIHSS	National Institutes of Health Stroke Scale
OR	odds ratio

Periprocedural vasospasm is a common complication during endovascular treatment (ET) for acute ischemic stroke.[1] Data on the incidence of vasospasm is limited, with reports varying from 3% to 20%.[2–4] Vasospasm is typically triggered by mechanical stress from aspiration catheters, stent retrievers, or both during recanalization attempts.[1,3,5] In ischemic stroke, vasospasm has been associated with younger patient age, lower prestroke modified Rankin Scale (mRS) scores, and multiple recanalization attempts.[6] However, its clinical relevance remains uncertain.[7,8] Although smaller retrospective studies have suggested a benign course, more recent observational data indicate potential associations with poorer outcomes and reduced recanalization rates.[4,9]

Nimodipine, a calcium channel blocker and vasodilator, commonly administered intraarterially for the treatment of vasospasm following subarachnoid hemorrhage, is occasionally used for vasospasm occurring during ET for acute ischemic stroke, too, particularly when the vasospasm is considered severe.[10] Recent data suggest that intraarterial nimodipine effectively resolves vasospasm without increasing the risk of intracranial hemorrhage. However, some studies have reported increased infarct growth associated with its use. Currently, there are no established guidelines on whether patients should receive intraarterial nimodipine and in which constellations in the setting of periprocedural vasospasm.

In this study, we aimed to (1) identify variables independently associated with the occurrence of vasospasm, (2) assess the impact of vasospasm on clinical and radiological outcomes, and (3) assess the impact of intraarterial nimodipine on clinical and radiological outcomes in patients with vasospasm.

METHODS

Study Design

The data that support the findings of this study are available from the corresponding author on reasonable request. We used data from the German Stroke Registry–Endovascular Treatment, an investigator-initiated, prospective, observational, multicenter registry involving 25 centers.[11] The registry includes consecutive patients with acute ischemic stroke who underwent ET (URL: https://www.clinicaltrials.gov; Unique identifier: NCT03356392). Ethical approval was centrally obtained from the Ethics Committee of LMU Munich (protocol 689-15), which served as the lead committee. Additional approvals were secured from local ethics committees according to regional requirements. Data collection was conducted under a waiver of informed consent, granted by the institutional review boards of participating centers. Data quality was ensured through a standardized computational protocol to check for plausibility, integrity, and completeness, with queries sent to individual centers to resolve inconsistencies. We used the STROBE checklist when writing our report.[12]

Clinical and Radiological Assessments

Baseline clinical, imaging, and treatment characteristics were recorded as reported by local neurologists and neurointerventionalists at each center. Alberta Stroke Program Early CT Scores were assessed using either computed tomography or magnetic resonance imaging. Occlusion type and site were determined from baseline imaging (computed tomography or magnetic resonance imaging) and conventional angiographic data. Treatment decisions were based on current national and international guidelines. Periprocedural vasospasm was diagnosed via conventional angiography during ET. The administration of intraarterial nimodipine was at the discretion of the treating neurointerventionalist. Patients with periprocedural administration of nitroglycerin derivatives were excluded from the comparison of outcomes based on intraarterial nimodipine use. Vascular risk factors (arterial hypertension, dyslipidemia, diabetes, atrial fibrillation, and smoking) were defined according to standardized criteria (Table S1). Clinical assessments included the National Institutes of Health Stroke Scale (NIHSS) and the mRS. The NIHSS was performed at admission, 24 hours, and at discharge, while the mRS was recorded as prestroke modified Rankin Scale, at discharge, and at 90 days. The 90-day mRS was obtained either through an in-person visit or a structured telephone interview conducted by each center.

Outcomes

The primary outcome was the shift in the distribution of mRS scores at 90 days, analyzed using inverse probability of treatment weighting (IPTW)-adjusted ordinal regression analysis. Secondary outcomes included dichotomized mRS scores (0–1 and 0–2), early neurological deterioration (END; defined as an increase of ≥4 points in the NIHSS at 24 hours compared with baseline), symptomatic intracranial hemorrhage (defined per ECASS [European Cooperative Acute Stroke Study] II criteria as any hemorrhage on 24-hour follow-up imaging accompanied by a ≥4-point NIHSS worsening[13]), all-cause mortality, successful reperfusion (modified Thrombolysis in Cerebral Infarction score of 2b–3), and additional procedural complications. Additional procedural complications were defined as a composite of vessel dissection or perforation and clot migration or embolization diagnosed via conventional angiography. Secondary outcomes were analyzed using IPTW-adjusted logistic regression models.

Statistics

Baseline characteristics were compared between patients with and without reported vasospasm, and among those with vasospasm, between patients who did and did not receive intraarterial nimodipine. Categorical variables are presented as counts and percentages, and continuous variables as means with SD or medians with interquartile ranges, as appropriate. To reduce confounding, IPTW was applied. Propensity scores for vasospasm were estimated using logistic regression based on the following covariates: age, sex, prestroke modified Rankin Scale, hypertension, diabetes, atrial fibrillation, active smoking, time from admission to groin puncture, nonterminal internal carotid artery occlusion, M2 occlusion of the middle cerebral artery (MCA), and basilar artery (BA) occlusion. For the comparison between patients with and without intraarterial nimodipine administration, the propensity model included age, time from admission to groin puncture, type of anesthesia, and proximal MCA-M1 occlusion. Stabilized weights were applied to construct a weighted pseudo-population. Covariate balance was assessed using standardized mean differences and was adequate after weighting (Tables S2 and S3; Figures S1 through S4). Primary outcome analyses were performed in the IPTW-weighted data set using survey-weighted logistic regression for binary outcomes and proportional odds models for the ordinal mRS score. Models were adjusted for clinically relevant variables and those showing differences between groups in univariate analyses. Effect estimates are reported as odds ratios (OR) with 95% CIs, based on complete case analysis. As a sensitivity analysis, multiple imputation was used to handle missing baseline covariates. Five imputed data sets were generated using predictive mean matching and chained equations. IPTW with stabilized weights was applied within each imputed data set. Regression models were fit separately, and results were combined using Rubin rules (Tables S4 and S5). To identify predictors of vasospasm, multivariable logistic regression was performed with covariate selection via Least Absolute Shrinkage and Selection Operator regression using 10-fold cross-validation. Missing data for these models were handled via multiple imputation (5 data sets), with final pooled estimates obtained using the Rubin rules. All analyses were conducted using R version 4.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Study Population

Eighteen thousand sixty-nine patients registered in the German Stroke Registry–Endovascular Treatment between June 2015 and December 2023 were reviewed. N=84 were excluded due to either not receiving ET (n=56) or being under 18 years of age or having missing age data (n=28), resulting in 17 985 patients included in the analysis comparing those with and without periprocedural vasospasm. Among the 578 patients who had vasospasm reported, 64 were excluded due to periprocedural administration of nitroglycerin derivatives (n=62) or missing intraarterial medication data (n=2), resulting in 514 patients for the comparison of intraarterial nimodipine administration versus no intraarterial nimodipine use (Figure 1).

