



Universiteit
Leiden
The Netherlands

Prognostic value of thrombus volume and interaction with first-line endovascular treatment device choice

Voorst, H. van; Bruggeman, A.A.E.; Andriessen, J.; Hoving, J.W.; Konduri, P.R.; Yang, W.J.; ... ; Majoie, C.B.L.M.

Citation

Voorst, H. van, Bruggeman, A. A. E., Andriessen, J., Hoving, J. W., Konduri, P. R., Yang, W. J., ... Majoie, C. B. L. M. (2023). Prognostic value of thrombus volume and interaction with first-line endovascular treatment device choice. *Stroke*, 54(4), 1056-1065.
doi:10.1161/STROKEAHA.122.041606

Version: Publisher's Version
License: [Creative Commons CC BY 4.0 license](https://creativecommons.org/licenses/by/4.0/)
Downloaded from:

Note: To cite this publication please use the final published version (if applicable).

CLINICAL AND POPULATION SCIENCES

Prognostic Value of Thrombus Volume and Interaction With First-Line Endovascular Treatment Device Choice

Henk van Voorst¹ MD; Agnetha A.E. Bruggeman¹ MD, PhD; Jurr Andriessen¹ MD; Jan W. Hoving¹ MD; Praneeta R. Konduri¹ MSc; Wenjin Yang¹ MD; Manon Kappelhof¹ MD, PhD; Nerea, Arrarte Terreros¹ PhD; Yvo B.W.E.M. Roos¹ MD, PhD; Wim H. van Zwam¹ MD, PhD; Aad van der Lugt¹ MD, PhD; Anouk van der Hoorn¹ MD, PhD; Jelis Boiten, MD, PhD; Stefan Roosendaal¹ MD, PhD; Sjoerd Jenniskens¹ MD, PhD; Matthan W.A. Caan¹ PhD; Henk A. Marquering¹ PhD; Bart J. Emmer¹ MD, PhD; Charles B.L.M. Majoie¹ MD, PhD; on behalf of the MR CLEAN Registry Investigators*

BACKGROUND: A larger thrombus in patients with acute ischemic stroke might result in more complex endovascular treatment procedures, resulting in poorer patient outcomes. Current evidence on thrombus volume and length related to procedural and functional outcomes remains contradicting. This study aimed to assess the prognostic value of thrombus volume and thrombus length and whether this relationship differs between first-line stent retrievers and aspiration devices for endovascular treatment.

METHODS: In this multicenter retrospective cohort study, 670 of 3279 patients from the MR CLEAN Registry (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) for endovascularly treated large vessel occlusions were included. Thrombus volume (0.1 mL) and length (0.1 mm) based on manual segmentations and measurements were related to reperfusion grade (expanded Treatment in Cerebral Infarction score) after endovascular treatment, the number of retrieval attempts, symptomatic intracranial hemorrhage, and a shift for functional outcome at 90 days measured with the reverted ordinal modified Rankin Scale (odds ratio >1 implies a favorable outcome). Univariable and multivariable linear and logistic regression were used to report common odds ratios (cORs)/adjusted cOR and regression coefficients (B/aB) with 95% CIs. Furthermore, a multiplicative interaction term was used to analyze the relationship between first-line device choice, stent retrievers versus aspiration device, thrombus volume, and outcomes.

RESULTS: Thrombus volume was associated with functional outcome (adjusted cOR, 0.83 [95% CI, 0.71–0.97]) and number of retrieval attempts (aB, 0.16 [95% CI, 0.16–0.28]) but not with the other outcome measures. Thrombus length was only associated with functional independence (adjusted cOR, 0.45 [95% CI, 0.24–0.85]). Patients with more voluminous thrombi had worse functional outcomes if endovascular treatment was based on first-line stent retrievers (interaction cOR, 0.67 [95% CI, 0.50–0.89]; $P=0.005$; adjusted cOR, 0.74 [95% CI, 0.55–1.0]; $P=0.04$).

CONCLUSIONS: In this study, patients with a more voluminous thrombus required more endovascular thrombus retrieval attempts and had a worse functional outcome. Patients with a lengthier thrombus were less likely to achieve functional independence at 90 days. For more voluminous thrombi, first-line stent retrieval compared with first-line aspiration might be associated with worse functional outcome.

GRAPHIC ABSTRACT: A [graphic abstract](#) is available for this article.

Key Words: functional status ■ ischemic stroke ■ prognosis ■ stents ■ thrombosis

Correspondence to: Henk van Voorst, MD, Department of Radiology and Nuclear Medicine, Amsterdam University Medical Center, University of Amsterdam, Office L0147, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands. Email h.vanvoorst@amsterdamumc.nl

*A list of the MR CLEAN Registry investigators is given in the Appendix.

Supplemental Material is available at <https://www.ahajournals.org/doi/suppl/10.1161/STROKEAHA.122.041606>.

For Sources of Funding and Disclosures, see page 1063.

© 2023 American Heart Association, Inc.

Stroke is available at www.ahajournals.org/journal/str

Nonstandard Abbreviations and Acronyms

AD	aspiration device
cOR	common odds ratio
CT	computed tomography
CTA	computed tomography angiography
eTICI	expanded Treatment in Cerebral Infarction
EVT	endovascular treatment
FAR	first-attempt reperfusion
IQR	interquartile range
LL	log-likelihood
MR CLEAN	Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands
mRS	modified Rankin Scale
sICH	symptomatic intracranial hemorrhage
SR	stent retriever

The size of a thrombus occluding an artery in acute ischemic stroke has been suggested as a prognostic marker for patients with a large vessel occlusion receiving endovascular treatment (EVT) as it could result in a more complex and prolonged procedure.^{1–9} Moreover, an EVT procedure requiring more retrieval attempts or achieving suboptimal reperfusion is associated with more ischemic damage,¹⁰ infarct growth,¹¹ remote embolization,¹¹ and complications such as intracranial hemorrhages,¹² negatively affecting patient functional outcomes. If thrombus volume or length is associated with any of these procedural outcomes, it might be possible to improve patient care by altering EVT strategies or optimizing device choices.

Thrombus length was associated with worse functional outcomes in some studies,^{1,3} whereas in other studies, no association was found.^{4,5} Similarly, 3 studies found that thrombus volume was associated with less successful reperfusion, more retrieval attempts, and a lower first-attempt reperfusion (FAR) effect,^{2,6,9} whereas 2 other studies did not find any association with procedural or patient outcomes.^{7,8} Thus, the prognostic value of thrombus volume remains a matter of debate. Additionally, it remains unclear whether thrombus volume has a stronger prognostic value than thrombus length. Furthermore, current evidence suggests that similar patient outcomes can be achieved using either a stent retriever (SR) or aspiration device (AD).^{13–15} It is unclear whether the effect of thrombus volume on procedural and functional outcome differs between first-line EVT with an SR or AD.

We aimed to study the prognostic value of thrombus volume as an alternative to thrombus length regarding

procedural and functional outcomes. Furthermore, we aimed to determine whether the associations between thrombus volume and procedural and functional outcomes differ between SR- and AD-based first-line EVT.

METHODS

Study Design and Patient Inclusion

We used data from patients included in the MR CLEAN Registry (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; March 18, 2014, to November 1, 2017). The MR CLEAN Registry was a national, multicenter, observational prospective registry including patients treated with EVT from 17 stroke centers in the Netherlands after the completion of the MR CLEAN trial.¹⁶ For this study, patients from the MR CLEAN Registry parts 1 and 2 were considered; inclusion dates ranged between March 2014 and January 2017.¹⁶ The Central Medical Ethics Committee of Erasmus MC, Rotterdam, the Netherlands, evaluated the study protocol of the MR CLEAN Registry and granted permission to carry out the study as a registry (MEC-2014-235). We conducted this study in line with the Strengthening the Reporting of Observational Studies in Epidemiology guideline.¹⁷ Data will be made available upon reasonable request while adhering to privacy regulations.

