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Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Nerea Arrarte Terreros ,[1,2] Agnetha A E Bruggeman ,[2] Henk van Voorst ,[1,2] Praneeta R Konduri,[1,2] Ivo G H Jansen,[2] Manon Kappelhof ,[1,2] Manon L Tolhuisen ,[1,2] Nikki Boodt,[3,4] Diederik W J Dippel ,[3] Aad van der Lugt,[4] Wim H van Zwam ,[5] Robert J van Oostenbrugge,[6,7] H. Bart van der Worp,[8] Bart J Emmer,[2] Frederick J A Meijer,[9] Yvo B W E M Roos,[10] Ed van Bavel,[1] Henk A Marquering,[1,2] Charles B L M Majoie,[2] MR CLEAN Registry investigators

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For numbered affiliations see end of article.

Correspondence to
Nerea Arrarte Terreros, Department of Biomedical Engineering and Physics; Department of Radiology and Nuclear Medicine, Amsterdam UMC, location AMC, 1105 AZ Amsterdam, The Netherlands; n.arrarteterreros@amsterdamumc.nl

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ABSTRACT

Background A thrombus in the M1 segment of the middle cerebral artery (MCA) can occlude this main stem only or extend into the M1-M2 bifurcation. The occlusion pattern may affect endovascular treatment (EVT) success, as a bifurcated thrombus may be more prone to fragmentation during retrieval.

Objective To investigate whether bifurcated thrombus patterns are associated with EVT procedural and clinical outcomes.

Methods Occlusion patterns of MCA thrombi on CT angiography from MR CLEAN Registry patients were classified into three groups: main stem occlusion, bifurcation occlusion extending into one M2 branch, and bifurcation occlusion extending into both M2 branches. Procedural parameters, procedural outcomes (reperfusion grade and embolization to new territory), and clinical outcomes (24-48 hour National Institutes of Health Stroke Scale [$NIHSS_{FU}$] score, change in NIHSS scores between 24 and 48 hours and baseline Δ[NIHSS], and 90-day modified Rankin Scale [mRS] scores) were compared between occlusion patterns.

Results We identified 1023 patients with an MCA occlusion of whom 370 (36%) had a main stem occlusion, 151 (15%) a single branch, and 502 (49%) a double branch bifurcation occlusion. There were no statistically significant differences in retrieval method, procedure time, number of retrieval attempts, reperfusion grade, and embolization to new territory between occlusion patterns. Patients with main stem occlusions had lower $NIHSS_{FU}$ scores than patients with single (7 vs 11, p=0.01) or double branch occlusions (7 vs 9, p=0.04). However, there were no statistically significant differences in ΔNIHSS or in 90-day mRS scores.

Conclusions In our population, EVT procedural and long-term clinical outcomes were similar for MCA bifurcation occlusions and MCA main stem occlusions.

INTRODUCTION

Middle cerebral artery (MCA) occlusions are the most common large vessel occlusions in patients with acute ischemic stroke (AIS).[1] The configuration of the MCA is highly variable across patients.[2] Most often, the M1 main stem bifurcates into two M2 segments: the frontoparietal M2 and the temporal M2 (figure 1A).

A thrombus in the MCA can occlude the main stem only or extend into one or two of the M2 branches. This difference in occlusion pattern may affect endovascular treatment (EVT) success. For example, when the thrombus extends into both M2 branches, one stent retriever (or aspiration device) cannot capture both branches simultaneously, as it can only be extended into one branch. During EVT, the interventionalist positions the treatment device in one branch, expecting that the thrombus segment occluding the other branch will come along. However, these bifurcated thrombi can be refractory to retrieval, requiring multiple retrieval attempts aimed at alternating branches.[3–5] Increasing the number of retrieval attempts may reduce the chance of good outcome by increasing the procedure time, the risk of thrombus fragmentation and of other procedural complications.[6]

The use of two stent retrievers simultaneously has been reported for difficult cases where the bifurcated thrombus cannot be removed by a single stent retriever.[3–5 7–9] However, this novel technique has been reported only in individual case studies, which makes it questionable whether it is a safe technique to use.