Comparison of Patients With and Without Periprocedural Vasospasm

Univariate Analysis

Of the 17 985 patients included in the analysis, 578 (3.2%) had vasospasm reported, while 17 407 (96.8%) had not (Table 1). Patients with vasospasm were on average younger (mean age, 68.2 years versus 73.8 years; $P<0.001$) and had a lower rate of prestroke dependency (prestroke modified Rankin Scale score, 3–5; 9.2% versus 16.4%; $P<0.001$). Sex distribution (51.6% female versus 51.8% female) and baseline NIHSS scores (14 versus 14) were similar between groups. Arterial hypertension (77.1% versus 70.0%; $P<0.001$), diabetes (23.0% versus 19.3%; $P=0.041$), and atrial fibrillation (41.7% versus 33.8%; $P<0.001$) were more common among patients without vasospasm, whereas active smoking was more frequent among those with vasospasm (25.1% versus 16.6%; $P<0.001$). In terms of procedural timings, patients with vasospasm had slightly shorter times from admission to groin puncture (69 minutes versus 72 minutes; $P=0.017$), but longer times from groin puncture to recanalization (48 minutes versus 42 minutes; $P<0.001$). Among patients with anterior circulation stroke, those with vasospasm had lower Alberta Stroke Program Early CT Scores on admission (median, 8 versus 9; $P=0.002$). Regarding occlusion sites, nonterminal internal carotid artery occlusions (5.8% versus 3.6%; $P=0.028$) and BA occlusions (8.2% versus 4.5%; $P<0.001$) were more frequent in patients without vasospasm. In contrast, MCA-M2 occlusions were more common among those with vasospasm (26.0% versus 16.9%; $P<0.001$), and the first pass recanalization rate was higher in patients without vasospasm (47.6% versus 38.0%; $P<0.001$). Contact aspiration was more frequently used as the first-line thrombectomy approach in patients without vasospasm (17.0% versus 10.2%; $P<0.001$), whereas first-line stent retriever thrombectomy was more common in patients with vasospasm (34.9% versus 26.2%; $P<0.001$).

Multivariate Analysis

After IPTW, periprocedural vasospasm was associated with worse functional outcomes at 90 days (median mRS, 4 versus 4; $P=0.042$; adjusted OR [aOR], 1.25 [95% CI, 1.02–1.53]; $P=0.030$), higher mortality (36.2% versus 29.7%; $P=0.018$; aOR, 1.35 [95% CI, 1.05–1.75]; $P=0.021$), and a higher rate of additional procedural complications (22.2% versus 6.8%; $P<0.001$; aOR, 3.96 [95% CI, 3.05–5.14]; $P<0.001$). Rates of favorable functional outcomes were numerically higher in patients without vasospasm (mRS, 0–1: 24.8% versus 22.7%; $P=0.339$; mRS 0–2: 36.3% versus 31.9%; $P=0.080$). No significant differences were observed between groups in the rates of END, symptomatic intracranial