Patients aged ≥ 18 years with an intracranial vessel occlusion in the anterior circulation—internal carotid artery, internal carotid artery terminus, middle cerebral artery (M1/M2/M3), or anterior cerebral artery (A1/A2)—who received EVT within 6.5 hours after stroke onset were included. Furthermore, for the current study, patients were required to have a baseline noncontrast computed tomography (CT) and CT angiography (CTA) available with a slice thickness ≤ 1.0 mm. Patients were excluded if spontaneous reperfusion was visible on digital subtraction angiography before EVT, the occlusion site could not be reached for EVT, data regarding primary device choice were missing, or if a different first-line approach than SR or AD was used. The EVT device choice was at the discretion of the treating neurointerventionist. Patients received intravenous alteplase (0.9 mg/kg) before EVT if they presented < 4.5 hours after stroke onset and had no contraindications according to the European Stroke Organization guidelines.¹⁸ Since our database did not include accurate data for secondary device choice or combined device use, all treatment approach analyses consider the first-line device choice. Patients treated with a combined approach, aspiration on one of the catheters during SR EVT, were included in the SR group.

Imaging Assessment

All baseline imaging was assessed by an independent central core laboratory of neuroradiologists who were blinded for all clinical data except the occlusion side. The following imaging parameters were reported: occluded arterial segment, Alberta Stroke Program Early CT Score, CTA collateral score, reperfusion grade on the final digital subtraction angiography (expanded Treatment in Cerebral Infarction [eTICI] score), and the presence of symptomatic intracranial hemorrhage (sICH).

Thrombus Measurements

Thrombi were segmented manually by an expert dedicated core laboratory (H.v.V., A.A.E.B., W.Y., J.A., P.R.K., N.A.T., J.W.H., M.K., and J.B.) using 3-dimensional imaging software ITK-SNAP¹⁹ with coregistered baseline noncontrast CT and CTA using Elastix.²⁰ The data processing and segmentation methods have been described previously.⁹ In short, thrombi were segmented considering both CTA and noncontrast CT in axial, coronal, and sagittal views (Figure 1). Patients were excluded if the visibility of the thrombus was poor due to very poor or uncorrectable alignment of CTA and noncontrast CT, severe movement, or beam hardening artifacts, an incomplete field of view on CT imaging resulting in incomplete thrombus visibility, excessive noise leading to very-poor-quality imaging, no thrombus present on imaging according to the core laboratory, and no visible hyperdense artery sign in combination with an absent collateral filling or insufficient CTA contrast opacification. In cases that were difficult to segment, a consensus reading under the supervision of C.B.L.M.M. or B.J.E. was held. Following previous work by Dutra et al,³ we excluded patients with a thrombus restricted to the petrous, cavernous, and clinoid segments of the internal carotid artery because volume measurement in these segments is less reliable due to blooming artifacts of the surrounding bone. Thrombus length, density, and perviousness were measured and reported previously.^{3,21}

Outcome Measures and Statistical Analyses

Our primary outcome was functional outcome as measured with the ordinal modified Rankin Scale (mRS) 90 days after acute ischemic stroke. Ordinal mRS values were inverted and studied with a shift analysis in line with previous studies of the MR CLEAN Registry.^{16,22} Using an inverted mRS results in odds ratios below 1 for worse functional outcome. Our secondary outcome measures were functional independence (mRS score, ≤ 2), ordinal eTICI post-EVT, successful reperfusion post-EVT (eTICI score, $\geq 2B$), FAR, sICH, and the number of thrombus retrieval attempts. Odds ratios and slopes with 95% CIs from logistic and linear regression models were reported for both univariable unadjusted (common odds ratio [cOR]/B) and multivariable adjusted analysis (adjusted cOR/aB). Multivariable analyses were used to statistically adjust for potential confounders. The following variables were used for adjustments: age, sex, prestroke mRS, collateral score, baseline National Institutes of Health Stroke Scale, Alberta Stroke Program Early CT Score, first-line EVT device (SR versus AD), administration of intravenous thrombolysis, time from symptom onset to arterial puncture, occlusion location, thrombus perviousness,²³ and

the number of months since start of the MR CLEAN Registry to correct for the improving outcomes of EVT through time.

First, since thrombus length is easier and faster to measure manually than volume, we compared the prognostic relationship of thrombus length and volume with the outcome measures. Second, we evaluated the interaction of thrombus volume with first-line EVT device on the outcome measures by introducing a multiplicative interaction term in the regression models. To assess whether device choice modified the relationship of thrombus volume with outcome, thrombus volume and device choice were also added as independent variables to the models with the multiplicative interaction terms.²⁴ Log-likelihood (LL) values were reported to describe and compare the goodness of fit of the (logistic) regression models to the data. Based on the LL, we compare models using thrombus volume and thrombus length and models with (thrombus volume–device choice) multiplicative interaction term to those without.

Baseline characteristics were described with median and interquartile range (IQR) or mean and SD for non-normally and normally distributed variables, respectively. Mann-Whitney *U* test, independent *t* test, χ^2 test, Kruskal-Wallis test, and ANOVA test were used to compare the baseline characteristics between our study cohort and the remainder of the MR CLEAN Registry population. Multiple imputation considering all the variables used for statistical adjustment, all the studied variables, and outcome measures were used for handling missing values in the regression analyses. Multiple imputation was performed using the R package mice. We imputed 5 data sets and used 4 knots for modeling nonlinear relationships. All statistical analyses were performed in R (R Statistical Software, V3.6.3, R: a language and environment for statistical computing; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Inclusion and Baseline Characteristics

Of all 3279 patients in the MR CLEAN Registry, 670 were included in this study (Figure 2). Table 1 compares the baseline characteristics of the included patients to those of the remainder of the MR CLEAN Registry and the first-line AD and SR groups. Table S1 describes the thrombus volume per occlusion location. Patients included in the current study had a lower collateral score, were less often treated with thrombolysis before EVT (71.9% versus 75.8%), were included earlier in the MR CLEAN Registry (months since the start of registry: median, 28

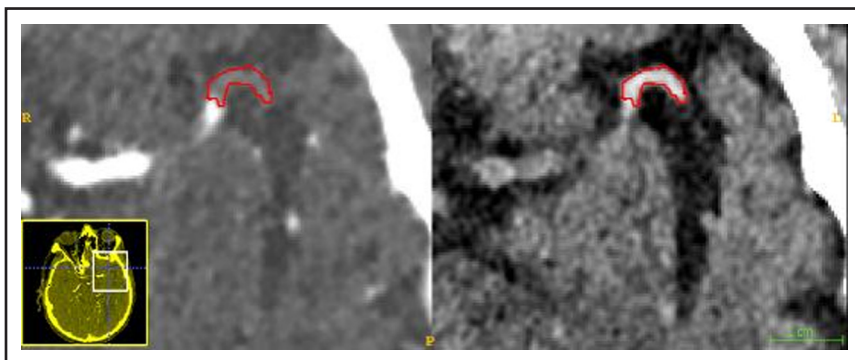


Figure 1. Example of a patient with a left middle cerebral artery occlusion.

A combination of the hyperdense artery sign on noncontrast computed tomography (right) and contrast filling defect on computed tomography angiography (left) to define the proximal thrombus border was used.

