OPEN ACCESS

Original research

Thrombectomy patients with minor stroke: factors of early neurological deterioration

Christian Heitkamp ,[1] Laurens Winkelmeier ,[1] Fabian Flottmann ,[1] Maximilian Schell,[2] Helge Kniep ,[1] Gabriel Broocks,[1,3] Christian Thaler ,[1] Paul Steffen,[1] Goetz Thomalla,[2] Jens Fiehler ,[1] Tobias D Faizy ,[1,4] for the German Stroke Registry-Endovascular Treatment (GSR-ET)

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/jnis-2024-021930).

[1]Department of Diagnostic and Interventional Neuroradiology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
[2]Department of Neurology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany
[3]Department of Neuroradiology, HELIOS Medical Center, Campus of MSH Medical School Hamburg, Schwerin, Germany
[4]Department of Neuroradiology, University Hospital Muenster, Muenster, Germany

Correspondence to
Dr Christian Heitkamp; c.heitkamp@uke.de

Received 2 May 2024
Accepted 15 June 2024

To cite: Heitkamp C, Winkelmeier L, Flottmann F, *et al*. *J NeuroIntervent Surg* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/jnis-2024-021930

ABSTRACT

Background A sizeable proportion of stroke patients with large vessel occlusion present with minor neurological deficits. Whether mechanical thrombectomy (MT) is beneficial in these patients is controversial. We aimed to investigate factors of early neurological deterioration (END) in thrombectomy patients with minor stroke and hypothesized that END is linked to unfavorable functional outcomes.

Methods Multicenter cohort study screening all patients prospectively enrolled in the German Stroke Registry–Endovascular Treatment (n=13 082) between 2015 and 2021. Patients who underwent MT for anterior circulation vessel occlusion with baseline National Institutes of Health Stroke Scale (NIHSS) score of <6 were included. END was defined as an increase in NIHSS score of ≥4 within the first 24 hours after MT. Multivariable regression analyses were performed to investigate factors associated with END and its association with unfavorable functional outcomes 90 days after treatment (modified Rankin Scale (mRS) score ≥2).

Results Among 817 patients included, 24% exhibited END and 48% had unfavorable functional outcomes. Prestroke mRS (adjusted odds ratio (aOR) [95% CI] 1.42 [1.13 to 1.78]), baseline NIHSS (aOR [95% CI] 0.83 [0.73 to 0.94]), time from admission to groin puncture (aOR [95% CI] 1.04 [1.02 to 1.07]), general anesthesia (aOR [95% CI] 1.68 [1.08 to 2.63]), number of passes (aOR [95% CI] 1.15 [1.03 to 1.29]), adverse events during treatment (aOR [95% CI] 1.89 [1.19 to 3.01]), successful recanalization (aOR [95% CI] 0.29 [0.17 to 0.50]), and intracranial hemorrhage on follow-up imaging (aOR [95% CI] 3.40 [1.90 to 6.07]) were independently associated with END. END was independently linked to unfavorable functional outcomes (aOR [95% CI] 7.51 [4.57 to 12.34]).

Conclusions Almost a quarter of thrombectomy patients with minor stroke developed END. These patients had twice the odds of experiencing unfavorable functional outcomes.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Early neurological deterioration (END) in thrombectomy patients with National Institutes of Health Stroke Scale (NIHSS) scores of ≥6 on admission occurs in up to 40% of cases and is a strong predictor of unfavorable functional outcomes after 90 days. Thrombectomy in patients with minor stroke, defined by an admission NIHSS score of <6, is controversial and research regarding incidence and factors of END in this patient group remains scarce. The objective of this study was to determine the factors associated with an increased risk of END in patients with a minor stroke.

WHAT THIS STUDY ADDS

⇒ Almost a quarter of thrombectomy patients with minor stroke developed END, doubling the likelihood of unfavorable functional outcomes 90 days after treatment. Our study provides patient-specific risk factors independently associated with END after endovascular treatment.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study provides clinicians with valuable information about the incidence and risk factors of END in patients with minor stroke who underwent mechanical thrombectomy. In the ongoing debate on whether or not mechanical thrombectomy is beneficial in patients with a minor stroke, these findings may help clinicians in identifying patients who require special clinical attention following thrombectomy.

INTRODUCTION

A considerable fraction of patients with acute ischemic stroke and large vessel occlusion (AIS-LVO) present with only minor neurological deficits.[1 2] Although most patients achieve functional independence after 3 months following best medical treatment alone, milder deficits can still substantially reduce daily life activities and quality of life.[3–5] The optimal treatment strategy for these patients remains the subject of current debate, as only a few patients with National Institutes of Health Stroke Scale (NIHSS) score <6 were randomized in the pivotal mechanical thrombectomy (MT) trials.[3] Until the ongoing randomized trials ENDOLOW (Endovascular Therapy for Low NIHSS Ischemic Strokes)[4] and MOSTE (Minor Stroke Therapy Evaluation)[5] provide first-level evidence as to whether MT is beneficial or may even harm patients with

minor stroke, MT is currently considered on a case-by-case basis after thorough assessment of clinical and radiological parameters.[6] In anticipation of data from these upcoming randomized trials, retrospective studies might help to identify prognostic factors of an unfavorable clinical course after MT that may ultimately lead to poor long-term outcomes.