In this study, we aim to investigate whether MCA bifurcation occlusions are different from MCA main stem occlusions for EVT procedural and clinical outcomes. Such information may support the development of (and need for) novel EVT techniques.

METHODS

Patient selection

Patients included in this study were recruited from the MR CLEAN Registry, a multicenter prospective observational registry of all patients undergoing EVT for AIS in the Netherlands.[10] This registry was approved by the central medical ethics committee of the Erasmus Medical Center Rotterdam, which served as the review board of all participating centers and granted permission to carry out the study as a registry (MEC-2014-235). All patients or legal representatives were provided with oral and written information on the registry and had the opportunity to withdraw consent to use their data.

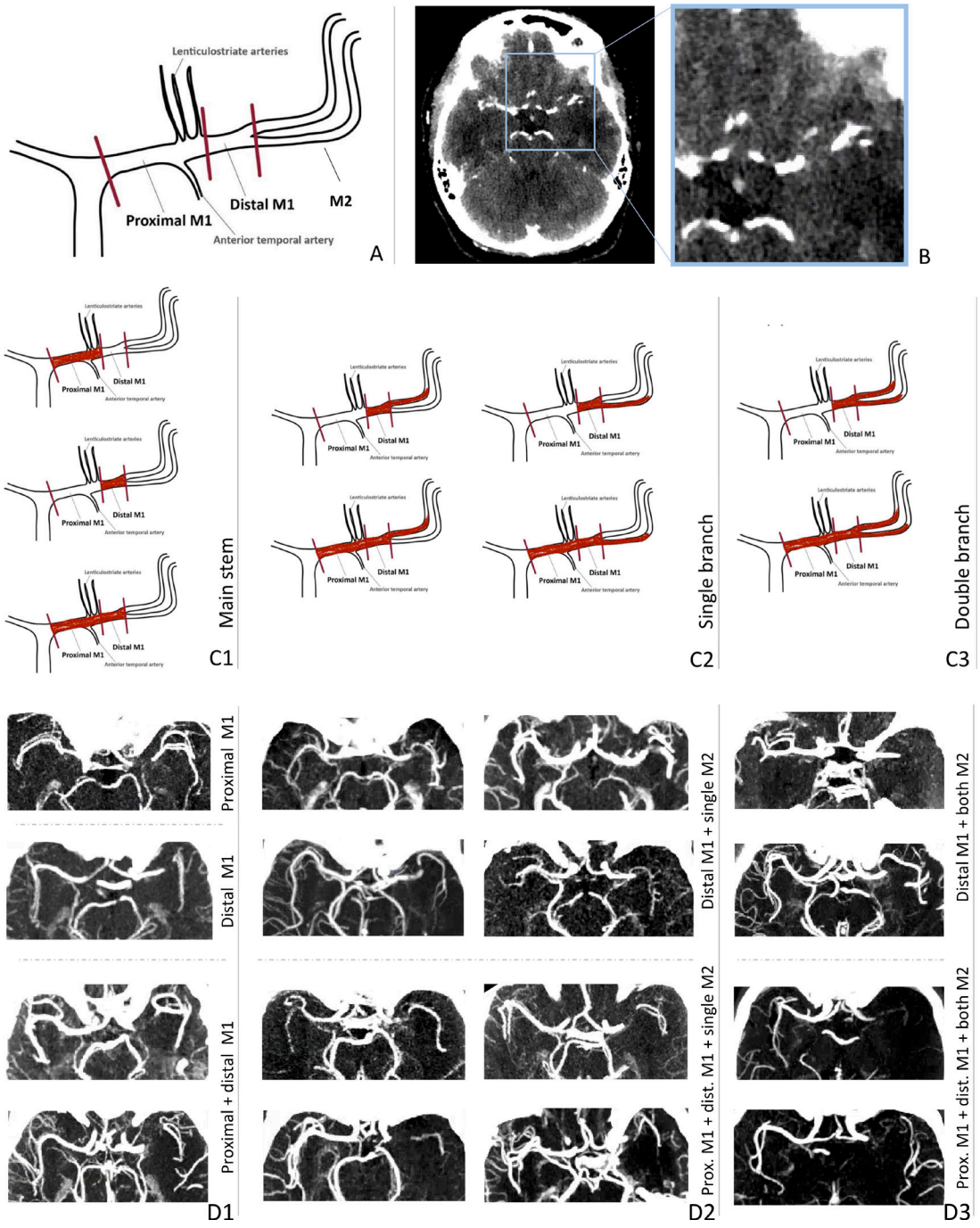

Figure 1 (A) Middle cerebral artery (MCA) configuration: proximal M1, distal M1 and the M2 bifurcation: frontoparietal M2 and temporal M2. (B) Axial view of a CT angiography (CTA) scan showing a proximal M1 occlusion, identifiable by a sudden stop of contrast filling. (C) Classification of MCA occlusion patterns: C1, main stem; C2, single branch; and C3, double branch occlusions. (D) Examples of thin-slab maximum intensity projections of CTA scans showing each occlusion pattern. Some scans are mirrored so all occlusions can be found on the right. (D1) Main stem occlusions where proximal M1, distal M1, or both proximal and distal M1 are occluded, from top to bottom. (D2) Single branch occlusion where the proximal and/or distal M1 and only one M2 branch (temporal or frontoparietal) are occluded. (D3) Double branch occlusion where the proximal and/or distal M1 and both M2 branches are occluded.

We included patients with AIS aged 18 years or older, with an MCA occlusion, who underwent EVT with a stent retriever (with or without aspiration) or aspiration device between March 2014 and November 2017. Patients without contraindications received 0.9 mg/kg of intravenous alteplase prior to EVT. The EVT approach and choice of material was left to the individual interventionalist. Source data for this study are not available owing to privacy regulations, but analysis methods, codes, and results are available from the corresponding author on reasonable request.

Data collection

All patients underwent a standard stroke imaging protocol at baseline, consisting of baseline non-contrast computed tomography (NCCT) and CT angiography (CTA). The MR CLEAN Registry imaging core laboratory, which has been involved in

all major clinical studies of the MR CLEAN Registry, assessed occlusion location, clot burden score (CBS), Alberta Stroke Program Early CT Score (ASPECTS), and collateral score. Core laboratory members were blinded to all clinical information except symptom side.[10]