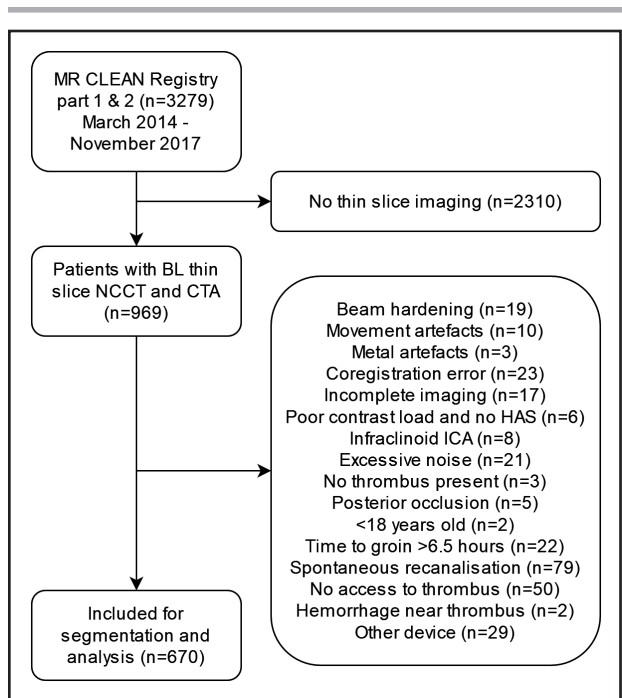


Figure 2. Inclusion flowchart.

Thin-slice imaging was defined as ≤ 1.0 mm slice thickness. BL indicates baseline; CTA, computed tomography angiography; HAS, hyper dense artery sign; ICA, internal carotid artery; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; and NCCT, noncontrast computed tomography.

[IQR, 20–36] versus 30 [IQR, 21–38]), were treated faster (minutes from onset to groin puncture: mean, 194 [SD, 78] versus 219 [SD, 105]), and had less thrombus retrieval attempts (median, 2 [IQR, 1–3] versus 1 [IQR, 1–3]). Compared with the first-line AD group, patients in the SR group were included earlier (months since start: median, 27 [IQR, 19–35] versus 34 [IQR, 23–38]) and had a lower thrombus perviousness (median, 3 [IQR, 1–10] versus 7 [IQR, 0–14]) with denser thrombi (Hounsfield units: mean, 50 [SD, 10] versus 47 [SD, 11]).

Prognostic Value of Thrombus Volume and Length

Table 2 describes the associations of thrombus volume and length with the outcome measures. Thrombus volume was associated with worse functional outcome (cOR, 0.80 [95% CI, 0.71–0.91]; acOR, 0.83 [95% CI, 0.71–0.97]), whereas thrombus length was not (cOR, 0.87 [95% CI, 0.75–1.01]). Thrombus length was only associated with a lower probability of functional independence (mRS score ≤ 2 acOR, 0.45 [95% CI, 0.24–0.85]) and not with any of the other outcome measures. Thrombus volume was associated with a lower probability of functional independence (mRS score ≤ 2 acOR, 0.78 [95% CI, 0.64–0.96]) and number of retrieval attempts (aB, 0.16 [95% CI, 0.04–0.28]). The

statistically significant relationship between thrombus volume and a lower probability of FAR was only present in the unadjusted model but was absent after adjustment for confounders (cOR, 0.79 [95% CI, 0.67–0.94]; acOR, 0.86 [95% CI, 0.71–1.05]). Specifically, the adjustment variable months since start of the registry had a strong relationship with an improved probability of FAR (acOR, 1.02 [95% CI, 1.01–1.04]; $P=0.008$), possibly explaining part of the initially observed relation with thrombus volume. The LL was higher for all (logistic) regression models with significant associations that used thrombus volume compared with thrombus length as an independent variable except for the models using functional independence (mRS score ≤ 2): thrombus volume versus length, unadjusted model LL: mRS, 11.66 versus 7.13; mRS score ≤ 2 , 10.87 versus 11.22; FAR, 8.41 versus 0.25; number of retrieval attempts, 16.43 versus 2.96; adjusted model LL: mRS, 257.98 versus 256.99; mRS score ≤ 2 , 201.79 versus 204.70; FAR, 41.77 versus 39.46; number of retrieval attempts, 50.44 versus 43.60. Tables S2 through S4 contain more extensive goodness-of-fit measures.

Thrombus Volume and Device Choice

Table 3 describes the results from unadjusted and adjusted (logistic) regression models with the multiplicative interaction term (device choice [SR, 1 versus AD, 0] \times thrombus volume). The multiplicative interaction term of first-line device choice and thrombus volume was significantly associated with worse functional outcome (mRS: cOR, 0.67 [95% CI, 0.5–0.89]; $P=0.005$; acOR, 0.74 [95% CI, 0.55–1.0]; $P=0.04$) but not with any other outcome measure. The ordinal logistic regression models for functional outcome had a higher LL when the interaction term was added (with interaction term versus without mRS models: unadjusted LL, 19.84 versus 11.60; adjusted LL, 262.11 versus 257.98). This indicates that patients with more voluminous thrombi had worse functional outcomes when an SR was used as first-line EVT device compared with an AD.

Results for the (logistic) regression models including a multiplicative interaction term of device choice and volume with each outcome measure are presented for the unadjusted (cOR/B) and the adjusted (acOR/aB) analyses. The reference device choice was an AD; results represent the effect of SR multiplied by thrombus volume per 0.1 mL (cOR, common odds ratio in unadjusted analysis; B, slope of the regression for continuous outcome in unadjusted analysis; acOR, adjusted common odds ratio after adjustment for confounders; aB, slope of the regression line after adjustment for confounders). Odds ratios are reported for the first 6 rows; the slope of the regression line is reported for number of attempts since it is a continuous outcome.