The NIHSS score after 24 hours was found to be an important predictor of long-term functional outcomes in AIS-LVO patients presenting with an NIHSS of ≥6 and can be compared with the baseline NIHSS to estimate the short-term clinical course of patients.[7 8] A recently published study of patients with minor stroke comparing MT+intravenous thrombolysis (IVT) with IVT alone observed a significantly higher rate of early neurological deterioration (END) in patients who underwent MT, despite similar long-term outcomes.[9] On the contrary, other studies of patients with minor stroke have shown that END is significantly associated with worse long-term outcomes.[10 11] To date, there is a lack of data regarding factors that are associated with END in patients with minor stroke treated by MT. Our objective was to assess prognostic factors of END and whether END is associated with unfavorable long-term functional outcomes in patients with minor stroke who were treated by MT.

METHODS

Study design and participating centers

This multicenter cohort study analyzed patients who were prospectively enrolled in the German Stroke Registry-Endovascular Treatment (GSR-ET) between June 2015 and December 2021. The GSR-ET is an ongoing, prospective, open-label, multicenter registry including patients who underwent MT at one of 25 comprehensive stroke centers in Germany (ClinicalTrials.gov identifier: NCT03356392).[12] All AIS-LVO patients with subsequent MT and an age of ≥18 years are included in the registry by the respective stroke center. Approval for the GSR-ET was granted by the ethics committee at Ludwig Maximilian University, Munich, Germany. Local ethics committees granted approval for all participating sites in accordance with their respective local regulations. Informed consent for this study was waived after review of the ethics committee of each participating center. This study was conducted in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guideline for observational studies. All procedures adhered to the guidelines set by the Health Insurance Portability and Accountability Act (HIPAA) and the Declaration of Helsinki.

Study inclusion criteria

The inclusion criteria for this study were defined as follows:1) acute ischemic stroke patients with an occlusion in the anterior circulation due to an isolated occlusion of the intracranial internal carotid artery (ICA) or of the M1 or M2 segment of the middle cerebral artery (MCA), 2) baseline NIHSS<6, 3) complete data on baseline NIHSS, prestroke modified Rankin Scale (mRS) score, NIHSS after 24 hours, recanalization status, and mRS after 90 days. We did not include patients with tandem occlusion or rescue MT (defined as MT following END) in our study. A detailed illustration of the inclusion and exclusion criteria can be found in online supplemental figure S1.

Clinical and radiological data acquisition

Patient characteristics, radiological parameters, and clinical outcomes were obtained from the GSR-ET database. Local investigators at each participating center assessed baseline imaging, digital subtraction angiograms, as well as follow-up imaging. The recanalization status was determined by the treating neurointerventionalist using the Thrombolysis in Cerebral Infarction (TICI) score. Successful recanalization was defined as a final TICI score of 2b-3. The patient's clinical status was assessed at admission, after 24 hours, and after 90 days using NIHSS and mRS.

Outcome measures

Primary outcome was an END, defined as an increase in NIHSS score of ≥4 within the first 24 hours following MT. The secondary outcome was an unfavorable functional outcome 90 days after MT, defined by an mRS score of ≥2, in line with previous research on patients with minor stroke.[1 11 13]

Statistical analysis

Patient characteristics, radiological findings, treatment details, and clinical outcomes were compared across study outcomes. Continuous variables were analyzed using the Mann–Whitney U test, and categorical variables were examined with the chi-square test. Data distribution normality was evaluated through Shapiro–Wilk tests. Continuous variables are displayed as medians with interquartile ranges (IQRs), while categorical variables are presented in counts and percentages. A subgroup analysis was conducted, including only successfully recanalized patients (TICI 2b-3), to evaluate the incidence of END in this patient group. Multivariable logistic regression analyses were performed to identify independent factors of END and unfavorable functional outcome. Variables that were clinically meaningful and significant with a p-value of below 0.05 in the group comparison between patients who exhibited END and those who did not (table 1) were included in the models. Following this objective, the independent variables with END as the dependent variable were NIHSS at admission, prestroke mRS, atrial fibrillation, occlusion of intracranial ICA, time from admission to groin puncture, administration of tissue plasminogen activator (tPA), general anesthesia, number of passes, successful recanalization, adverse event during treatment, and intracranial hemorrhage (ICH) on follow-up imaging after 24 hours. Covariates adjusting the model for unfavorable functional outcome were selected a priori and included age, prestroke mRS, NIHSS at admission, diabetes mellitus, time from symptom onset/last seen well to admission, general anesthesia, administration of tPA, successful recanalization, END, and ICH.

We provided adjusted odds ratios (aORs) together with associated p-values and 95% confidence intervals (CIs) for every independent variable. Statistical significance was considered when the p-value was below 0.05. The variance inflation factor for each independent variable was calculated to mitigate the possibility of multicollinearity in the regression model. The data analysis was conducted using Stata (Stata/MP18, StataCorp, TX, USA).