Occlusion pattern classification

MCA segments were defined as follows: proximal M1, distal M1, M2-frontoparietal, and M2-temporal (figure 1A). M3 and more distal MCA segments were not considered in this study. The MR CLEAN Registry central imaging core laboratory assessed which MCA segments were occluded based on the contrast-filling defects found on baseline CTA (figure 1B). The central imaging core laboratory in charge of the CTA modality consisted of 31 interventional neuroradiologists with at least 5 years of experience assessing CTA scans in daily clinical practice. Each observer assessed a subset of the total number of these CTA scans. For the scoring, three views (axial, sagittal, and coronal) were used, aided with a maximum intensity projection of the CTA scan, if available. To ensure scoring-homogeneity, the observers were provided with training and guidelines of relevant definitions of each occlusion segment, including the scheme shown in figure 1A. The scoring of bifurcating M2 branches was performed based on the perfusion territory (frontoparietal vs temporal). This criterion was also applied for special cases like trifurcations or early bifurcations. If the scoring was not clear, the scoring was reviewed by a senior radiologist. Based on the scored occluded segment(s), we distinguished between patients with:

- An MCA **main stem** occlusion, where the proximal M1, distal M1, or both segments are occluded, but no M2 branches are occluded.
- A bifurcated thrombus with occlusion of the M1 segment and only one M2 branch (temporal or frontoparietal), i.e., **single branch** occlusion.
- A bifurcated thrombus with occlusion of the M1 segment and both M2 branches (temporal and frontoparietal), i.e., **double branch** occlusion.

A complete overview of these patterns is displayed in figure 1C,D.

EVT outcomes

For each occlusion pattern group, we compared the retrieval method (stent retriever vs aspiration), duration of EVT procedure, number of retrieval attempts, reperfusion grade, and presence of an embolus in a new (previously unaffected) vascular territory (ENT). Both reperfusion grade and ENT were assessed by the MR CLEAN Registry imaging core laboratory. Reperfusion grade after EVT was scored on digital subtraction angiography (DSA) according to the expanded Thrombolysis in Cerebral Infarction (eTICI) scale, ranging from 0 (no reperfusion) to 3 (complete reperfusion) and including a 2c score (99% reperfusion).[10] If only one DSA view was available a maximum of 2a was scored. The presence of ENT was identified on the last DSA run and defined as a remaining occlusion not matching the primary target occlusion on the first DSA run.