Table 1. Baseline Characteristics

	Remainder MR CLEAN registry	Included cohort (AD+SR)	P value	AD	SR	P value
No. of patients	2609	670		198	472	
Baseline characteristics						
Age, y; mean (SD)	69 (14)	68 (15)	0.33	68 (165)	69 (15)	0.82
Sex, n (%)			0.86			0.30
Women	1257 (48.2%)	326 (48.7%)		103 (52.0%)	223 (47.2%)	
Men	1352 (51.8%)	344 (51.3%)		95 (48.0%)	249 (52.8%)	
History of diabetes, n (%)			0.59			0.11
No	2165 (83.5%)	558 (84.4%)		172 (88.2%)	386 (82.8%)	
Yes	429 (16.5%)	103 (15.6%)		23 (11.8%)	80 (17.2%)	
Prestroke mRS score, n (%)			0.87			0.37
0	1730 (67.7%)	440 (67.7%)		124 (66.0%)	316 (68.4%)	
1	343 (13.4%)	81 (12.5%)		19 (10.1%)	62 (13.4%)	
2	192 (7.5%)	49 (7.5%)		18 (9.6%)	31 (6.7%)	
3	163 (6.4%)	48 (7.4%)		14 (7.4%)	34 (7.4%)	
4	105 (4.1%)	28 (4.3%)		12 (6.4%)	16 (3.5%)	
5	24 (0.9%)	4 (0.6%)		1 (0.5%)	3 (0.6%)	
Systolic blood pressure, mm Hg; mean (SD)	150 (25)	149 (24)	0.45	150 (24)	148 (24)	0.54
Baseline NIHSS, median (IQR)	16 (11 to 19)	16 (11 to 20)	0.30	17 (11 to 20)	15 (11 to 19)	0.18
Baseline ASPECTS, median (IQR)	9 (7 to 10)	9 (7 to 10)	0.16	9 (7 to 10)	9 (7 to 10)	0.76
Collateral score, n (%)			0.03			0.65
0	146 (6.0%)	41 (6.3%)		14 (7.3%)	27 (5.9%)	
1	857 (35.4%)	243 (37.4%)		75 (39.1%)	168 (36.7%)	
2	923 (38.1%)	267 (41.1%)		72 (37.5%)	195 (42.6%)	
3	496 (20.5%)	99 (15.2%)		31 (16.1%)	68 (14.8%)	
Occlusion location, n (%)			0.63			0.09
ICA	135 (5.5%)	26 (4.0%)		3 (1.6%)	23 (5.0%)	
ICA-T	527 (21.4%)	136 (20.9%)		42 (21.9%)	94 (20.4%)	
M1	1428 (57.9%)	387 (59.4%)		120 (62.5%)	267 (58.0%)	
M2	357 (14.5%)	98 (15.0%)		24 (12.5%)	74 (16.1%)	
Other: A1, A2, or M3	20 (0.8%)	5 (0.8%)		3 (1.6%)	2 (0.4%)	
Thrombolysis given, n (%)			0.04			0.26
No	629 (24.2%)	188 (28.1%)		49 (24.9%)	139 (29.5%)	
Yes	1970 (75.8%)	480 (71.9%)		148 (75.1%)	332 (70.5%)	
Months since start registry, median (IQR)	30 (21 to 38)	28 (20 to 36)	<0.01	34 (23 to 38)	27 (19 to 35)	<0.001
Time from onset to groin puncture, min; mean (SD)	219 (105)	194 (78)	<1×10 ⁻⁹	192 (76)	195 (79)	0.60
Manual thrombus measurements						
Thrombus length, mm; median (IQR)	18 (11 to 28)	18 (11 to 29)	0.65	19 (10 to 32)	17 (11 to 27)	0.55
Thrombus perviousness, HU; median (IQR)	4 (−2 to 13)	4 (−1 to 12)	0.58	7 (0 to 14)	3 (−1 to 10)	<0.01
Thrombus density, HU; mean (SD)	50 (9.6)	49 (10.0)	0.10	47 (11)	50 (10)	<0.01
Thrombus volume, mL; median (IQR)				0.08 (0.04 to 0.14)	0.09 (0.05 to 0.15)	0.07
Primary device choice, n (%)			0.21			
AD	514 (27.0%)	198 (29.6%)		198 (100.0%)		
SR	1392 (73.0%)	472 (70.4%)			472 (100.0%)	

Data are stratified by the included cohort and the remainder of the registry and by endovascular device choice: AD or SR. AD indicates aspiration device; ASPECTS, Alberta Stroke Program Early CT Score; HU, Hounsfield unit; ICA, internal carotid artery; ICA-T, internal carotid artery terminus; IQR, interquartile range; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; and SR, stent retriever.

Table 2. Prognostic Value of Thrombus Volume and Thrombus Length

Outcome	Thrombus volume (per 0.1 mL)		Thrombus length (per 0.1 mm)	
	cOR/B (95% CI)	acOR/aB (95% CI)	cOR/B (95% CI)	acOR/B (95% CI)
Functional outcome (ordinal mRS, lower is worse)	0.80 (0.71 to 0.91)‡	0.83 (0.71 to 0.97)*	0.87 (0.75 to 1.01)	0.65 (0.41 to 1.03)
Functional independence (mRS score ≤2)	0.78 (0.67 to 0.91)†	0.78 (0.64 to 0.96)*	0.77 (0.63 to 0.95)†	0.45 (0.24 to 0.85)*
Reperfusion rate (ordinal eTICI score)	0.92 (0.82 to 1.04)	0.90 (0.78 to 1.03)	0.96 (0.83 to 1.11)	0.89 (0.57 to 1.38)
Successful reperfusion (eTICI score ≥2B)	0.94 (0.81 to 1.08)	0.90 (0.75 to 1.07)	1.02 (0.85 to 1.24)	1.08 (0.6 to 1.94)
First-attempt reperfusion	0.79 (0.67 to 0.94)†	0.86 (0.71 to 1.05)	1.01 (0.85 to 1.19)	1.02 (0.6 to 1.73)
Symptomatic intracranial hemorrhage	1.06 (0.8 to 1.4)	1.07 (0.76 to 1.5)	1.28 (0.88 to 1.85)	2.15 (0.68 to 6.8)
Number of thrombus retrieval attempts	0.2 (0.1 to 0.31)‡	0.16 (0.04 to 0.28)†	0.04 (−0.05 to 0.13)	0.02 (−0.10 to 15)

Functional outcome: reversed mRS so that an OR below 1 and B below 0 corresponds to worse functional outcome. Odds ratios are reported for the first 6 rows, the slope of the regression line is reported for the number of attempts. acOR indicates adjusted common odds ratio; cOR, common odds ratio; eTICI, expanded Treatment in Cerebral Infarction; mRS, modified Rankin Scale; and OR, odds ratio.

**P*<0.05, †*P*<0.01, ‡*P*<0.0001.

DISCUSSION

Thrombus volume had a stronger association with poor procedural and worse functional outcomes than thrombus length. Moreover, more voluminous thrombi were associated with more retrieval attempts, a lower probability of achieving functional independence, and a worse ordinal functional outcome. Thrombus volume and length were not associated with eTICI, slCH, and FAR. Our findings might indicate that more voluminous thrombi cause a more difficult EVT procedure, resulting in more permanent and severe neurological deficits. When SR was used, functional outcome was more affected by volume compared with when an AD was used as first-line EVT device. We did not identify a potential statistically significant causal factor in eTICI, slCH, FAR, or number of thrombus retrieval attempts that might explain the interaction of device choice and volume on functional outcome.

Our findings regarding thrombus length and outcomes are in line with some previous studies^{1,3} but not with other previous studies.^{4,5} Regarding associations of thrombus volume with outcome measures, our

nonsignificant results are partially conflicting for the effect on successful reperfusion and FAR^{2,6} and for our association with functional outcome.^{7,8} Part of these deviations are likely due to the much larger sample size we adopted compared with other studies.^{4,5,7,8} The nonsignificant association between thrombus volume and successful reperfusion found in our study might be due to the improvement of EVT care; compared with the study by Yoo et al,² successful reperfusion was much higher in our cohort. Although we found an effect between thrombus volume and FAR, this effect became nonsignificant after adjusting for potential confounders, partially conflicting with findings by Baek et al⁶ who used less extensive statistical adjustments than we did. Findings from this study might indicate that patients with larger thrombi achieve a worse functional outcome due to more retrieval attempts irrespective of reperfusion status. The association between more retrieval attempts and a worse functional outcome irrespective of the reperfusion status has been described previously.¹⁰ This association might be due to an increased rate of (unobserved) hemorrhagic complications,¹² a more time-consuming intervention, or due to an

Table 3. Interaction of Device Choice on the Relationship of Thrombus Volume With Outcome

Outcome measure	Multiplicative interaction term first-line device choice (SR=1 vs AD=0) and thrombus volume (0.1 mL)			
	cOR/B	<i>P</i> value	acOR/aB	<i>P</i> value
Functional outcome (ordinal mRS score <1 indicates worse functional outcome)	0.67 (0.5 to 0.89)*	0.005*	0.74 (0.55 to 1)*	0.047*
Functional independence (mRS score ≤2)	0.76 (0.54 to 1.06)	0.108	0.86 (0.59 to 1.27)	0.454
Reperfusion rate (ordinal eTICI score)	1.13 (0.86 to 1.48)	0.381	1.19 (0.91 to 1.57)	0.210
Successful reperfusion (eTICI score ≥2B)	1.04 (0.74 to 1.46)	0.807	1.1 (0.78 to 1.55)	0.569
First-attempt reperfusion	0.95 (0.66 to 1.37)	0.789	1.04 (0.71 to 1.52)	0.845
Symptomatic intracranial hemorrhage	1.59 (0.71 to 3.54)	0.385	1.69 (0.76 to 3.78)	0.202
Number of thrombus retrieval attempts	0.15 (−0.07 to 0.38)	0.398	0.10 (−0.13 to 0.33)	0.184

acOR indicates adjusted common odds ratio; AD, aspiration device; cOR, common odds ratio; eTICI, expanded Treatment in Cerebral Infarction; mRS, modified Rankin Scale; and SR, stent retriever.