RESULTS

Baseline characteristics of patients

Of 13 082 patients enrolled in the GSR-ET, a total of 817 patients met the inclusion criteria (online supplemental figure S1). Median age was 72 (IQR 62–80) years and the sex ratio was balanced (51% male). The median NIHSS on admission was 4 (IQR 2–5) and the median ASPECTS (Alberta Stroke Program Early CT Score) was 9 (8–10). The most frequent vessel occlusion sites were the M1 (43%) and M2 (45%) segment of the MCA. Vessel recanalization was successfully (TICI≥2b) achieved in 703 (86%) patients and complete (TICI3) in 435 (53%) patients. Adverse events during endovascular treatment

Table 1 Patients' baseline, procedural, and outcome characteristics

Characteristics	Total (n=817)	No END (n=625)	END (n=192)	P-value
Baseline patient characteristics				
Age (years)	72 (62–80)	72 (61–80)	73 (62–81)	0.55
Male sex	419 (51%)	321 (51%)	98 (51%)	0.94
Prestroke mRS	0 (0–0)	0 (0–0)	0 (0–1)	0.002
NIHSS at admission	4 (2–5)	4 (2–5)	3 (2–4)	0.002
Hypertension	611 (75%)	461 (74%)	150 (78%)	0.22
Diabetes mellitus	171 (21%)	124 (20%)	47 (25%)	0.15
Dyslipidemia	369 (45%)	286 (46%)	83 (44%)	0.60
Atrial fibrillation	286 (35%)	232 (37%)	54 (29%)	0.029
Time from symptom onset/last seen well to admission (min)	180 (80–379)	172 (77–375)	220 (87–408)	0.22
Imaging characteristics				
ASPECTS	9 (8–10)	9 (8–10)	9 (8–10)	0.23
Left hemispheric stroke	446 (55%)	336 (54%)	110 (57%)	0.39
Occlusion site				
Intracranial ICA	99 (12%)	64 (10%)	35 (18%)	0.003
M1	354 (43%)	271 (43%)	83 (43%)	0.97
M2	364 (45%)	290 (46%)	74 (39%)	0.055
Treatment characteristics				
Administration of tPA	334 (41%)	270 (43%)	64 (34%)	0.017
Time from admission to groin puncture (min)	81 (55–122)	79 (53–115)	90 (57–231)	<0.001
General anesthesia	522 (66%)	382 (63%)	140 (74%)	0.008
Number of passes	1 (1–3)	1 (1–2)	2 (1–3)	<0.001
TICI 0	55 (7%)	29 (5%)	26 (14%)	<0.001
TICI 1	20 (2%)	11 (2%)	9 (5%)	0.022
TICI 2a	39 (5%)	24 (4%)	15 (8%)	0.024
TICI 2b	268 (33%)	211 (34%)	57 (30%)	0.29
TICI 3	435 (53%)	350 (56%)	85 (44%)	0.004
Successful recanalization (TICI 2b-3)	703 (86%)	561 (90%)	142 (74%)	<0.001
Adverse event during treatment	147 (18%)	96 (15%)	51 (27%)	<0.001
Vasospasm	42 (5%)	34 (5%)	8 (4%)	0.48
Clot migration and embolization	28 (3%)	17 (3%)	11 (6%)	0.045
Dissection or perforation	27 (3%)	14 (2%)	13 (7%)	0.002
Follow-up characteristics				
24-hour NIHSS	3 (1–6)	2 (1–4)	13 (9–19)	<0.001
Groin hematoma after 24 hours	12 (1%)	10 (2%)	2 (1%)	0.57
ICH after 24 hours	72 (9%)	39 (6%)	33 (17%)	<0.001
Recurrent stroke	35 (4%)	22 (4%)	13 (7%)	0.052
Outcome characteristics				
mRS score at 90-day follow-up	1 (0–3)	1 (0–2)	3 (2–5)	<0.001
mRS score 0–1	425 (52%)	387 (62%)	38 (20%)	<0.001
mRS score 0–2	547 (67%)	482 (77%)	65 (34%)	<0.001
mRS score 5–6	111 (14%)	47 (8%)	64 (33%)	<0.001

Data are presented as median (interquartile range) for continuous measures and n (%) for categorical measures. Characteristics were compared by using either Mann–Whitney U test (1) for continuous variables or a chi-square test (2) for categorical variables. Statistical significance: p<0.05.
ASPECTS, Alberta Stroke Program Early CT Score; END, early neurological deterioration; ICA, internal carotid artery; ICH, intracranial hemorrhage; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; TICI, Thrombolysis in Cerebral Infarction; tPA, tissue plasminogen activator.

occurred in 147 (18%) patients including vasospasm, clot migration, and embolization as well as dissection or perforation. The median NIHSS score after 24 hours was 3 (IQR 1–6) and follow-up imaging revealed ICH in 72 (9%) patients. Table 1 displays further baseline, procedural, and outcome characteristics.

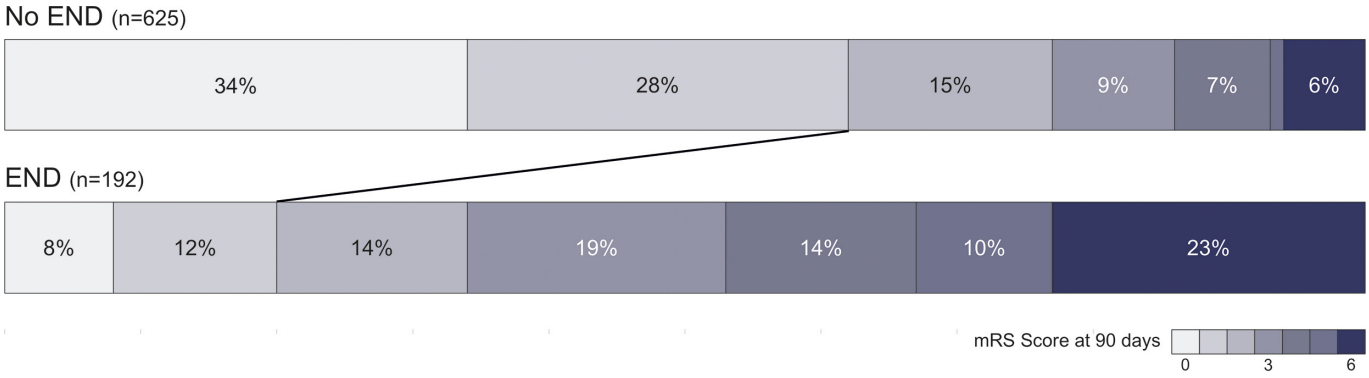


Figure 1 Distribution of the modified Rankin Scale (mRS) at 90 days stratified by early neurological deterioration (END). Patients with END had more often unfavorable functional outcomes at 90 days (mRS 2–6; line; 80% vs 38%; p<0.001).