Functional outcome

Stroke severity at 24 to 48 hours' follow-up was assessed using the National Institutes of Health Stroke Scale ($NIHSS_{FU}$).[11] Change in NIHSS score between hospital presentation and follow-up was calculated according to: $\Delta NIHSS = NIHSS_{FU} - NIHSS_{BL}$. A negative ΔNIHSS value implies clinical improvement and a positive value means clinical deterioration. Patients' functional outcome was assessed with the modified Rankin scale (mRS) at 90 days through telephone or in-person interviews by trained nurses.[12] Presence of symptomatic intracranial hemorrhage (sICH) on follow-up NCCT was assessed by the MR CLEAN Registry core laboratory using the Heidelberg bleeding criteria for hemorrhage classification.[13]

Statistical analyses

In this exploratory study, we compared baseline clinical characteristics, EVT outcomes, and patient functional outcomes for the three occlusion patterns. Numerical data were reported as medians with IQR, and categorical data as numbers and percentages. The Kruskal-Wallis test was used to compare numerical data and the χ^2 test (or Fisher exact test) for categorical data. Statistical significance was set at $p<0.05$. If a variable was statistically significantly different between the three groups, a post hoc analysis was performed to assess the pairwise differences: Mann-Whitney U test for numerical data, and pairwise χ^2 test (with Bonferroni corrections) for categorical data. To further evaluate the effect of observed baseline differences, we performed a subgroup analysis to investigate if similar trends in outcome variables are observed after stratification based on age. We further performed a subgroup analysis where we stratified the population based on the used first-line EVT approach (stent retriever (with or without aspiration) or aspiration alone). In addition, for each occlusion pattern, we assessed the impact of proximal M1 occlusions. All analyses were performed with IBM SPSS statistics package software (version 26.0).

RESULTS

Our study population consisted of 1023 patients. The patient inclusion flow chart can be found in the online supplemental figure S1. Of all included patients, 370/1023 (36%) patients had an MCA main stem occlusion, 151/1023 (15%) had a single branch occlusion, and 502/1023 (49%) had a double branch occlusion (online supplemental table S1).

Baseline characteristics

Baseline characteristics of the three subgroups can be found in table 1. Patients with main stem occlusions were slightly younger than patients with single branch (70 years vs 74 years, $p=0.03$) and double branch occlusions (70 years vs 73 years, $p=0.03$). Patients with main stem occlusions had a higher collateral score than patients with single branch and double branch occlusions ($p<0.01$). Main stem occlusions resulted in higher CBS than single branch (8 vs 7, $p<0.01$) and double branch occlusions (8 vs 6, $p<0.01$).

EVT outcomes

Stent retrievers were used as a first-line device in 72% of patients with main stem occlusions, in 75% of patients with single branch, and in 73% of patients with double branch occlusions ($p=0.77$). There were no statistically significant differences in duration of EVT procedure, number of retrieval attempts, reperfusion grade, and presence of ENT between the three groups (table 2).

Functional outcome

Patients with a main stem occlusion had lower $NIHSS_{FU}$ scores than patients with single branch (7 vs 11, $p=0.01$) and double branch occlusions (7 vs 9, $p=0.04$) (figure 2A).