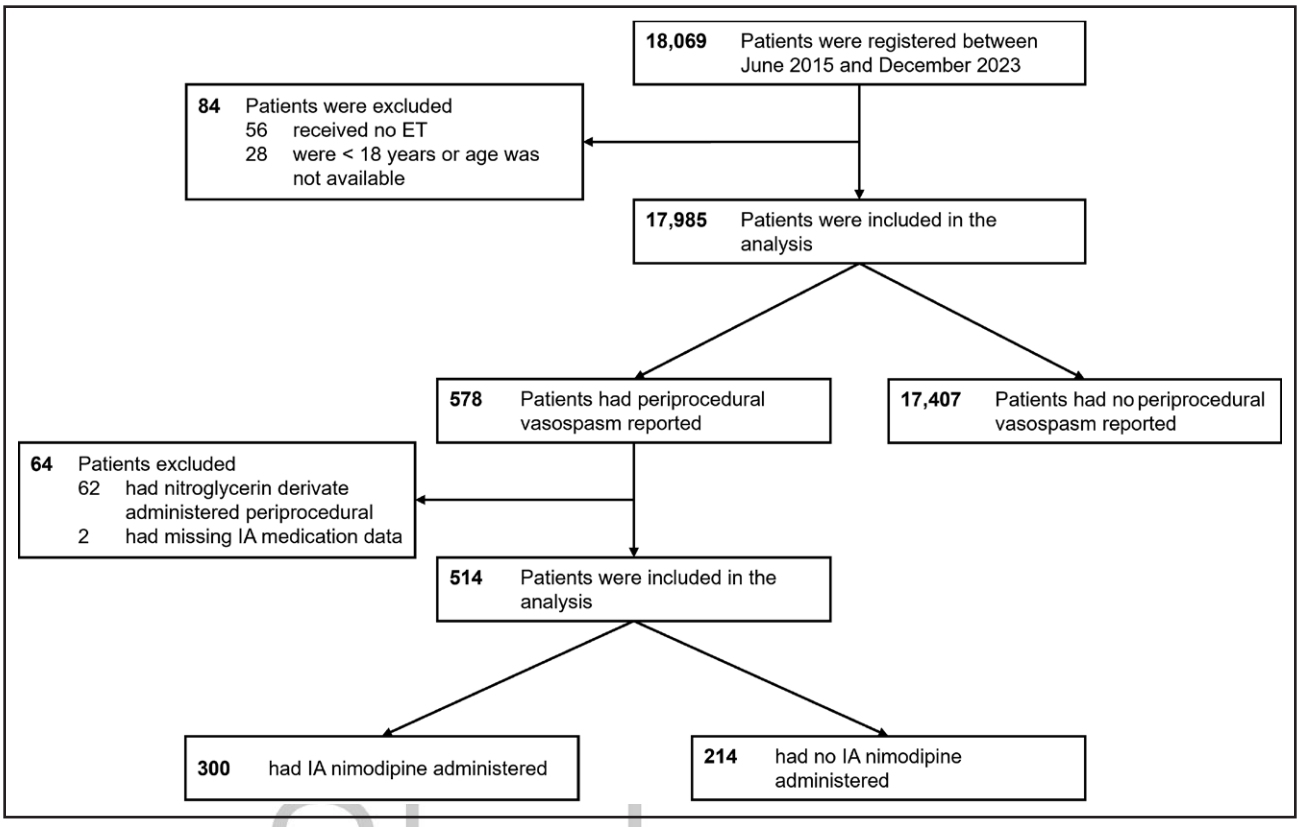

Figure 1. Patient selection flowchart.
IA indicates intraarterial; and ET endovascular treatment.

hemorrhage, or successful recanalization (Table 2). The sensitivity analysis yielded similar results (Table S4).

Predictors of Periprocedural Vasospasm

In the multivariable model, younger age (OR, 0.79 [95% CI, 0.74–0.85]; *P*<0.001 per 10-year increase), active smoking (OR, 1.28 [95% CI, 1.02–1.60]; *P*=0.034), MCA-M2 occlusion (OR, 1.53 [95% CI, 1.24–1.89]; *P*<0.001), first-line stent retriever thrombectomy (OR, 1.41 [95% CI, 1.16–1.72]; *P*<0.001), and a higher number of recanalization attempts (OR, 1.07 [95% CI, 1.03–1.11]; *P*=0.003 per 1 additional recanalization attempt) were independently associated with higher odds of vasospasm. In contrast, first pass recanalization (OR, 0.75 [95% CI, 0.59–0.96]; *P*=0.022), first-line contact aspiration thrombectomy (OR, 0.64 [95% CI, 0.46–0.89]; *P*=0.007), BA occlusion (OR, 0.50 [95% CI, 0.30–0.77]; *P*=0.001), and nonterminal internal carotid artery occlusion (OR, 0.57 [95% CI, 0.34–0.91]; *P*=0.016) were associated with reduced odds of vasospasm (Figure 2). The highest predicted probability of vasospasm (16.7%) was observed in patients aged ≤60 years who were active smokers, had MCA-M2 occlusions, and required >5 recanalization attempts. In contrast, the lowest predicted probability (0.4%) was seen in nonsmoking patients over 70 years of age who achieved first-pass recanalization of non-MCA-M2 occlusions (Figure 3). Predicted probabilities for vasospasm across individual variables are presented in Figure S5.

Comparison of Patients With and Without Periprocedural Intraarterial Nimodipine Administration

Univariate Analysis

Of the 514 patients included in this analysis, 300 (58.4%) received intraarterial nimodipine during ET, while 214 (41.6%) did not (Table 3). Patients with intraarterial nimodipine administration were younger (mean age, 66.7 years versus 70.1 years; *P*=0.015), whereas all other baseline characteristics were similarly distributed. Admission to groin puncture times were slightly longer in the intraarterial nimodipine group (72 minutes versus 66 minutes; *P*=0.014), and proximal MCA-M1 occlusions were less frequent (28.0% versus 37.9%; *P*=0.021). Additionally, patients who received intraarterial nimodipine more often received general anesthesia (86.9% versus 70.5%; *P*<0.001).

Multivariate Analysis

In the unweighted cohort, patients with periprocedural vasospasm who received intraarterial nimodipine had

Table 1. Univariate Comparison of Patients With and Without Periprocedural Vasospasm

	Vasospasm, N=578 (3.2%)	No vasospasm, N=17 407 (96.8%)	*P* value
Baseline characteristics			
Age, y, mean (SD)	68.2 (15.5)	73.8 (13.8)	<0.001*,†
Female sex, n (%)	298/578 (51.6)	9009/17 396 (51.8)	0.933‡
pmRS, median (IQR)	0 (0–1)	0 (0–2)	<0.001*,†
Prestroke dependency, n (%)	51/553 (9.2)	2684/16 329 (16.4)	<0.001‡†
NIHSS, median (IQR)	14 (9–18)	14 (8–18)	0.508*
Vascular risk factors, n (%)			
Arterial hypertension	392/560 (70.0)	12 801/16 612 (77.1)	<0.001‡†
Diabetes	108/560 (19.3)	3787/16 484 (23.0)	0.041‡†
Dyslipidemia	250/558 (44.8)	6741/16 419 (41.1)	0.080‡
Atrial fibrillation	189/560 (33.8)	6849/16 445 (41.7)	<0.001‡†
Active smoking	132/526 (25.1)	2510/15 139 (16.6)	<0.001‡†
Procedural time intervals, min, median (IQR)			
Last known normal to admission	186 (78–354)	180 (78–372)	0.998*
Admission to groin puncture	69 (46–94)	72 (48–103)	0.017*,†
Groin puncture to recanalization	48 (30–78)	42 (24–66)	<0.001*,†
Last known normal to recanalization	288 (210–504)	306 (216–528)	0.350*
Stroke, imaging, and treatment characteristics			
ASPECTS (for anterior circulation stroke), median (IQR)	8 (7–10)	9 (7–10)	0.002*,†
Occlusion type, n (%)			
ICA, terminal segment	102/578 (17.7)	2625/17 407 (15.1)	0.099‡
Non-terminal ICA	21/578 (3.6)	1007/17 407 (5.8)	0.028‡†
M1 proximal	188/578 (32.5)	5036/17 407 (28.9)	0.063‡
M1 distal	102/578 (17.7)	2602/17 407 (15.0)	0.076‡
M2	150/578 (26.0)	2941/17 407 (16.9)	<0.001‡†
Anterior cerebral artery	27/578 (4.7)	577/17 407 (3.3)	0.078‡
Posterior cerebral artery	12/578 (2.1)	596/17 407 (3.4)	0.080‡
Basilar artery	26/578 (4.5)	1434/17 407 (8.2)	<0.001‡†
Vertebral artery	5/578 (0.9)	297/17 407 (1.7)	0.138‡
Common carotid artery	38/578 (6.6)	1107/17 407 (6.4)	0.795‡
Tandem occlusion, n (%)	86/560 (15.4)	2652/16 091 (16.5)	0.524‡
Carotid artery stenting, n (%)	76/578 (13.2)	2163/17 407 (12.4)	0.608‡
Occlusion side, n (%)			0.367‡
Left	290/541 (53.6)	7884/15 080 (52.3)	
Right	251/541 (46.4)	7196/15 080 (47.7)	
Intravenous thrombolysis, n (%)	264/574 (46.0)	8007/9202 (46.5)	0.832‡
Type of anesthesia, n (%)			0.913‡
General anesthesia	462/568 (81.3)	13 231/16 320 (81.1)	
Conscious sedation	106/568 (18.7)	3089/16 320 (18.9)	
First-line thrombectomy approach			
Contact aspiration	58/568 (10.2)	2643/15 543 (17.0)	<0.001‡†
Stent retriever	198/568 (34.9)	4070/15 543 (26.2)	<0.001‡†
Combined or cross-over	312/568 (55.0)	8830/15 543 (64.2)	0.374‡
Recanalization attempts, n (IQR)	2 (1–3)	2 (1–3)	<0.001*,†
First pass recanalization, n (%)	205/539 (38.0)	7410/15 560 (47.6)	<0.001‡†