Primary and secondary outcomes

A total of 192 (24%) patients experienced END. These patients had a higher prestroke mRS score (IQR 0–1 vs 0–0; p=0.002), lower NIHSS score at admission (3 vs 4; p=0.002), and less often atrial fibrillation as a comorbidity (29% vs 37%; p=0.029) compared with patients who did not exhibit END. The intracranial ICA was more often occluded in patients with END (18% vs 10%; p=0.003). Regarding treatment characteristics, patients with END were less often treated with intravenous tPA (34% vs 43%; p=0.017), time from admission to groin puncture was longer (90 min vs 79 min; p=0.017), and they underwent more often general anesthesia (74% vs 63%; p=0.008). There was a higher number of passes (2 vs 1; p<0.001) performed in END patients, successful recanalization was less often achieved (74% vs 90%; p<0.001), and adverse events during endovascular treatment were more frequent (27% vs 15%; p<0.001). On follow-up imaging after 24 hours, patients with END were more often diagnosed with ICH (17% vs 6%; p<0.001). Patients with END were more likely to achieve unfavorable functional outcomes at 90 days compared with those without END (mRS of 2–6: 80% vs 38%; p<0.001, figure 1).

Table 2 displays a subgroup analysis of successfully recanalized patients (TICI 2b-3). In this specific group of patients, END was slightly lower (20%) compared with the overall cohort (24%). Also refer to online supplemental table S1 for more details regarding group differences with respect to long-term functional outcomes. Noteworthy, END occurred more frequently in patients with unfavorable functional outcomes (39% vs 9%; p<0.001).

Independent factors associated with END and unfavorable functional outcomes (mRS of 2–6 90 days after treatment)

In multivariable logistic regression, a higher prestroke mRS score (aOR [95% CI] 1.42 [1.13 to 1.78]; p=0.003), longer time from admission to groin puncture (aOR [95% CI] 1.04 [1.02 to 1.07]; p=0.001), general anesthesia (aOR [95% CI] 1.68 [1.08 to 2.63]; p=0.022), higher number of passes (aOR [95% CI] 1.15 [1.03 to 1.29]; p=0.012), adverse events during treatment (aOR [95% CI] 1.89 [1.19 to 3.01]; p=0.007), and the occurrence of ICH within 24 hours (aOR [95% CI] 3.40 [1.90 to 6.07]; p<0.001) increased the odds of END (figure 2). A higher NIHSS score at admission (aOR [95% CI] 0.83 [0.73 to 0.94]; p=0.004) and successful recanalization (aOR [95% CI] 0.29 [0.17 to 0.50]; p<0.001) decreased the odds of END.

Multivariable logistic regression analysis with unfavorable functional outcome as the dependent variable highlights the strong association between END and unfavorable functional outcomes at 90 days (aOR [95% CI] 7.51 [4.57 to 12.34]; p<0.001). Figure 2 displays further independently associated factors of unfavorable functional outcome.

DISCUSSION

In this multicenter study of 817 AIS-LVO patients who presented with a NIHSS score of <6 and were treated by MT, 192 (24%) patients experienced END and 392 (48.0%) patients had unfavorable functional outcomes after 90 days. The first 24 hours after endovascular therapy proved to be prognostically relevant, as the occurrence of END was found to be an independent factor that is strongly associated with unfavorable long-term functional outcomes. To date, studies on END with regard to minor strokes predominantly focused on patients who were treated by IVT alone where incidences of END range between 13% and 24%.[2 10 14] In our study of patients treated with MT, we observed a comparable incidence and our findings confirm the results of previous research that END is strongly associated with unfavorable long-term functional outcomes.[2 15 16]

The limited inclusion of patients with minor stroke in landmark endovascular trials has left uncertainty as to whether endovascular therapy is beneficial in these patients.[3] Thus, the decision to obtain endovascular treatment is currently based on a careful case-by-case evaluation,[17] pending the results of ongoing prospective studies such as ENDOLOW[4] and MOSTE.[5] To determine the factors that contribute to a negative clinical course after MT, we report patient-specific factors that contribute to END after MT in patients with minor stroke due to LVO.