*Statistical significance (*P*<0.05).

impaired microvascular reperfusion and thus persistent brain tissue ischemia.²⁵ Moreover, more physical strain and damage to the vessel wall during the intervention could induce inflammatory cascades that results in an impaired microvascular reperfusion.^{25,26} To the best of our knowledge, this is the first study performing an interaction analysis on first-line device choice and thrombus volume. Our findings on the relationship between thrombus volume and outcomes considering the device choice were in line with Dutra et al where a higher clot burden score, associated with a less voluminous thrombi, was associated with better outcomes when an SR was used.³ Part of these findings related to the interaction of thrombus volume and first-line EVT device could be explained based on pathophysiological and physical mechanisms. Namely, an important difference between SR- and AD-based EVT is the way the thrombus is removed. In AD EVT, only the proximal part of the thrombus is touched with a device causing suction while in SR EVT, a stent is deployed in and past the thrombus to provide traction. This implies a larger contact surface of SR devices with the thrombus. The contact surface could relate to functional outcome in 3 different ways: first, due to the larger contact surface, the use of SR could lead to an easier and more successful intervention for patients with more voluminous thrombi. Second, the larger contact surface could cause more friction and adhesion during EVT, resulting in a higher chance of intracerebral hemorrhages and activation of inflammatory cascades associated with the no-reflow phenomenon after the procedure and in turn affect functional outcome.^{25,27} Third, a previous study advocated that the thrombus length/SR length ratio should be as small as possible to have a greater chance to achieve FAR,²⁸ potentially improving outcome. Our findings are in line with the second theory as the interaction between first-line EVT device choice and thrombus volume indicated increasingly worse functional outcome for SR- compared with AD-treated patients for more voluminous thrombi. However, since we did not include asymptomatic intracranial hemorrhage or the occurrence of no reflow as an outcome measure, we could not verify this proposed causal pathway to functional outcome. In addition, we could not verify the value of the length/SR length ratio presented in the third theory due to lacking data. An alternative explanation for the interaction effect between first-line device and thrombus volume could lie in a selection effect. If the interventionalist would prefer AD for smaller or easier-to-treat thrombi, indirectly the more profound effect of thrombus volume in first-line SR compared with first-line AD EVT could have been affected. Additionally, SR was the EVT standard before the introduction of AD. Due to the improvement of EVT workflows, interventionalists' experience, and patient outcomes over time, this might also have affected the interaction of first-line SR with

thrombus volume. However, we did not observe a difference in thrombus volume and thrombus characteristics between the first-line AD EVT and SR EVT patients. Furthermore, we adjusted our (logistic) regression models for EVT experience by using months since the start of the MR CLEAN Registry. Therefore, the effects of patient selection are likely to be limited in this study.

Our study has limitations. First, this study considers a selected cohort as a post hoc analysis of the MR CLEAN Registry. Thus, the found effects might be caused by inclusion bias. Furthermore, deviations in the baseline characteristics between our population and the remainder of the MR CLEAN Registry might complicate the ability to generalize our findings to the broader population. Second, only data on the first-line device choice were available. Switching from AD to SR when the initial attempts failed or combined used of AD and SR could have occurred but were not registered and considered in this study. Third, there were no interventionalist-specific data available. If such data were available, it would become possible to correct or stratify for interventionalist-based effects. Procedural outcome might depend on the interventionalist experience with either device and their relationship to thrombus volume. Ideally, the interaction of device choice and thrombus volume would be tested in a randomized trial with interventionalists having proper training or experience with AD and SR devices. Fourth, the use of AD or SR as first-line device was not a random choice but at the discretion of the treating interventionalist. This might be a source of bias in the reported interaction effects. Fifth, thrombus measurements were performed with single-phase CTA for patients with deviating collateral statuses. Therefore, if a hyperdense artery sign was absent, in some cases, it was difficult to determine the distal thrombus border due to a lack of contrast filling causing potential volume measurement errors. Ideally, multiphase CTA or CT perfusion should be used to determine the distal part of the thrombus. Finally, the difficulty to remove a thrombus could also be related to factors other than thrombus size, such as thrombus composition and occlusion patterns such as bifurcation and trifurcation thrombi. These factors require further studies. Future research should focus on more fine-grained device choice modeling and should consider interventionalist-specific differences or at least differences in EVT experience. Furthermore, the optimal moment to switch from SR to AD—or vice versa—and its relationship to thrombus volume remains a subject for future research.

CONCLUSIONS

In this multicenter retrospective cohort study, thrombus volume in patients with endovascularly treated acute ischemic stroke was associated with worse functional outcome and more EVT attempts but not with first-attempt recanalization, sICHs, or reperfusion rate. Thrombus length was only associated with functional

independence. Patients with more voluminous thrombi had worse functional outcome when treated with a first-line stent retrieval compared with a first-line AD. This might indicate that thrombus volume could be used to optimize first-line EVT device choice. A randomized clinical trial is required to assess whether voluminous thrombi are best treated with first-line SRs or ADs.

ARTICLE INFORMATION

Received October 11, 2022; final revision received January 18, 2023; accepted February 6, 2023.

Affiliations

Department of Radiology and Nuclear Medicine (H.v.V., A.A.E.B., J.A., J.W.H., P.R.K., W.Y., M.K., N.A.T., S.R., H.A.M., B.J.E., C.B.L.M.M.), Department of Biomedical Engineering and Physics (H.v.V., P.R.K., M.K., N.A.T., M.W.A.C., H.A.M.), and Department of Neurology (Y.B.W.E.M.R.), Amsterdam UMC, University of Amsterdam, the Netherlands. Neurovascular Center, Changhai Hospital, Naval Medical University, Shanghai, China (W.Y.). Department of Radiology and Nuclear Medicine, Cardiovascular Research Institute Maastricht, Maastricht University Medical Center, the Netherlands (W.H.v.Z.). Department of Radiology and Nuclear Medicine, Erasmus University Medical Center, Rotterdam, the Netherlands (A.v.d.L.). Department of Radiology and Nuclear Imaging (A.v.d.H.) and Department of Neurology (J.B.), University Medical Center Groningen, the Netherlands. Department of Radiology and Nuclear Medicine, Radboud UMC, Nijmegen, the Netherlands (S.J.).

Sources of Funding

This study was partly funded by the CONTRAST consortium. The CONTRAST consortium is supported by the Netherlands Cardiovascular Research Initiative (CVON), an initiative of the Dutch Heart Foundation, the Brain Foundation Netherlands, Medtronic, and Cerenovus. The MR CLEAN Registry was partly funded by the TWIN Foundation and by Erasmus MC University Medical Center, Maastricht University Medical Center, and Amsterdam UMC.

Disclosures

Dr van der Lugt received funding from the Dutch Heart Foundation, Brain Foundation Netherlands, the Netherlands Organization for Health Research and Development, and Health-Holland (Topsector Life Sciences & Health) and unrestricted grants from Penumbra, Inc, Stryker, Medtronic, Thrombolytic Science, and Cerenovus for research, all paid to the institution. Consultation fees were received by Dr van der Lugt from Stryker and Bracco Imaging. Amsterdam UMC received a grant from Stryker for research led by Drs Majoie and Roos. DR Majoie, Roos, Emmer, Caan, and Marquering are shareholders of NicoLab. Maastricht University MC received funds from Philips and Stryker for consultations and for an international grant/contract by Johnson and Johnson by Dr van Zwam.