ASPECTS indicates Alberta Stroke Program Early CT Score; ICA, internal carotid artery; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; and pmRS, premodified Rankin Scale.

*Wilcoxon rank-sum test.

†Significant differences.

‡χ^2 test.

Table 2. Primary and Secondary Outcomes (Periprocedural Vasospasm Versus No Vasospasm)

	Vasospasm, N=578 (3.2%)	No vasospasm, N=17 407 (96.8%)	*P* value	IPTW adjusted effect estimate (95% CI)	*P* value
Primary outcome					
mRS, median (IQR)	4 (2–6)	4 (2–6)	0.042*†	1.25 (1.02–1.53)‡	0.030*§
Secondary outcomes					
mRS score 0–1	22.7%	24.8%	0.339‖	0.88 (0.68–1.13)‡	0.319§
mRS score 0–2	31.9%	36.3%	0.080‖	0.80 (0.63–1.01)‡	0.056§
END	19.8%	20.0%	0.903‖	0.98 (0.75–1.28)‡	0.892§
sICH	4.6%	3.3%	0.162‖	1.44 (0.89–2.33)¶	0.142§
Mortality	36.2%	29.7%	0.018*,‖	1.35 (1.05–1.75)‡	0.021*§
mTICI 2b–3	84.4%	85.8%	0.531‖	0.95 (0.70–1.37)#	0.921§
Additional procedural complications**	22.2%	6.8%	<0.001*,‖	3.96 (3.05–5.14)#	<0.001*,§

Analyses were conducted in the weighted sample of the total study population. END indicates early neurological deterioration; IPTW, inverse probability of treatment weighting; IQR, interquartile range; mRS, modified Rankin Scale; mTICI, modified Thrombolysis In Cerebral Infarction; and sICH, symptomatic intracranial hemorrhage.

*Significant differences.

†Wilcoxon rank-sum test.

‡Adjusted for age, sex, and pmRS.

§Wald-test.

‖χ^2 test.

¶Adjusted for age, sex, pmRS, and hypertension.

#Adjusted for age, sex, pmRS, and recanalization attempts.

**Additional procedural complications were defined as a composite of vessel dissection or perforation and clot migration or embolization diagnosed via conventional angiography.

better functional outcomes at 90 days (median mRS score, 3 versus 4; *P*=0.027). However, this difference was no longer statistically significant after IPTW (median mRS score, 3 versus 4; *P*=0.186) and multivariable adjustment (aOR, 0.79 [95% CI, 0.54–1.15]; *P*=0.223; Table 4; Figure 4). Before IPTW, patients who received intraarterial nimodipine had higher rates of favorable functional outcomes (mRS score, 0–1: 28.7% versus 23.7%, *P*=0.030; mRS score, 0–2: 43.4% versus 30.6%, *P*=0.010). These differences were also not statistically significant after IPTW (mRS score, 0–1: 27.4% versus 26.4%, *P*=0.824; mRS score, 0–2: 43.6% versus 34.2%, *P*=0.081), and adjustment (mRS score, 0–1: aOR, 0.98 [95% CI, 0.56–1.72]; *P*=0.948; mRS score, 0–2: aOR, 1.57 [95% CI, 0.94–2.60]; *P*=0.080). Intraarterial nimodipine administration was independently associated with a significantly lower rate of END (15.5% versus 26.0%; *P*=0.015; aOR, 0.54 [95% CI, 0.31–0.91]; *P*=0.021) in IPTW-adjusted regression analysis. No other secondary outcome differed significantly between the IPTW-adjusted groups. The sensitivity analysis yielded similar results (Table S5).

DISCUSSION

In this real-world cohort, periprocedural vasospasm occurred in ≈3% of patients undergoing ET for acute ischemic stroke, corresponding to the lower end of previously reported rates.[1,2] Leveraging high-volume, multicenter data from routine clinical practice, our findings suggest that vasospasm may occur less frequently than

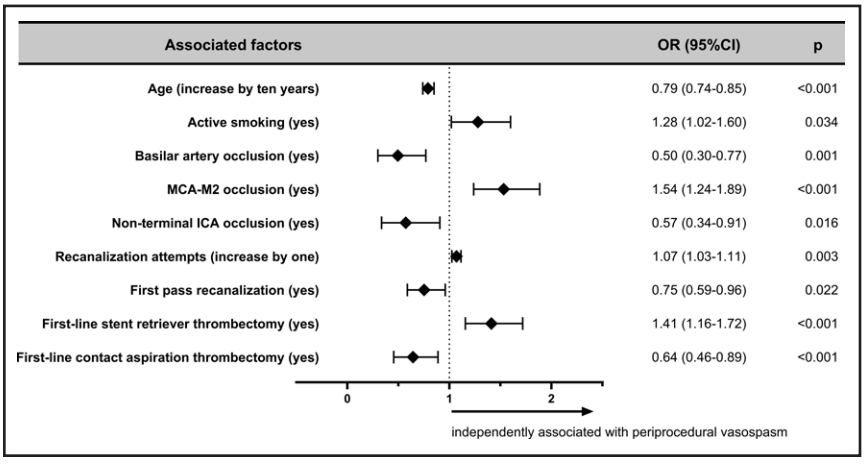

Figure 2. Predictors for periprocedural vasospasm.
Odds ratios (ORs), 95% CIs, and *P* values are shown for variables selected via Least Absolute Shrinkage and Selection Operator (LASSO) regression. Logistic regression analyses were based on 5 multiply imputed data sets, with final estimates pooled using Rubin rules. The Wald-test was used to test for statistical significance. ICA indicates internal carotid artery; and MCA middle cerebral artery.