We observed an independent association between higher prestroke mRS scores and both END and unfavorable functional outcomes. A higher prestroke mRS score has been discussed to indicate previous stroke or comorbidities, which could impede favorable early clinical recovery.[18] We observed that the occlusion of the intracranial ICA was significantly more frequent in patients with END. Equivalently, prior studies found that patients with minor stroke and proximal vessel occlusion sites are at a high risk of developing END.[10 19] However, these studies predominantly focused on patients treated by IVT alone. Failure of early recanalization of a proximal vessel by means of IVT may lead to an extension of ischemic tissue beyond the initial penumbra into the adjacent, previously asymptomatic tissue, ultimately resulting in an increment of NIHSS scores.[20 21] Interestingly in our study, after adjusting for other covariates including recanalization status, we did not find a significant correlation between a proximal vessel occlusion site and END. Yet, we found a

Table 2 Characteristics of patients with successful recanalization (Thrombolysis in Cerebral Infarction (TICI) 2b-3) stratified by early neurological deterioration

Characteristics	Total (n=703)	No END (n=561)	END (n=142)	P-value
Baseline patient characteristics				
Age (years)	72 (62–80)	72 (62–80)	73 (62–81)	0.32
Male sex	355 (50%)	287 (51%)	68 (48%)	0.49
Prestroke mRS	0 (0–0)	0 (0–0)	0 (0–1)	0.041
NIHSS at admission	4 (2–5)	4 (2–5)	3 (1–4)	0.006
Hypertension	529 (75%)	414 (74%)	115 (81%)	0.076
Diabetes mellitus	147 (21%)	109 (19%)	38 (27%)	0.051
Dyslipidemia	317 (45%)	252 (45%)	65 (46%)	0.81
Atrial fibrillation	254 (36%)	211 (38%)	43 (30%)	0.098
Time from symptom onset/last seen well to admission (min)	180 (79–395)	173 (77–380)	199 (87–408)	0.39
Imaging characteristics				
ASPECTS	9 (8–10)	9 (8–10)	10 (8–10)	0.81
Occlusion site				
Left hemispheric stroke	384 (55%)	304 (54%)	80 (56%)	0.65
Intracranial ICA	78 (11%)	54 (10%)	24 (17%)	0.014
M1	308 (44%)	241 (43%)	67 (47%)	0.36
M2	317 (45%)	266 (47%)	51 (36%)	0.014
Treatment characteristics				
Administration of tPA	291 (41%)	243 (43%)	48 (34%)	0.046
Time from admission to groin puncture (min)	80 (54–120)	79 (54–115)	89 (56–240)	0.003
General anesthesia	456 (67%)	347 (64%)	109 (78%)	0.002
Number of passes	1 (1–3)	1 (1–2)	2 (1–3)	<0.001
TICI 2b	268 (38%)	211 (38%)	57 (40%)	0.58
TICI 3	435 (62%)	350 (62%)	85 (60%)	0.58
Adverse event during treatment	118 (17%)	79 (14%)	39 (28%)	<0.001
Vasospasm	39 (6%)	32 (6%)	7 (5%)	0.72
Clot migration and embolization	24 (3%)	16 (3%)	8 (6%)	0.10
Dissection or perforation	18 (3%)	10 (2%)	8 (6%)	0.009
Follow-up characteristics				
24-hour NIHSS	2 (1–6)	2 (1–3)	12 (8–19)	<0.001
Groin hematoma after 24 hours	10 (1%)	9 (2%)	1 (1%)	0.42
ICH after 24 hours	66 (9%)	38 (7%)	28 (20%)	<0.001
Recurrent stroke	30 (4%)	21 (4%)	9 (6%)	0.17
Outcome characteristics				
mRS score at 90-day follow-up	1 (0–3)	1 (0–2)	3 (2–5)	<0.001
mRS score 0–1	395 (56%)	362 (65%)	33 (23%)	<0.001
mRS score 0–2	502 (71%)	446 (80%)	56 (39%)	<0.001
mRS score 5–6	81 (12%)	38 (7%)	43 (30%)	<0.001

Data are presented as median (interquartile range) for continuous measures, and n (%) for categorical measures. Characteristics were compared by using either Mann–Whitney U test (1) for continuous variables or a chi-square test (2) for categorical variables. Statistical significance: p<0.05.
ASPECTS, Alberta Stroke Program Early CT Score; END, early neurological deterioration; ICA, internal carotid artery; ICH, intracranial hemorrhage; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; TICI, Thrombolysis in Cerebral Infarction; tPA, tissue plasminogen activator.

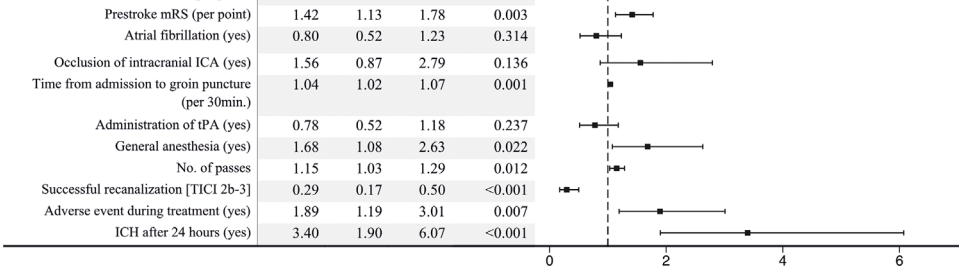
strong and inverse correlation between recanalization success and END. As higher penumbra salvage volume is largely driven by a complete vessel recanalization and restored blood supply to downstream brain parenchyma, successful recanalization prevents infarct progression and may therefore be protective with respect to an early increase in NIHSS scores.[21–23]

Numerous studies have evaluated whether local anesthesia, conscious sedation, or general anesthesia serves patients best in endovascular therapy. However, there is currently no definitive recommendation as to which procedure is most appropriate for respective subtypes of stroke patients.[24] Research suggests that patients with a baseline NIHSS of ≥6 are at an increased risk of END when administered general anesthesia.[25 26] Our study affirms these findings for patients with minor stroke. In patients presenting with LVO and minor stroke symptoms it is likely that cerebral perfusion is sustained to a certain extent by favorable