Supplemental Material

Supplemental Results
Tables S1–S4

APPENDIX

Group authors MR CLEAN Registry (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands):

Executive Committee:

Diederik W.J. Dippel (Department of Neurology, Erasmus MC University Medical Center), Aad van der Lugt (Department of Radiology, Erasmus MC University Medical Center), Charles B.L.M. Majoie (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Yvo B.W.E.M. Roos (Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam), Robert J. van Oostenbrugge (Department of Neurology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Wim H. van Zwam (Department of Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Jelis Boiten (Department of Neurology, Haaglanden MC, the Hague), Jan Albert Vos (Department of Radiology, St. Antonius Hospital, Nieuwegein). Study coordina-

tors: Ivo G.H. Jansen (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Maxim J.H.L. Mulder (Department of Neurology and Department of Radiology, Erasmus MC University Medical Center), Robert-Jan B. Goldhoorn (Department of Neurology and Department of Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Kars C.J. Compagne (Department of Radiology, Erasmus MC University Medical Center), Manon Kappelhof (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Josje Brouwer (Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam), Sanne J. den Hartog (Department of Neurology, Department of Radiology, and Department of Public Health, Erasmus MC University Medical Center), Wouter H. Hinsenvelde (Department of Neurology and Department of Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Local principal investigators: Diederik W.J. Dippel (Department of Neurology, Erasmus MC University Medical Center), Bob Roozenbeek (Department of Neurology, Erasmus MC University Medical Center), Aad van der Lugt (Department of Radiology, Erasmus MC University Medical Center), Adriaan C.G.M. van Es (Department of Radiology, Erasmus MC University Medical Center), Charles B.L.M. Majoie (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Yvo B.W.E.M. Roos (Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam), Bart J. Emmer (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Jonathan M. Coutinho (Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam), Wouter J. Schonewille (Department of Neurology, St. Antonius Hospital, Nieuwegein), Jan Albert Vos (Department of Radiology, St. Antonius Hospital, Nieuwegein), Marieke J.H. Wermer (Department of Neurology, Leiden University Medical Center), Marianne A.A. van Walderveen (Department of Radiology, Leiden University Medical Center), Julie Staals (Department of Neurology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Robert J. van Oostenbrugge (Department of Neurology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Wim H. van Zwam (Department of Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Jeannette Hofmeijer (Department of Neurology, Rijnstate Hospital, Arnhem), Jasper M. Martens (Department of Radiology, Rijnstate Hospital, Arnhem), Geert J. Lycklama à Nijeholt (Department of Radiology, Haaglanden MC, the Hague), Jelis Boiten (Department of Neurology, Haaglanden MC, the Hague), Sebastiaan F. de Bruijn (Department of Neurology, HAGA Hospital, the Hague), Lukas C. van Dijk (Department of Radiology, HAGA Hospital, the Hague), H. Bart van der Worp (Department of Neurology, University Medical Center Utrecht), Rob H. Lo (Department of Radiology, University Medical Center Utrecht), Ewoud J. van Dijk (Department of Neurology, Radboud University Medical Center, Nijmegen), Hieronymus D. Boogaarts (Department of Neurosurgery, Radboud University Medical Center, Nijmegen), J. de Vries (Department of Neurology, Isala Klinieken, Zwolle), Paul L.M. de Kort (Department of Neurology, Elisabeth-TweeSteden Ziekenhuis, Tilburg), Julia van Tuijl (Department of Neurology, Elisabeth-TweeSteden Ziekenhuis, Tilburg), Jo P. Peluso (Department of Radiology, Elisabeth-TweeSteden Ziekenhuis, Tilburg), Puck Franssen (Department of Neurology, Isala Klinieken, Zwolle), Jan S.P. van den Berg (Department of Neurology, Isala Klinieken, Zwolle), Boudewijn A.A.M. van Hasselt (Department of Radiology, Isala Klinieken, Zwolle), Leo A.M. Aerden (Department of Neurology, Reinier de Graaf Gasthuis, Delft), René J. Dallinga (Department of Radiology, Reinier de Graaf Gasthuis, Delft), Maarten Uyttenboogaart (Department of Neurology, University Medical Center Groningen), Omid Eschgi (Department of Radiology, University Medical Center Groningen), Reinoud P.H. Bokkers (Department of Radiology, University Medical Center Groningen), Tobien H.C.M.L. Schreuder (Department of Neurology, Atrium Medical Center, Heerlen), Roel J.J. Heijboer (Department of Radiology, Atrium Medical Center, Heerlen), Koos Keizer (Department of Neurology, Catharina Hospital, Eindhoven), Lonneke S.F. Yo (Department of Radiology, Catharina Hospital, Eindhoven), Heleen M. den Hertog (Department of Neurology, Isala Klinieken, Zwolle), Emiel J.C. Sturm (Department of Radiology, Medical Spectrum Twente, Enschede), Paul J.A.M. Brouwers (Department of Neurology, Medical Spectrum Twente, Enschede). Imaging Assessment Committee: Charles B.L.M. Majoie (chair; Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Aad van der Lugt (co-chair; Department of Radiology, Erasmus MC University Medical Center), Wim H. van Zwam (Department of Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Geert J. Lycklama à Nijeholt (Department of Radiology, Haaglanden MC, the Hague), Marianne A.A. van Walderveen (Department of Radiology, Leiden University Medical Center), Marieke E.S. Sprengers (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Sjoerd F.M. Jenniskens (Department of Radiology, Radboud University Medical Center, Nijmegen), René van den Berg (Department