Table 1 Baseline characteristics of the three occlusion pattern groups

Baseline characteristics	Main stem (n=370)	Single branch (n=151)	Double branch (n=502)	P value
Age – median (IQR)	**70 (59–79)**	**74 (62–82)**	**73 (63–80)**	**0.03**
Sex, female – no./total (%)	174/370 (47)	73/151 (48)	255/502 (51)	0.54
Medical history – no./total (%)				
Previous stroke	60/368 (16)	27/149 (18)	93/500 (19)	0.67
Diabetes mellitus	63/369 (17)	18/150 (12)	87/500 (17)	0.27
Hypertension	185/364 (51)	83/147 (56)	274/495 (55)	0.33
Atrial fibrillation	87/367 (24)	37/147(25)	132/499 (26)	0.66
Pre-stroke mRS score – no./total (%)				0.43
0	243/363 (67)	91/147 (62)	327/491 (67)	
1	57/363 (16)	25/147 (17)	63/491 (13)	
2	26/363 (7)	8/147 (5)	35/491 (7)	
≥3	37/363 (10)	23/147 (16)	66/491 (13)	
Systolic blood pressure† (mm Hg) – median (IQR)	150 (130–166)	149 (130–165)	146 (130–162)	0.77
Diastolic blood pressure‡ (mm Hg) – median (IQR)	80 (71–91)	80 (70–90)	80 (70–90)	0.44
$NIHSS_{BL}$§ – median (IQR)	15 (11–18)	16 (12–20)	15 (11–19)	0.11
$ASPECTS_{BL}$¶ – median (IQR)	9 (8–10)	9 (8–10)	9 (8–10)	0.99
CS – no./total (%)				**<0.01**
0	**8/358 (2)**	**0/150 (0)**	**28/492 (6)**	
1	**75/358 (21)**	**56/150 (37)**	**179/492 (36)**	
2	**143/358 (40)**	**80/150 (53)**	**209/492 (42)**	
3	**132/358 (37)**	**14/150 (10)**	**76/492 (15)**	
CBS	**8 (6–8)**	**7 (5–7)**	**6 (4–6)**	**<0.01**
Treatment and workflow				
IVT – no./total (%)	277/370 (75)	112/151 (74)	365/502 (73)	0.66
Transferred patients – no./total (%)	191/370 (52)	89/151 (59)	281/502 (56)	0.24
Stroke onset* to first hospital presentation** (min) – median (IQR)	55 (38–104)	57 (40–105)	57 (40–101)	0.72
Hospital presentation to IVT†† (min) – median (IQR)	25 (19–32)	23 (17–33)	24 (18–33)	0.41
Stroke onset* to groin puncture (min) – median (IQR)	193 (150–255)	209 (160–270)	192 (147–255)	0.12

*Time of stroke onset was defined as the time of witnessed symptom onset or, if unknown, as the time the patient was last seen well.
†Missing value: 26.
‡Missing value: 31.
§Missing value: 13.
¶Missing value: 1.
**Missing value: 185.
††Missing value: 429
ASPECTS, Alberta Stroke Programme Early CT Score; BL, baseline; CBS, clot burden score; CS, collateral score; CT, computed tomography; IQR, interquartile range; IVT, intravenous treatment with alteplase; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

However, there were no statistically significant differences in the ΔNIHSS scores for the three occlusion patterns (online supplemental table S2). Patients with main stem thrombi had slightly lower mRS scores at 90 days than patients with bifurcated thrombi (figure 2B), although these differences were not statistically significant (p=0.58). There were no significant differences in the occurrence of sICH (online supplemental file 2).

The subgroup analysis, stratified by the median age of the study population, showed similar trends in older patients (age >72 years): main stem occlusion had lower $NIHSS_{FU}$ scores than patients with single branch occlusions (8 vs 13, p=0.01), but were not significantly different from double branch occlusions (8 vs 11, p=0.07) after adjusting with Bonferroni corrections. For younger patients (age <72 years): the three groups showed a median $NIHSS_{FU}$ score of 7 (p=0.46) (online supplemental table S3).

Subgroup analysis: first-line EVT approach

Stent retriever

The results of the stent-retriever subgroup analysis can be found in online supplemental table S4. We found no differences in EVT outcomes. Patients with main stem occlusions had lower $NIHSS_{FU}$ scores than patients with single branch occlusions (7 vs 10, p=0.03), but were not significantly different from double branch occlusions (7 vs 9, p=0.07) after Bonferroni corrections. There were no differences in ΔNIHSS or in mRS scores. We found differences in the occurrence of sICH between the three groups; however these differences did not remain when performing a post hoc analysis with Bonferroni corrections.