A END

Independent variables	Adjusted Odds Ratio	95% Conf. Interval		p-value
NIHSS at admission (per point)	0.83	0.73	0.94	0.004
Prestroke mRS (per point)	1.42	1.13	1.78	0.003
Atrial fibrillation (yes)	0.80	0.52	1.23	0.314
Occlusion of intracranial ICA (yes)	1.56	0.87	2.79	0.136
Time from admission to groin puncture (per 30min.)	1.04	1.02	1.07	0.001
Administration of tPA (yes)	0.78	0.52	1.18	0.237
General anesthesia (yes)	1.68	1.08	2.63	0.022
No. of passes	1.15	1.03	1.29	0.012
Successful recanalization [TICI 2b-3]	0.29	0.17	0.50	<0.001
Adverse event during treatment (yes)	1.89	1.19	3.01	0.007
ICH after 24 hours (yes)	3.40	1.90	6.07	<0.001

Odds diagram



B Unfavorable functional outcome (mRS90 ≥2)

Independent variables	Adjusted Odds Ratio	95% Conf. Interval		p-value
Age (per year)	1.05	1.03	1.06	<0.001
Prestroke mRS (per point)	2.78	2.03	3.82	<0.001
NIHSS at admission (per point)	1.24	1.09	1.40	0.001
Diabetes mellitus (per point)	1.20	0.76	1.87	0.436
Time from symptom onset/last seen well to admission (per 30 min.)	1.02	1.01	1.04	0.010
General anesthesia (yes)	1.60	1.08	2.37	0.020
Administration of tPA (yes)	0.82	0.55	1.22	0.324
Successful recanalization [TICI 2b-3]	0.26	0.14	0.46	<0.001
END (yes)	7.51	4.57	12.34	<0.001
ICH after 24 hours (yes)	1.91	1.00	3.63	0.049

Odds diagram

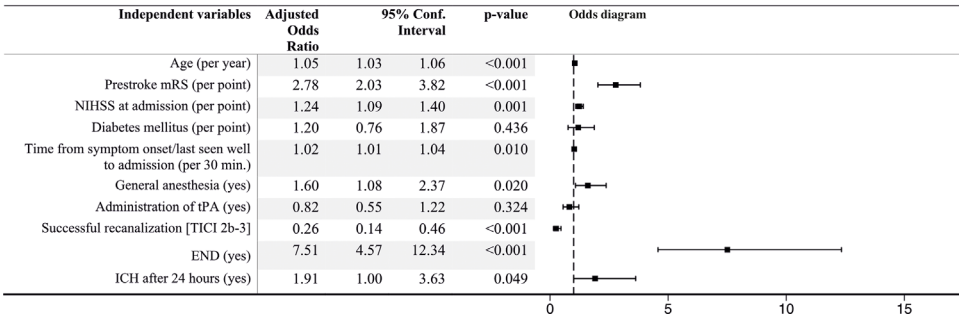


Figure 2 Multivariable logistic regression analyses with respective odds diagrams assessing independent factors of (A) early neurological deterioration and (B) unfavorable functional outcome (mRS≥2) in patients with minor stroke. Model A included 705 patients while Model B included 708 patients. END, early neurological deterioration; ICA, internal carotid artery; ICH, intracranial hemorrhage; mRS, modified Rankin Scale; mRS90, modified Rankin Scale at 90 days' follow-up; NIHSS, National Institutes of Health Stroke Scale; TICI, Thrombolysis in Cerebral Infarction; tPA, tissue plasminogen activator.

collaterals. During general anesthesia, a (transient) reduction in blood pressure may occur, which may result in an exhaustion of collateral supply, leading to infarct progression and ultimately early clinical worsening.[27 28] However, it is also important to consider a potential selection bias inherently linked to the retrospective design of our study: Interventionalists might select general anesthesia for patients whom they perceive as having a higher risk of complications. This decision may have been influenced by confounding factors, such as a deterioration of the patient's clinical status between admission and transport to the angiography unit, or a necessitation of general anesthesia due to other comorbidities, which per se might indicate poor prognosis. It is thus imperative to emphasize that the findings of this study do not justify any assertion regarding the superiority of one specific anesthetic regimen. General anesthesia may even derive benefit in patients with minor stroke who exhibit distal vessel occlusion that requires demanding catheter navigation and a calm patient. Consequently, the selection of an anesthetic regimen should be based on an assessment of patient-specific characteristics, to reduce the risk of adverse events, given the uncertainty of whether MT is superior to best medical management alone.

A higher number of passes during MT required to achieve successful recanalization was identified as an independent predictor of END in our investigation. This was also found for patients with a baseline NIHSS of ≥6.[25] The correlation between an increasing number of passes and END may be explained by higher probabilities of vessel wall injury with every pass, resulting in an endothelial dysfunction and clot fragmentation.[29] Presently, there is no established threshold indicating the number of passes beyond which the procedure should be discontinued. Future research is warranted to elucidate optimal thresholds for patients with minor stroke.

When evaluating patients with minor stroke for MT it is crucial to consider safety concerns and (peri-)procedural risks inherently linked to endovascular treatment.[17] Complications may occur and may foster embolism to new vascular territories or ICH.[30] A recently published meta-analysis of 5190 patients with minor stroke exhibits a three-fold increased risk of symptomatic ICH when patients were treated by MT.[1] In our study, both adverse events during treatment and the occurrence of ICH on 24 hours' follow-up imaging were independently associated with END.