of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Albert J. Yoo (Department of Radiology, Texas Stroke Institute, Texas), Ludo F.M. Beenen (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Alida A. Postma (Department of Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Stefan D. Roosendaal (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Bas F.W. van der Kallen (Department of Radiology, Haaglanden MC, the Hague), Ido R. van den Wijngaard (Department of Radiology, Haaglanden MC, the Hague), Adriaan C.G.M. van Es (Department of Radiology, Erasmus MC University Medical Center), Bart J. Emmer (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Jasper M. Martens (Department of Radiology, Rijnstate Hospital, Arnhem), Lonke S.F. Yo (Department of Radiology, Catharina Hospital, Eindhoven), Jan Albert Vos (Department of Radiology, St. Antonius Hospital, Nieuwegein), Joost Bot (Department of Radiology, Amsterdam UMC, Vrije Universiteit van Amsterdam, Amsterdam), Pieter-Jan van Doormaal (Department of Radiology, Erasmus MC University Medical Center), Anton Meijer (Department of Radiology, Radboud University Medical Center, Nijmegen), Elyas Ghariq (Department of Radiology, Haaglanden MC, the Hague), Reinoud P.H. Bokkers (Department of Radiology, University Medical Center Groningen), Marc P. van Proosdij (Department of Radiology, Noordwest Ziekenhuisgroep, Alkmaar), G. Menno Kriete-meijer (Department of Radiology, Catharina Hospital, Eindhoven), Jo P. Peluso (Department of Radiology, Elisabeth-TweeSteden Ziekenhuis, Tilburg), Hieronymus D. Boogaarts (Department of Neurosurgery, Radboud University Medical Center, Nijmegen), Rob Lo (Department of Radiology, University Medical Center Utrecht), Dick Gerrits (Department of Radiology, Medical Spectrum Twente, Enschede), Wouter Dinkelaar (Department of Radiology, Erasmus MC University Medical Center), Auke P.A. Appelman (Department of Radiology, University Medical Center Groningen), Bas Hammer (Department of Radiology, HAGA Hospital, the Hague), Sjoert Pegge (Department of Radiology, Radboud University Medical Center, Nijmegen), Anouk van der Hoorn (Department of Radiology, University Medical Center Groningen), Saman Vinke (Department of Neurosurgery, Radboud University Medical Center, Nijmegen). Writing Committee: Diederik W.J. Dippel (chair; Department of Neurology, Erasmus MC University Medical Center), Aad van der Lugt (Department of Radiology, Erasmus MC University Medical Center), Charles B.L.M. Majoie (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Yoo B.W.E.M. Roos (Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam), Robert J. van Oostenbrugge (Department of Neurology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Wim H. van Zwam (Department of Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Geert J. Lycklama à Nijeholt (Department of Radiology, Haaglanden MC, the Hague), Jelis Boiten (Department of Neurology, Haaglanden MC, the Hague), Jan Albert Vos (Department of Radiology, St. Antonius Hospital, Nieuwegein), Wouter J. Schonewille (Department of Neurology, St. Antonius Hospital, Nieuwegein), Jeannette Hofmeijer (Department of Neurology, Rijnstate Hospital, Arnhem), Jasper M. Martens (Department of Radiology, Rijnstate Hospital, Arnhem), H. Bart van der Worp (Department of Neurology, University Medical Center Utrecht), Rob H. Lo (Department of Radiology, University Medical Center Utrecht). Adverse Event Committee: Robert J. van Oostenbrugge (chair; Department of Neurology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Jeannette Hofmeijer (Department of Neurology, Rijnstate Hospital, Arnhem), H. Zwenneke Flach (Department of Radiology, Isala Klinieken, Zwolle). Trial methodologist: Hester F. Lingsma (Department of Public Health, Erasmus MC University Medical Center). Research nurses and local trial coordinators: Nazihah el Ghannouti (Erasmus MC University Medical Center), Martin Sterrenberg (Erasmus MC University Medical Center), Wilma Pelikaan (Department of Neurology, St. Antonius Hospital, Nieuwegein), Rita Sprengers (Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam), Marjan Elfrink (Department of Neurology, Rijnstate Hospital, Arnhem), Michelle Simons (Department of Neurology, Rijnstate Hospital, Arnhem), Marjolein Vossers (Department of Radiology, Rijnstate Hospital, Arnhem), Joke de Meris (Department of Neurology, Haaglanden MC, the Hague), Tamara Vermeulen (Department of Neurology, Haaglanden MC, the Hague), Annet Geerlings (Department of Neurology, Radboud University Medical Center, Nijmegen), Gina van Vemde (Department of Neurology, Isala Klinieken, Zwolle), Tiny Simons (Department of Neurology, Atrium Medical Center, Heerlen), Gert Messchendorp (Department of Neurology, University Medical Center Groningen), Nynke Nicolaij (Department of Neurology, University Medical Center Groningen), Hester Bongenaar (Department of Neurology, Catharina Hospital, Eindhoven), Karin Bodde (Department of Neurology, Reinier de Graaf Gasthuis, Delft), Sandra Kleijn (Department of Neurology, Medical Spectrum Twente, Enschede), Jasmijn Lodico (Department of Neurology, Medical Spectrum Twente, Enschede), Hanneke Droste (Department of Neurology, Medi-

cal Spectrum Twente, Enschede), Maureen Wollaert (Department of Neurology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Sabrina Verheesen (Department of Neurology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), D. Jeurissen (Department of Neurology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]), Erna Bos (Department of Neurology, Leiden University Medical Center), Yvonne Drabbe (Department of Neurology, HAGA Hospital, the Hague), Michelle Sandiman (Department of Neurology, HAGA Hospital, the Hague), Nicoline Aaldering (Department of Neurology, Rijnstate Hospital, Arnhem), Berber Zweedijk (Department of Neurology, University Medical Center Utrecht), Jovoca Vervoort (Department of Neurology, Elisabeth-TweeSteden Ziekenhuis, Tilburg), Eva Ponjee (Department of Neurology, Isala Klinieken, Zwolle), Sharon Romviel (Department of Neurology, Radboud University Medical Center, Nijmegen), Karin Kanselaar (Department of Neurology, Radboud University Medical Center, Nijmegen), Denn Barning (Department of Radiology, Leiden University Medical Center). PhD and medical students: Esmee Venema (Department of Public Health, Erasmus MC University Medical Center), Vicky Charlos (Department of Neurology and Department of Public Health, Erasmus MC University Medical Center), Ralph R. Geuskens (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Tim van Straaten (Department of Neurology, Radboud University Medical Center, Nijmegen), Saliha Ergezen (Erasmus MC University Medical Center), Roger R.M. Harmsma (Erasmus MC University Medical Center), Daan Muijres (Erasmus MC University Medical Center), Anouk de Jong (Erasmus MC University Medical Center), Olvert A. Berkhemer (Department of Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht [CARIM]; Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam; Department of Neurology, Erasmus MC University Medical Center), Anna M.M. Boers (Department of Biomedical Engineering and Physics and Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), J. Huguet (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), P.F.C. Groot (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Marieke A. Mens (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Katinka R. van Kranendonk (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Kilian M. Treurniet (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Manon L. Tolhuisen (Department of Biomedical Engineering and Physics and Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Heitor Alves (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Annick J. Weterings (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Eleonora L.F. Kirkels (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Eva J.H.F. Voogd (Department of Neurology, Rijnstate Hospital, Arnhem), Lieve M. Schupp (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Sabine Collette (Department of Neurology and Department of Radiology, University Medical Center Groningen), Adrien E.D. Groot (Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam), Natalie E. LeCouffe (Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam), Praneeta R. Konduri (Department of Biomedical Engineering and Physics, Amsterdam UMC, University of Amsterdam, Amsterdam), Haryadi Prasetya (Department of Biomedical Engineering and Physics, Amsterdam UMC, University of Amsterdam, Amsterdam), Nerea Arrarte-Terreros (Department of Biomedical Engineering and Physics, Amsterdam UMC, University of Amsterdam, Amsterdam), Lucas A. Ramos (Department of Biomedical Engineering and Physics, Amsterdam UMC, University of Amsterdam, Amsterdam).

REFERENCES

1. Yoo AJ, Khatri P, Mocco J, Zaidat OO, Gupta R, Frei D, Lopes D, Shownkeen H, Berkhemer OA, Meyer D, et al; THERAPY Trial Investigators. Impact of thrombus length on outcomes after intra-arterial aspiration thrombectomy in the THERAPY trial. *Stroke*. 2017;48:1895–1900. doi: 10.1161/STROKEAHA.116.016253
2. Yoo J, Baek JH, Park H, Song D, Kim K, Hwang IG, Kim YD, Kim SH, Lee HS, Ahn SH, et al. Thrombus volume as a predictor of nonrecanalization after intravenous thrombolysis in acute stroke. *Stroke*. 2018;49:2108–2115. doi: 10.1161/STROKEAHA.118.021864