Table 2 EVT outcomes: first-line device used, duration of EVT procedure, number of retrieval attempts, eTICI scores, and ENT

EVT outcomes	Main stem, n=370	Single branch, n=151	Double branch, n=502	P value
First-line device				0.77
Stent retriever	268/370 (72)	114/151 (75)	368/502 (73)	
Aspiration	102/370 (28)	37/151 (25)	134/502 (27)	
Procedural time* (min) – median (IQR)	55 (36–80)	60 (37–89)	56 (38–83)	0.62
Retrieval attempts – no./total (%)				0.38
1	146/343 (42)	67/144 (47)	194/476 (41)	
2	68/343 (20)	28/144 (19)	127/476 (27)	
3	61/343 (18)	24/144 (17)	72/476 (15)	
4	33/343 (10)	10/144 (7)	34/476 (7)	
≥5	35/343 (10)	15/144 (10)	49/476 (10)	
eTICI scores – no./total (%)				0.55
0	27/362 (7)	14/148 (9)	35/494 (7)	
1	14/362 (4)	7/148 (5)	8/494 (2)	
2a	72/362 (20)	30/148 (20)	105/494 (21)	
2b	73/362 (20)	31/148 (21)	107/494 (22)	
2c	43/362 (12)	14/148 (9)	67/494 (14)	
3	133/362 (37)	52/148 (35)	172/494 (35)	
ENT – no./total (%)	11/336 (3)	6/138 (4)	22/465 (5)	0.59

*Missing values: 71.
ENT, embolization to new (previously unaffected) vascular territory; eTICI, expanded Thrombolysis in Cerebral Infarction; EVT, endovascular treatment; IQR, interquartile range.

Aspiration

We found no differences in EVT or functional outcomes for the three occlusion patterns for patients treated with aspiration. Results of the aspiration subgroup analysis can be found in online supplemental table S5.

Impact of proximal M1 occlusions

We found similar EVT procedural and functional outcomes in main stem and single branch patients with and without an occluded proximal M1 segment. The results can be found in the online supplemental tables S6 and S7.

We found significant differences in the distribution of eTICI scores in patients with a double branch occlusion: double branch patients with a proximal M1 occlusion had less often 2a scores than patients without a proximal M1 occlusion (12% vs 25%, p=0.04 after Bonferroni corrections). Double branch patients with a proximal M1 occlusion also had higher median $NIHSS_{FU}$ scores than patients without a proximal M1 occlusion (11 vs 8, p<0.01). However, we found similar ΔNIHSS and 90-day mRS scores in both groups. The results can be found in the online supplemental table S8.

DISCUSSION

In this study, we found no differences in EVT procedural outcomes based on MCA occlusion pattern groups, when comparing main stem, single branch, and double branch occlusions. We found that patients with main stem occlusions had better NIHSS scores at 24-48 hours than patients with bifurcated thrombi; however, there were no differences in ΔNIHSS scores or in long-term functional outcomes as measured with the 90-day mRS.

MCA main stem and bifurcation occlusions have previously been compared in 62 patients, where lower rates of successful recanalization were found in patients with bifurcated thrombi than in main stem thrombi, but no differences in long-term functional outcomes.[14] Studies comparing M1 and M2 occlusions have reported similar results for recanalization and complication rates.[15 16] Proximal and distal M1 occlusions have also been associated with similar post-EVT clinical outcomes.[17] Other studies showed that shorter distance from the internal cerebral artery terminus to an MCA occlusion is related to higher rates of successful recanalization after EVT.[18]

Successful recanalization of an MCA artery depends on multiple factors besides the occlusion pattern/location - to enumerate a few: MCA tortuosity has been associated with reduced stent-retriever thrombectomy success.[19] Smaller thrombi have been related to fewer EVT attempts, higher rates of successful recanalization, and better functional outcomes after EVT.[20 21] Red blood cell-rich thrombi may be more prone to fragmentation during retrieval than fibrin-rich thrombi.[22] The occlusion dynamics (ie, the way the thrombus occludes the vessel) might affect thrombus