As MT evolves and devices improve, new indications and frontiers are constantly being discussed (e.g., treatment of medium vessel occlusions and low NIHSS patients). Conversely, developments in medical management (for instance the advanced use of tenecteplase) and patient monitoring also need to be taken into account when deciding whether or not to perform MT, as in our context in patients with minor stroke. Eventually, upcoming prospective randomized trials will shed new light on proper patient selection and treatment management of patients with minor stroke for whom MT may be beneficial or for whom the risks outweigh the benefits. Our retrospective, multicenter study provides valuable additional information about the clinical course of patients with minor stroke, and we present various factors that should advocate caution as to which patients may be at risk for END after MT treatment.

LIMITATIONS

This study is subject to limitations. The study's retrospective and nonrandomized design potentially introduces selection bias,

diminishing the overall generalizability of the primary findings. Additionally, all clinical parameters, including mRS, occlusion site, and NIHSS, were reported at individual sites, which may be susceptible to site-related bias resulting in limited interrater reliability. Due to the retrospective nature of our study, we encountered instances of missing data and therefore cannot detail all adverse events during treatment, apart from vasospasm, clot migration, embolization, and dissection or perforation. Comorbidities that may occur early in the clinical course, such as infectious diseases or cardiorespiratory adverse events, which could increase the NIHSS score, were not documented. Regrettably, our data do not provide information on intracranial atherosclerosis as stroke etiology, which may be overrepresented in patients with minor stroke and LVO. Our study does not incorporate information regarding thrombus length or collateral parameters, both of which have been found to influence END in previous studies.[10]

CONCLUSIONS

Early neurological deterioration, defined by a NIHSS score increase of ≥4 within the first 24 hours after MT, occurred in almost a quarter of patients with minor stroke undergoing MT. These patients had twice the odds of experiencing unfavorable functional outcomes. Factors associated with END include a higher prestroke mRS score, general anesthesia, higher number of passes during MT to achieve successful recanalization, and the occurrence of adverse events during treatment.

X Laurens Winkelmeier @WinkelmeierMD and Jens Fiehler @Fie0815

Acknowledgements The authors acknowledge the German Stroke Registry (GSR) investigators and the GSR steering committee. See online supplemental figure S2.

Contributors CH, LW, JF, GT, and TDF developed the study concept and design. CH, FF, MS, HK, CT, PS, and GB acquired, analyzed, and interpreted the data. CH, LW, GB, GT, and TDF drafted the manuscript. The project was supervised by JF, GT, and TDF. CH is the guarantor for this article. All authors have agreed to the conditions of authorship and endorse the final version of the article.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests FF reported receiving personal fees from Eppdata GmbH outside the submitted work. HK reported an ownership stake in Eppdata GmbH and compensation from Eppdata GmbH for consultant services outside the submitted work. GB reported receiving compensation as a speaker from Balt and personal fees from Eppdata GmbH outside the submitted work. CT reported receiving personal fees from Eppdata GmbH outside the submitted work. GT reported receiving personal fees from Acandis, Alexion, Amarin, Bayer, Boehringer Ingelheim, Bristol Myers Squibb/Pfizer, Daiichi Sankyo, Portola, and Stryker outside the submitted work. JF reported an ownership stake in Eppdata GmbH and grants and personal fees from Acandis, Cerenovus, MicroVention, Medtronic, Stryker, Phenox, and grants from Route 92 outside the submitted work. TDF reported grants from the German Research Foundation (DFG) (Project Number: 411621970) and personal fees from Eppdata GmbH outside the submitted work.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and approval for the German Stroke Registry-Endovascular Treatment (GSR-ET) was granted by the ethics committee at Ludwig Maximilian University, Munich, Germany (689-15). Local ethics committees granted approval for all participating sites in accordance with their respective local regulations. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iDs
Christian Heitkamp http://orcid.org/0000-0002-8988-0918
Laurens Winkelmeier http://orcid.org/0000-0002-9103-5983
Fabian Flottmann http://orcid.org/0000-0001-8358-8089
Helge Kniep http://orcid.org/0000-0001-5258-2370
Christian Thaler http://orcid.org/0000-0002-7102-9316
Jens Fiehler http://orcid.org/0000-0001-8533-7478
Tobias D Faizy http://orcid.org/0000-0002-1631-2020