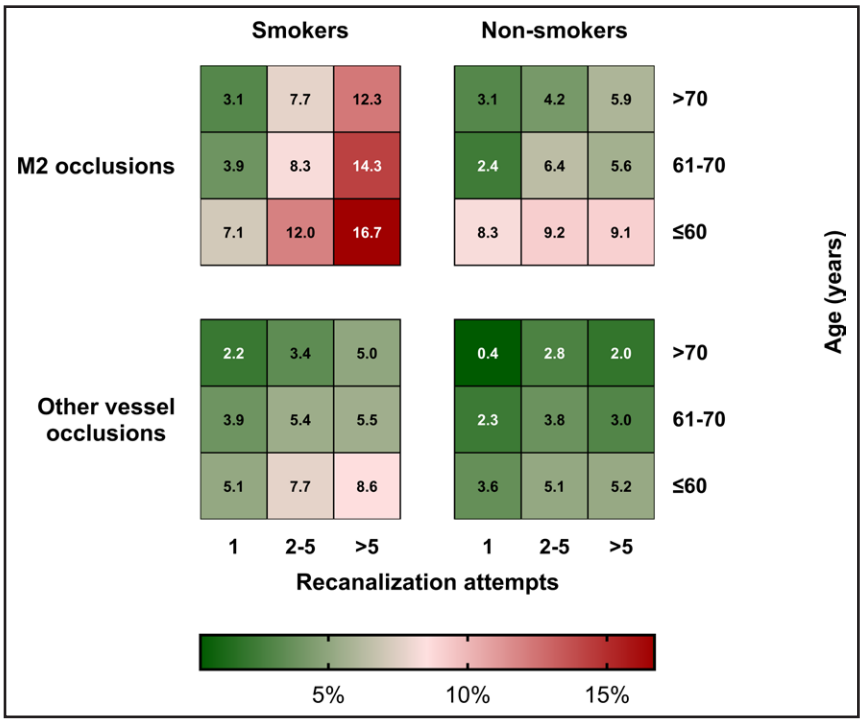

Figure 3. Heatmap of predicted probabilities for vasospasm. Predicted probabilities (%) for periprocedural vasospasm are shown stratified by type of vessel occlusion, smoking status, age intervals, and number of recanalization attempts. Predicted probabilities derived from a pooled logistic regression model using multiple imputation.

reported in smaller or single-center studies, although underreporting within the registry cannot be ruled out.

Vasospasm was associated with worse functional outcomes, increased all-cause mortality, and higher rates of other periprocedural complications. These findings support earlier reports that challenge the notion of vasospasm as a benign event and underline the need to recognize it as a serious complication of ET in patients with stroke.[4,10] While vasospasm was not associated with increased rates of ICH, previous data suggest that the impact on clinical outcomes may be mediated by vasospasm-related infarct growth.[14]

We identified several factors independently associated with vasospasm, including younger age, active smoking, distal (M2 segment) occlusions, first-line stent retriever thrombectomy, and a higher number of recanalization attempts. In contrast, first pass recanalization, first-line contact aspiration thrombectomy, proximal internal carotid artery, and BA occlusions were associated with a lower risk of vasospasm. Both younger age and cigarette smoking, the latter potentially due to the effect of pro-inflammatory substances in tobacco that may increase susceptibility to vessel wall stress, have been previously identified as predictors of vasospasm in subarachnoid hemorrhage.[15–17] In our cohort, younger patients also had lower rates of vascular risk factors such as diabetes and hypertension, which may result in less intracranial atherosclerotic disease. This, in turn, could increase vessel wall compliance and susceptibility to shear stress, thereby contributing to a higher risk of vasospasm.[6] More recanalization attempts were associated with increased odds of vasospasm, likely due to cumulative vessel strain, whereas first-pass recanalization success reduced this risk, consistent with previous studies and highlighting the importance of the first-pass effect.[18] The association of vasospasm with distal vessel occlusions (eg, M2) may be explained by the increased mechanical stress on vessel walls during catheter navigation and thrombectomy maneuvers in smaller vessels. This is particularly relevant in light of recent trials comparing ET and best medical treatment to best medical management alone for distal occlusions, and should be considered when evaluating treatment decisions in this population.[19,20] Conversely, the lower rate of vasospasm in BA occlusions may be due to the more frequent use of aspiration-only thrombectomy in these individuals. Aspiration catheters are associated with a lower risk of vasospasm than stent retrievers, most likely due to less mechanical vessel wall stress, which may explain this protective effect. This aligns with our observation that first-line contact aspiration thrombectomy was associated with lower rates of vasospasm, whereas first-line stent retriever thrombectomy increased the risk of vasospasm.[6] Given the significant impact of vasospasm on clinical outcomes, the identification of these associated factors may aid neurointerventionalists in identifying high-risk patients and in anticipating and managing this complication during endovascular stroke treatment. Furthermore, prophylactic nimodipine administration in high-risk populations may warrant investigation in future clinical trials.