3. Dutra BG, Tolhuisen ML, Alves HCBR, Treurniet KM, Kappelhof M, Yoo AJ, Jansen IGH, Dippel DWJ, Van Zwam WH, van Oostenbrugge RJ, et al; MR CLEAN Registry Investigators†. Thrombus imaging characteristics and outcomes in acute ischemic stroke patients undergoing endovascular treatment. *Stroke*. 2019;50:2057–2064. doi: 10.1161/STROKEAHA.118.024247
4. Seker F, Pfaff J, Wolf M, Schönenberger S, Nagel S, Herweh C, Pham M, Bendszus M, Möhlenbruch MA. Impact of thrombus length on recanalization and clinical outcome following mechanical thrombectomy in acute ischemic stroke. *J Neurointerv Surg*. 2017;9:937–939. doi: 10.1136/neurintsurg-2016-012591
5. Spiotta AM, Vargas J, Hawk H, Turner R, Chaudry MI, Battenhouse H, Turk AS. Hounsfield unit value and clot length in the acutely occluded vessel and time required to achieve thrombectomy, complications and outcome. *J Neurointerv Surg*. 2014;6:423–427. doi: 10.1136/neurintsurg-2013-010765
6. Baek JH, Yoo J, Song D, Kim YD, Nam HS, Kim BM, Kim DJ, Lee HS, Heo JH. Predictive value of thrombus volume for recanalization in stent retriever thrombectomy. *Sci Rep [Internet]*. 2017;7:1–8. doi: 10.1038/s41598-017-16274-9
7. Mokin M, Morr S, Natarajan SK, Lin N, Snyder KV, Hopkins LN, Siddiqui AH, Levy EI. Thrombus density predicts successful recanalization with Solitaire stent retriever thrombectomy in acute ischemic stroke. *J Neurointerv Surg*. 2015;7:104–107. doi: 10.1136/neurintsurg-2013-011017
8. Borst J, Berkhemer OA, Santos EMM, Yoo AJ, Den Blanken M, Roos YBWEM, Van Bavel E, Van Zwam WH, Van Oostenbrugge RJ, et al. Value of thrombus CT characteristics in patients with acute ischemic stroke. *Am J Neuroradiol*. 2017;38:1758–1764. doi: 10.3174/ajnr.A5331
9. van Voorst H, Bruggeman AAE, Yang W, Andriessen J, Welberg E, Dutra BG, Konduri PR, Arrarte Terreros N, Hoving JW, Tolhuisen ML, et al. Thrombus radiomics in patients with anterior circulation acute ischemic stroke undergoing endovascular treatment [Internet]. *J Neurointerv Surg*. 2022;1–7. <http://www.ncbi.nlm.nih.gov/pubmed/35882552>.
10. Flottmann F, Brekenfeld C, Broocks G, Leischner H, McDonough R, Faizy TD, Deb-Chatterji M, Alegiani A, Thomalla G, Mpotsaris A, et al. Good clinical outcome decreases with number of retrieval attempts in stroke thrombectomy: beyond the first-pass effect. *Stroke*. 2021;52:482–490. doi: 10.1161/STROKEAHA.120.029830
11. Ben Hassen W, Touloupas C, Benzakoun J, Boulouis G, Bretzner M, Bricout N, Legrand L, Rodriguez C, Le Berre A, Seners P, et al. Impact of repeated clot retrieval attempts on infarct growth and outcome after ischemic stroke. *Neurology*. 2021;97:e444–e453. doi: 10.1212/WNL.00000000000012321
12. Maros ME, Brekenfeld C, Broocks G, Leischner H, McDonough R, Deb-Chatterji M, Alegiani A, Thomalla G, Fiehler J, Flottmann F. Number of retrieval attempts rather than procedure time is associated with risk of symptomatic intracranial hemorrhage. *Stroke*. 2021;52:1580–1588. doi: 10.1161/STROKEAHA.120.031242
13. Bernsen MLE, Goldhoorn RJB, Lingsma HF, Van Oostenbrugge RJ, Van Zwam WH, Uyttenboogaart M, Roos YBWEM, Martens JM, Hofmeijer J. Importance of occlusion site for thrombectomy technique in stroke: comparison between aspiration and stent retriever. *Stroke*. 2021;52:80–90. doi: 10.1161/STROKEAHA.120.030031
14. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019;50:e344–e418. doi: 10.1161/STR.0000000000000211
15. Turc G, Bhogal P, Fischer U, Khatri P, Lobotesis K, Mazighi M, Schellinger PD, Toni D, De Vries J, White P, et al. European Stroke Organisation (ESO) - European Society for Minimally Invasive Neurological Therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischemic stroke [published online February 26, 2019]. *J Neurointerv Surg*. 2019;1–30. doi: 10.1136/neurintsurg-2018-014569
16. Jansen IGH, Mulder MJHL, Goldhoorn RJB. Endovascular treatment for acute ischaemic stroke in routine clinical practice: prospective, observational cohort study (MR CLEAN registry). *BMJ*. 2018;360:k949. doi: 10.1136/bmj.k949
17. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Bull World Health Organ*. 2007;85:867–872. doi: 10.2471/BLT.07.045120
18. Berge E, Whiteley W, Audebert H, Marchis GD, Fonseca AC, Padiglioni C, Ossa NP de la, Strbian D, Tsvigoulis G, Turc G. European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke. *Eur Stroke J*. 2021;6:1–LXII. doi: 10.1177/2396987321989865
19. Yushkevich PA, Piven J, Hazlett HC, Smith RG, Ho S, Gee JC, Gerig G. User-guided 3D active contour segmentation of anatomical structures: significantly improved efficiency and reliability. *Neuroimage*. 2006;31:1116–1128. doi: 10.1016/j.neuroimage.2006.01.015
20. Klein S, Staring M, Murphy K, Viergever MA, Pluim JPW. Elastix: a toolbox for intensity-based medical image registration. *IEEE Trans Med Imaging*. 2010;29:196–205. doi: 10.1109/TMI.2009.2035616
21. Arrarte Terreros N, Bruggeman AAE, Kappelhof M, Tolhuisen ML, Brouwer J, Hoving JW, Konduri PR, Van Kranendonk KR, Dutra BG, Alves HCBR, et al. Thrombus imaging characteristics within acute ischemic stroke: similarities and interdependence. *J Neurointerv Surg*. 2022;1–9.
22. Saver JL. Novel end point analytic techniques and interpreting shifts across the entire range of outcome scales in acute stroke trials. *Stroke*. 2007;38:3055–3062. doi: 10.1161/STROKEAHA.107.488536
23. Santos EMM, Marquering HA, den Blanken MD, Berkhemer OA, Boers AMM, Yoo AJ, Beenen LF, Treurniet KM, Wismans C, van Noort K, et al. Thrombus permeability is associated with improved functional outcome and recanalization in patients with ischemic stroke. *Stroke [Internet]*. 2016;47:732–741. Accessed December 6, 2019. <http://www.ncbi.nlm.nih.gov/pubmed/26846859>
24. Cox DR. Interaction. *Int Stat Rev/Rev Int Stat [Internet]*. 1984;52:1–24. Accessed January 18, 2023. <http://www.jstor.org/stable/1403235>
25. Kloner RA, King KS, Harrington MG. No-reflow phenomenon in the heart and brain. *Am J Physiol Heart Circ Physiol*. 2018;315:H550–H562. doi: 10.1152/ajpheart.00183.2018
26. Ng FC, Churilov L, Yassi N, Kleinig TJ, Thijs V, Wu T, Shah D, Dewey H, Sharma G, Desmond P, et al. Prevalence and significance of impaired microvascular tissue reperfusion despite macrovascular angiographic reperfusion (no-reflow). *Neurology*. 2022;98:E790–E801. doi: 10.1212/WNL.00000000000013210
27. Yoo AJ, Andersson T. Thrombectomy in acute ischemic stroke: challenges to procedural success. *J Stroke*. 2017;19:121–130. doi: 10.5853/jos.2017.00752
28. Belachew NF, Dobrocky T, Meinel TR, Hakim A, Vynckier J, Arnold M, Seiffge DJ, Wiest R, Piechowiak EI, Fischer U, et al. Risks of undersizing stent retriever length relative to thrombus length in patients with acute ischemic stroke. *Am J Neuroradiol*. 2021;42:2181–2187. doi: 10.3174/ajnr.A7313