REFERENCES

1 Safouris A, Palaiodimou L, Nardai S, *et al*. Medical management versus endovascular treatment for large-vessel occlusion anterior circulation stroke with low NIHSS. *Stroke* 2023;54:2265–75.
2 Saleem Y, Nogueira RG, Rodrigues GM, *et al*. Acute neurological deterioration in large vessel occlusions and mild symptoms managed medically. *Stroke* 2020;51:1428–34.
3 Goyal M, Menon BK, van Zwam WH, *et al*. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* 2016;387:1723–31.
4 Nogueira RG. Endovascular therapy for low NIHSS ischemic strokes (ENDOLOW). 2022. Available: https://clinicaltrials.gov/ct2/show/NCT04167527
5 University Hospital, Montpellier. Evaluation of acute mechanical revascularization in large vessel occlusion stroke with minor symptoms (NIHSS<6) in patients last seen well < 24 hours. 2022. Available: https://clinicaltrials.gov/ct2/show/NCT03796468
6 Feil K, Matusevicius M, Herzberg M, *et al*. Minor stroke in large vessel occlusion: a matched analysis of patients from the German Stroke Registry–Endovascular Treatment (GSR–ET) and patients from the Safe Implementation of Treatments in Stroke–International Stroke Thrombolysis Register (SITS–ISTR). *Eur J Neurol* 2022;29:1619–29.
7 Kniep H, Meyer L, Bechstein M, *et al*. How much of the thrombectomy related improvement in functional outcome is already apparent at 24 hours and at hospital discharge *Stroke* 2022;53:2828–37.
8 Heitkamp C, Winkelmeier L, Heit JJ, *et al*. Early neurological deterioration in patients with acute ischemic stroke is linked to unfavorable cerebral venous outflow. *Eur Stroke J* 2024;9:162–71.
9 Volny O, Zerna C, Tomek A, *et al*. Thrombectomy vs medical management in low NIHSS acute anterior circulation stroke. *Neurology* 2020;95:e3364–72.
10 Seners P, Ben Hassen W, Lapergue B, *et al*. Prediction of early neurological deterioration in individuals with minor stroke and large vessel occlusion intended for intravenous thrombolysis alone. *JAMA Neurol* 2021;78:321–8.
11 Broccolini A, Brunetti V, Colò F, *et al*. Early neurological deterioration in patients with minor stroke due to isolated M2 occlusion undergoing medical management: a retrospective multicenter study. *J Neurointerv Surg* 2024;16:38–44.
12 Alegiani AC, Dorn F, Herzberg M, *et al*. Systematic evaluation of stroke thrombectomy in clinical practice: the German Stroke Registry Endovascular Treatment. *Int J Stroke* 2019;14:372–80.
13 Seners P, Arquizan C, Fontaine L, *et al*. Perfusion imaging and clinical outcome in acute minor stroke with large vessel occlusion. *Stroke* 2022;53:3429–38.
14 Kim J-T, Heo S-H, Yoon W, *et al*. Clinical outcomes of patients with acute minor stroke receiving rescue IA therapy following early neurological deterioration. *J Neurointerv Surg* 2016;8:461–5.
15 Nagel S, Bouslama M, Krause LU, *et al*. Mechanical thrombectomy in patients with milder strokes and large vessel occlusions. *Stroke* 2018;49:2391–7.
16 Pfaff J, Herweh C, Pham M, *et al*. Mechanical thrombectomy in patients with acute ischemic stroke and lower NIHSS scores: recanalization rates, periprocedural complications, and clinical outcome. *AJNR Am J Neuroradiol* 2016;37:2066–71.
17 Seners P, Cereda CW. Thrombectomy in stroke with a large vessel occlusion and mild symptoms: "striving to better, oft we mar what's well". *Stroke* 2023;54:2276–8.
18 Kniep H, Meyer L, Broocks G, *et al*. Thrombectomy for M2 occlusions: predictors of successful and futile recanalization. *Stroke* 2023;54:2002–12.
19 Mazya MV, Cooray C, Lees KR, *et al*. Minor stroke due to large artery occlusion. When is intravenous thrombolysis not enough? Results from the SITS International Stroke Thrombolysis Register. *Eur Stroke J* 2018;3:29–38.
20 Fu J, Zhou Y, Li Q, *et al*. Perfusion changes of unexplained early neurological deterioration after reperfusion therapy. *Transl Stroke Res* 2020;11:195–203.
21 Kim J-M, Bae J-H, Park K-Y, *et al*. Incidence and mechanism of early neurological deterioration after endovascular thrombectomy. *J Neurol* 2019;266:609–15.
22 Feyen L, Katoh M, Haage P, *et al*. Thrombectomy of mild stroke. *Clin Neuroradiol* 2023;33:687–94.

23 Winkelmeier L, Faizy TD, Brekenfeld C, *et al*. Comparison of thrombolysis in cerebral infarction (TICI) 2B and TICI 3 reperfusion in endovascular therapy for large ischemic anterior circulation strokes. *J Neurointerv Surg* 2023. 10.1136/jnis-2023-020724. [Epub ahead of print 30 Sep 2023].
24 Goyal N, Malhotra K, Ishfaq MF, *et al*. Current evidence for anesthesia management during endovascular stroke therapy: updated systematic review and meta-analysis. *J Neurointerv Surg* 2019;11:107–13.
25 Girot J-B, Richard S, Gariel F, *et al*. Predictors of unexplained early neurological deterioration after endovascular treatment for acute ischemic stroke. *Stroke* 2020;51:2943–50.
26 Sun D, Tong X, Huo X, *et al*. Unexplained early neurological deterioration after endovascular treatment for acute large vessel occlusion: incidence, predictors, and clinical impact: data from ANGEL-ACT Registry. *J Neurointerv Surg* 2022;14:875–80.
27 Petersen NH, Ortega-Gutierrez S, Wang A, *et al*. Decreases in blood pressure during thrombectomy are associated with larger infarct volumes and worse functional outcome. *Stroke* 2019;50:1797–804.
28 Crosby G, Muir KW. Anesthesia and neurologic outcome of endovascular therapy in acute ischemic stroke. *Neurology* 2016;87:648–9.
29 Winkelmeier L, Faizy TD, Broocks G, *et al*. Association between recanalization attempts and functional outcome after thrombectomy for large ischemic stroke. *Stroke* 2023;54:2304–12.
30 Happi Ngankou E, Gory B, Marnat G, *et al*. Thrombectomy complications in large vessel occlusions: incidence, predictors, and clinical impact in the ETIS Registry. *Stroke* 2021;52:e764–8.