To our knowledge, this is the largest study to date comparing patients with periprocedural vasospasm during ET who received intraarterial nimodipine administration to those who did not. Furthermore, previous studies

Table 3. Univariate Comparison of Patients With and Without IA Nimodipine Administration

	IA nimodipine, N=300 (58.4%)	No IA nimodipine, N=214 (41.6%)	*P* value
Baseline characteristics			
Age, y, mean (SD)	66.7 (16.0)	70.1 (15.0)	0.015*,†
Female sex, n (%)	162 (54.0)	104 (48.6)	0.245‡
pmRS, median (IQR)	0 (0–1)	0 (0–1)	0.645†
Prestroke dependency, n (%)	29/294 (9.9)	20/196 (10.2)	1.000‡
NIHSS, median (IQR)	14 (9–18)	14 (9–18)	0.979†
Vascular risk factors, n (%)			
Arterial hypertension	198/297 (66.7)	144/199 (72.4)	0.199‡
Diabetes	50/297 (16.8)	40/199 (20.1)	0.406‡
Dyslipidemia	131/297 (44.1)	79/197 (40.1)	0.404‡
Atrial fibrillation	104/297 (35.0)	70/199 (35.2)	1.000‡
Active smoking	65/282 (23.1)	45/181 (24.9)	0.656‡
Procedural time intervals, min, median (IQR)			
Last known normal to admission	186 (78–462)	186 (90–330)	0.678†
Admission to groin puncture	72 (54–102)	66 (42–90)	0.014*,†
Groin puncture to recanalization	48 (30–78)	48 (30–78)	0.357†
Last known normal to recanalization	294 (210–600)	228 (204–468)	0.270†
Stroke, imaging, and treatment characteristics			
ASPECTS (for anterior circulation stroke), median (IQR)	8 (7–10)	9 (7–10)	0.160†
Occlusion type, n (%)			
ICA, terminal segment	52/300 (17.3)	42/214 (19.6)	0.563‡
Nonterminal ICA	15/300 (5.0)	6/214 (2.8)	0.262‡
M1 proximal	84/300 (28.0)	81/214 (37.9)	0.021*,‡
M1 distal	59/300 (19.7)	35/214 (16.4)	0.357‡
M2	80/300 (26.7)	51/214 (23.8)	0.475‡
Anterior cerebral artery	15/300 (5.0)	6/214 (2.8)	0.262‡
Posterior cerebral artery	6/300 (2.0)	6/214 (2.8)	0.567‡
Basilar artery	15/300 (5.0)	7/214 (3.3)	0.384‡
Vertebral artery	2/300 (0.7)	2/214 (1.0)	1.000‡
Common carotid artery	11/300 (7.5)	16/214 (3.7)	0.071‡
Tandem occlusion, n (%)	43/294 (14.6)	29/203 (14.3)	1.000‡
Carotid artery stenting, n (%)	40/300 (13.3)	23/214 (10.8)	0.415
Occlusion side, n (%)			0.461‡
Left	154/279 (55.2)	106/206 (51.5)	
Right	125/279 (44.8)	100/206 (48.5)	
Intravenous thrombolysis, n (%)	136/297 (45.8)	101/213 (47.4)	0.712‡
Type of anesthesia, n (%)			<0.001*,‡
General anesthesia	258/297 (86.9)	148/210 (70.5)	
Conscious sedation	39/297 (13.1)	62/210 (29.5)	
Recanalization attempts, n (IQR)	2 (1–3)	2 (1–3)	0.782†
First pass recanalization, n (%)	77/200 (38.5)	109/276 (39.5)	0.850‡

ASPECTS indicates Alberta Stroke Program Early CT Score; IA, intraarterial; ICA, internal carotid artery; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; and pmRS, premodified Rankin Scale.

*Significant differences.

†Wilcoxon rank-sum test.

‡χ^2 test.

have been limited by the absence of direct comparisons between treated and untreated patients, and thus were unable to distinguish the effects of intraarterial nimodipine from those of vasospasm itself.[4,10,14] In this study, intraarterial nimodipine administration was associated with reduced neurological deterioration at 24

Table 4. Primary and Secondary Outcomes (Periprocedural IA Nimodipine Bolus Versus No IA Nimodipine Administration)

	Unweighted cohorts			Weighted cohorts				
	IA nimodipine, N=300 (58.4%)	No IA nimodipine, N=214 (41.6%)	*P* value	IA nimodipine	No IA nimodipine	*P* value	IPTW adjusted effect estimate (95% CI)	*P* value
Primary outcome								
mRS, median (IQR)	3 (1–6)	4 (2–6)	**0.027***,†	3 (1–6)	4 (2–6)	0.186†	0.79 (0.54–1.15)‡	0.223§
Secondary outcomes								
mRS score 0–1, n (%)	74/258 (28.7)	41/173 (23.7)	**0.030***,‖	27.4%	26.4%	0.824‖	0.98 (0.56–1.72)‡	0.948§
mRS score 0–2, n (%)	112/258 (43.4)	53/173 (30.6)	**0.010***,‖	43.6%	34.2%	0.081‖	1.57 (0.94–2.60)‡	0.080§
END, n (%)	47/280 (16.8)	42/183 (23.0)	0.130‖	15.5%	26.0%	**0.015***,‖	0.54 (0.31–0.91)‡	**0.021***,§
sICH, n (%)	12/300 (3.6)	15/214 (7.0)	0.200‖	3.9%	10.9%	**0.010***,‖	0.41 (0.17–1.01)¶	0.053§
Mortality, n (%)	66/258 (25.6)	57/173 (32.9)	0.120‖	23.5%	28.4%	0.284‖	0.79 (0.46–1.35)‡	0.389§
mTICI 2b–3, n (%)	253/297 (85.2)	183/211 (86.7)	0.700‖	85.9%	87.3%	0.694‖	1.12 (0.61–2.08)#	0.713§
Additional procedural complications, n (%)**	60/300 (20.0)	51/214 (23.8)	0.404‖	18.6%	22.9%	0.319‖	0.74 (0.44–1.25)#	0.263§

Analyses were conducted in the weighted sample of the total study population. END indicates early neurological deterioration; IA, intraarterial; IPTW, Inverse Probability of Treatment Weighting; IQR, interquartile range; mRS, modified Rankin Scale; mTICI, modified Thrombolysis In Cerebral Infarction; sICH, symptomatic intracranial hemorrhage.

*Significant differences.

†Wilcoxon rank-sum test.

‡Adjusted for age, sex, and pmRS.

§Wald-test.

‖χ^2 test.

¶Adjusted for age, sex, pmRS, and hypertension.

#Adjusted for age, sex, pmRS, and recanalization attempts.