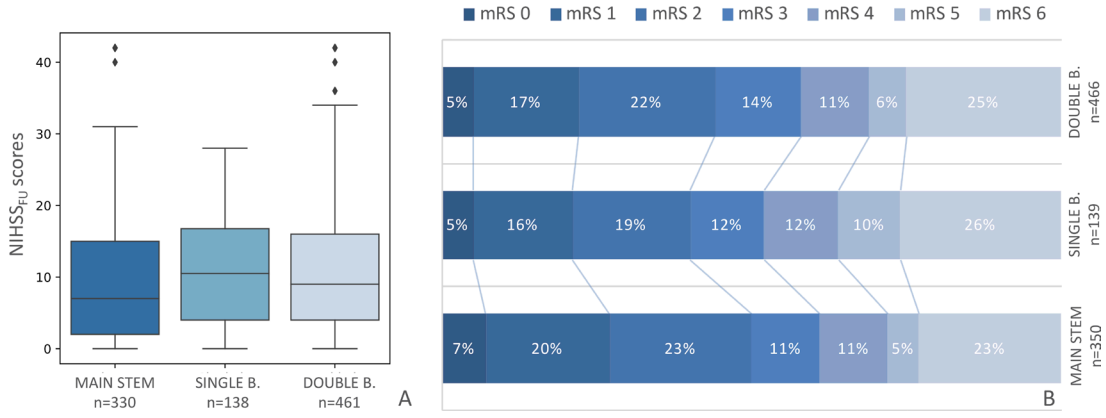

Figure 2 2(A) Neurological deficit assessed by the National Institutes of Health Stroke Scale (NIHSS) scores at 24–48 hours ($NIHSS_{FU}$) for patients with main stem, single branch, and double branch middle cerebral artery (MCA) occlusions. Patients with main stem occlusions have lower $NIHSS_{FU}$ scores than patients with single branch (p=0.01) and double branch (p=0.04) occlusions. (B) Functional outcome assessed by the modified Rankin scale (mRS) at 90 days for patients with a main stem, single branch, and double branch MCA occlusions. Between-group differences are not significant (p=0.58).

removal: emboli can be bent and folded while traveling along the vascular system before they obstruct a vessel.[23 24] Ultimately, all these thrombus characteristics result in a wide spectrum of biomechanical responses, which may affect thrombus-device interaction, and therefore thrombus retrieval.[25–27]

We found higher $NIHSS_{FU}$ scores in patients with MCA main stem thrombi than in those with bifurcated thrombi, while the 90-day mRS scores remained similar. NIHSS scores at 24-48 hours may better reflect consequences of the procedure than mRS scores at 3 months. The mRS score lacks specificity compared with the NIHSS score, since it accounts for all patient disabilities (even if they are not related to the AIS) and is a more coarse scale, including 7 rather than 42 levels.[28] The longer the time between treatment and outcome assessment, the more probable that the outcome score will be affected by other factors, such as patient comorbidities or adverse effects at a later stage.

On the other hand, given that the procedural parameters were similar between the three groups, the observed difference in $NIHSS_{FU}$ scores might be due to other between-group differences, e.g., age, and not because of the occlusion patterns. The stratification analysis showed that when comparing patients with similar ages, the distribution of $NIHSS_{FU}$ scores remain different only for older patients.

The occlusion pattern can affect the length and complexity of procedures (which are associated with functional outcome), and it can also directly affect the functional outcome of the patient, regardless of the treatment. Main stem occlusions are less extensive (higher CBS) than bifurcation occlusions. A higher CBS has previously been related to better patient functional outcome.[29] However, we found no such differences in functional outcome among the occlusion pattern groups.

In patients with double branch occlusions, we found that patients without an occluded proximal M1 segment had more eTICI 2a scores than patients with an occluded proximal M1, while the other eTICI categories remained similar. An eTICI score of 2a implies partial reperfusion (≤50%) of the target vascular territory. A bifurcated thrombus also occluding the proximal M1 segment could potentially better integrate with the stent since it has a larger stent-thrombus contact area, and therefore has a lower chance of fracture during retrieval than a shorter thrombus occluding only the distal M1 segment and the bifurcation. On the other hand, this finding could also be due to other factors, e.g., an uneven distribution of the single DSA views over the patients might also have caused this difference in eTICI 2a scores. Nevertheless, the ΔNIHSS and 90-day mRS scores remained similar for both groups.