**Additional procedural complications were defined as a composite of vessel dissection or perforation and clot migration or embolization diagnosed via conventional angiography.

hours. Although we observed trends toward improved functional outcomes, these did not reach statistical significance in weighted analyses. Importantly, we also did not find an increased risk of symptomatic intracranial hemorrhage associated with nimodipine, contrary to concerns raised by some authors who hypothesized that vasodilation in infarcted tissue could potentially elevate the risk of bleeding by enhancing reperfusion.[21] The observed benefit of intraarterial nimodipine with regard to END may be attributed to prolonged vasodilatory effects, which may persist for several hours following ET. This conclusion is supported by its pharmacokinetic profile, with a reported half-life of ≈9 hours. Additionally, sustained increases in local vessel flow velocity have been reported several hours after ET, suggesting that vasospasm may continue, or even emerge, well beyond the procedure itself.[22,23] Together, these findings suggest that intraarterial nimodipine may have a beneficial effect in patients experiencing periprocedural vasospasm. Nonetheless, its use should be carefully considered, as nimodipine is associated with systemic hypotension and potential local cerebral steal phenomena—both of which may have negative effects during ET.[24,25]

Strengths of this study include its multicenter design, the inclusion of a large real-world patient population, and the consistency of findings across sensitivity analyses, which support the robustness of the results. Still, limitations apply. The observational nature of the study introduces the potential for residual confounding. Detailed

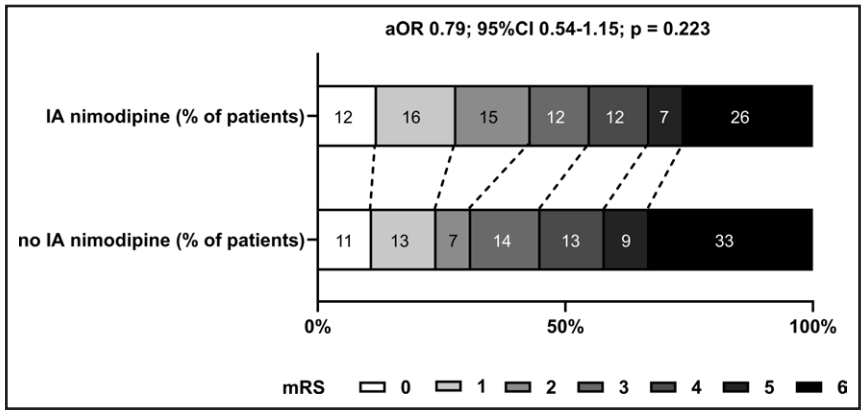

Figure 4. Distribution of scores on the modified Rankin Scale (mRS) at 90 days.
The adjusted effect estimate of the ordinal regression analysis indicates the odds of achieving higher mRS scores (worse clinical outcome) at 90 days. aOR indicates adjusted odds ratio; and IA, intraarterial.

angiographic data on the exact location and number of vasospasms and the rationale for intraarterial nimodipine administration were not available. Underreporting of vasospasm may have occurred, with events more often documented when considered severe or when nimodipine was administered, which may explain why the observed prevalence was at the lower end of rates reported in previous studies. Additionally, data on infarct volume at 24 hours is lacking, limiting our ability to directly confirm whether vasospasm-related infarct growth mediated the observed clinical outcomes. Regarding data on the first-line thrombectomy approach, we could not distinguish between patients who underwent an initial combined technique and those who transitioned (crossover approach), which may have influenced our results. Furthermore, we could not determine whether vasospasm resolved spontaneously in patients who did not receive nimodipine, nor could we account for the use of nimodipine in flush solutions, which has been suggested to prevent vasospasm in recent data and thus may have influenced our findings.[26]

CONCLUSIONS

Risk for periprocedural vasospasm is higher in younger patients with distal anterior circulation strokes who require multiple recanalization attempts and are active smokers. Vasospasm is associated with worse functional outcome and higher all-cause mortality, supporting its notion as a serious complication of endovascular stroke treatment. Intraarterial nimodipine administration appears to reduce rates of END without increasing the risk of intracerebral hemorrhage and may thus be considered as a therapeutic option in selected individuals.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S5
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STUDY GROUP

APPENDIX

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REFERENCES

1. Balami JS, White PM, McMeekin PJ, Ford GA, Buchan AM. Complications of endovascular treatment for acute ischemic stroke: prevention and management. *Int J Stroke*. 2018;13:348–361. doi: 10.1177/1747493017743051
2. Behme D, Gondecki L, Fiethen S, Kowoll A, Mpotsaris A, Weber W. Complications of mechanical thrombectomy for acute ischemic stroke-a retrospective single-center study of 176 consecutive cases. *Neuroradiology*. 2014;56:467–476. doi: 10.1007/s00234-014-1352-0
3. Emprechtinger R, Piso B, Ringleb PA. Thrombectomy for ischemic stroke: meta-analyses of recurrent strokes, vasospasms, and subarachnoid hemorrhages. *J Neurol*. 2017;264:432–436. doi: 10.1007/s00415-016-8205-1
4. Ferhat S, Bellanger G, Milnerowicz M, Kyheng M, Labreuche J, Sibon I, Khobzi M, Abousleiman JM, Popica DA, Moulin S, et al; ETIS investigators. Iatrogenic arterial vasospasm during mechanical thrombectomy requiring treatment with intra-arterial nimodipine might be associated with worse outcomes. *Eur J Neurol*. 2024;31:e16467. doi: 10.1111/ene.16467
5. Campbell BC, Hill MD, Rubiera M, Menon BK, Demchuk A, Donnan GA, Roy D, Thornton J, Dorado L, Bonafe A, et al. Safety and efficacy of solitaire stent thrombectomy: individual patient data meta-analysis of randomized trials. *Stroke*. 2016;47:798–806. doi: 10.1161/STROKEAHA.115.012360
6. Jesser J, Awounvo S, Vey JA, Vollherbst DF, Hilgenfeld T, Chen M, Nguyen TN, Schönenberger S, Bendszus M, Möhlenbruch MA, et al. Prediction and outcomes of cerebral vasospasm in ischemic stroke patients receiving anterior circulation endovascular stroke treatment. *Eur Stroke J*. 2023;8:684–691. doi: 10.1177/23969873231177766
7. Jesser J, Nguyen T, Dmytriw AA, Yamagami H, Miao Z, Sommer LJ, Stockero A, Pfaff JAR, Ospel J, Goyal M, et al. Treatment practice of vasospasm during endovascular thrombectomy: an international survey. *Stroke Vasc Neurol*. 2024;9:490–496. doi: 10.1136/svn-2023-002788
8. Happi Ngankou E, Gory B, Marnat G, Richard S, Bourcier R, Sibon I, Dargazanli C, Arquizan C, Maïer B, Blanc R, et al; ETIS Registry Investigators. Thrombectomy complications in large vessel occlusions: incidence, predictors, and clinical impact in the ETIS registry. *Stroke*. 2021;52:e764–e768. doi: 10.1161/STROKEAHA.121.034865
9. Uchikawa H, Kuroiwa T, Nishio A, Tempaku A, Kondo K, Mukasa A, Kamada H. Vasospasm as a major complication after acute mechanical thrombectomy with stent retrievers. *J Clin Neurosci*. 2019;64:163–168. doi: 10.1016/j.jocn.2019.03.011
10. Pilgram-Pastor SM, Piechowiak EI, Dobrocky T, Kaesmacher J, Den Hollander J, Gralla J, Mordasini P. Stroke thrombectomy complication management. *J Neurointerv Surg*. 2021;13:912–917. doi: 10.1136/neurintsurg-2021-017349
11. Alegiani AC, Dorn F, Herzberg M, Wollenweber FA, Kellert L, Siebert E, Nolte CH, von Rennenberg R, Hattingen E, Petzold GC, et al. Systematic evaluation of stroke thrombectomy in clinical practice: the German Stroke Registry Endovascular Treatment. *Int J Stroke*. 2019;14:372–380. doi: 10.1177/1747493018806199
12. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370:1453–1457. doi: 10.1016/s0140-6736(07)61602-x
13. Hacke W, Kaste M, Fieschi C, von Kummer R, Davalos A, Meier D, Larrue V, Bluhmki E, Davis S, Donnan G, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second European-Australasian

Acute Stroke Study Investigators. *Lancet*. 1998;352:1245–1251. doi: 10.1016/s0140-6736(98)08020-9
14. Jesser J, Potreck A, Vollherbst D, Seker F, Chen M, Schönenberger S, Do TD, Bendszus M, Möhlenbruch MA, Weyland CS. Effect of intra-arterial nimodipine on iatrogenic vasospasms during endovascular stroke treatment - angiographic resolution and infarct growth in follow-up imaging. *BMC Neurol*. 2023;23:5. doi: 10.1186/s12883-022-03045-x
15. Lasner TM, Weil RJ, Riina HA, King JT Jr, Zager EL, Raps EC, Flamm ES. Cigarette smoking-induced increase in the risk of symptomatic vasospasm after aneurysmal subarachnoid hemorrhage. *J Neurosurg*. 1997;87:381–384. doi: 10.3171/jns.1997.87.3.0381
16. Kale SP, Edgell RC, Alshekhlee A, Borhani Haghighi A, Sweeny J, Felton J, Kitchener J, Vora N, Bieneman BK, Cruz-Flores S, et al. Age-associated vasospasm in aneurysmal subarachnoid hemorrhage. *J Stroke Cerebrovasc Dis*. 2013;22:22–27. doi: 10.1016/j.jstrokecerebrovasdis.2011.05.024
17. Inagawa T. Risk factors for cerebral vasospasm following aneurysmal subarachnoid hemorrhage: a review of the literature. *World Neurosurg*. 2016;85:56–76. doi: 10.1016/j.wneu.2015.08.052
18. Jang KM, Choi HH, Nam TK, Byun JS. Clinical outcomes of first-pass effect after mechanical thrombectomy for acute ischemic stroke: a systematic review and meta-analysis. *Clin Neurol Neurosurg*. 2021;211:107030. doi: 10.1016/j.clineuro.2021.107030
19. Goyal M, Ospel JM, Ganesh A, Dowlatshahi D, Volders D, Möhlenbruch MA, Jumaa MA, Nimjee SM, Booth TC, Buck BH, et al; ESCAPE-MeVO Investigators. Endovascular treatment of stroke due to medium-vessel occlusion. *N Engl J Med*. 2025;392:1385–1395. doi: 10.1056/NEJMoa2411668
20. Psychogios M, Brehm A, Ribo M, Rizzo F, Strbian D, Räty S, Arenillas JF, Martínez-Galdámez M, Hajdu SD, Michel P, et al; DISTAL Investigators. Endovascular treatment for stroke due to occlusion of medium or distal vessels. *N Engl J Med*. 2025;392:1374–1384. doi: 10.1056/NEJMoa2408954
21. Neuberger U, Kickingereder P, Schönenberger S, Schieber S, Ringleb PA, Bendszus M, Pfaff J, Möhlenbruch MA. Risk factors of intracranial hemorrhage after mechanical thrombectomy of anterior circulation ischemic stroke. *Neuroradiology*. 2019;61:461–469. doi: 10.1007/s00234-019-02180-6
22. Gómez-Escalonilla C, Simal P, García-Moreno H, Sánchez TL, Canalejo DM, Jiménez MR, Hernández LS, Alfocea DT, Moreu M, Pérez-García C, et al. Transcranial Doppler 6 h after successful reperfusion as a predictor of infarct volume. *J Stroke Cerebrovasc Dis*. 2022;31:106149. doi: 10.1016/j.jstrokecerebrovasdis.2021.106149
23. Rossi S, Paolucci M, Arnone G, Bigliardi G, Longoni M, Pulito G, Azzini C, Coppo L, Russo M, Tsivgoulis G, et al; HYs Study Group. Prognostic value of cerebral hemodynamics assessment on 24-h transcranial color-coded Doppler following a successful thrombectomy. *Eur J Neurol*. 2025;32:e70224. doi: 10.1111/ene.70224
24. Rass V, Kindl P, Lindner A, Kofler M, Altmann K, Putnina L, Ianosi BA, Schiefecker AJ, Beer R, Pfausler B, et al. Blood pressure changes in association with nimodipine therapy in patients with spontaneous subarachnoid hemorrhage. *Neurocrit Care*. 2023;39:104–115. doi: 10.1007/s12028-023-01760-y
25. Forsman M, Fleischer JE, Milde JH, Steen PA, Michenfelder JD. The effects of nimodipine on cerebral blood flow and metabolism. *J Cereb Blood Flow Metab*. 1986;6:763–767. doi: 10.1038/jcbfm.1986.133
26. Sommer LJ, Jesser J, Nikoubashman O, Nguyen TN, Pinho J, Reich A, Wiesmann M, Weyland CS. Nimodipine as vasodilator in guide catheter flush to prevent vasospasm during endovascular stroke treatment. *Clin Neuroradiol*. 2024;34:809–815. doi: 10.1007/s00062-024-01424-0