The use of dual stents has been reported in the literature as a solution for refractory thrombi located in bifurcations.[3–5] This approach was not used in our patient cohort. In our patient cohort, bifurcation occlusions are not different from main stem occlusions for EVT outcomes, and therefore our results do not a priori encourage the use of a double stents for bifurcated thrombi. However, the thrombus imaging and histological characteristics of these refractory thrombi should be further studied and considered when developing novel EVT techniques.

Limitations

Occlusion patterns were scored on single-phase CTA by human eye. As such, some inaccuracy and interobserver variability might have been introduced. Poor distal contrast filling might have caused misclassification. Patients with a double branch occlusion might be misclassified if there is a main stem occlusion in combination with poor collateral distal filling. This might be reflected in the EVT outcomes: patients with double branch occlusions had similar outcomes to patients with main stem occlusions, and had better outcomes than patients with single branch occlusions. Assessment on multiphase CTA could improve the classification of the occlusion pattern. Combined CTA- and NCCT-based thrombus segmentations, although time consuming, could more accurately assess the occlusion pattern and additionally provide information on the clot burden. However, the occlusion segment classification presented in this study was performed as done in current clinical practice: based only on CTA scans.

Interobserver variability was not assessed in this study. However, previous studies have shown that, among experienced observers (>5 years), interobserver agreement was substantial for the assessment of CTA scans.[30]

The occlusion patterns illustrated in this study are an oversimplification of all the complex patterns that can be found.

CONCLUSION

In our population, EVT procedural and clinical outcomes are similar for patients with MCA main stem and patients with MCA bifurcation occlusions. More research should be conducted to justify the use of a more aggressive EVT approach for bifurcation thrombi.

Author affiliations
[1]Department of Biomedical Engineering and Physics, Amsterdam UMC, location AMC, Amsterdam, The Netherlands
[2]Department of Radiology and Nuclear Medicine, Amsterdam UMC, location AMC, Amsterdam, The Netherlands
[3]Department of Neurology, Erasmus MC, Rotterdam, The Netherlands
[4]Department of Radiology and Nuclear Medicine, Erasmus MC, Rotterdam, The Netherlands
[5]Department of Radiology, Maastricht UMC, Maastricht, The Netherlands
[6]Department of Neurology, Maastricht UMC, Maastricht, The Netherlands
[7]Cardiovascular Research Institute Maastricht, University of Maastricht, Maastricht, Netherlands
[8]Department of Neurology and Neurosurgery Brain Center, UMC Utrecht, Utrecht, The Netherlands
[9]Department of Medical Imaging, Radboud UMC, Nijmegen, The Netherlands
[10]Department of Neurology, Amsterdam UMC, location AMC, Amsterdam, The Netherlands

Correction notice This article has been corrected since it was first published. The open access licence has been updated to CC BY. 17th May 2023.

Collaborators MR CLEAN Registry investigators: Executive committee: Diederik WJ Dippel (Department of Neurology, Erasmus MC University Medical Center); Aad van der Lugt (Radiology, Erasmus MC University Medical Center); Charles BLM Majoie (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam); Yvo BWEM Roos (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 (Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht (CARIM)); Jelis Boiten (Neurology, Haaglanden MC, the Hague); Jan Albert Vos (Radiology, Sint Antonius Hospital, Nieuwegein). Study coordinators: Ivo GH Jansen (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam); Maxim JHL Mulder(Department of Neurology, Erasmus MC University Medical Center; Radiology, Erasmus MC University Medical Center); Robert- Jan B Goldhoorn (Department of Neurology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht (CARIM); Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht (CARIM)); Kars CJ Compagne (Radiology, Erasmus MC University Medical Center); Manon Kappelhof (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam); Josje Brouwer (Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam); Sanne J den Hartog (Department of Neurology, Radiology, Public Health, Erasmus MC University Medical Center); Wouter H Hinsenveld (Department of Neurology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht (CARIM); Radiology, Maastricht University Medical

Center and Cardiovascular Research Institute Maastricht (CARIM)),. Local principal investigators: Diederik WJ Dippel (Department of Neurology, Erasmus MC University Medical Center); Bob Roozenbeek (Department of Neurology, Erasmus MC University Medical Center); Aad van der Lugt (Radiology, Erasmus MC University Medical Center); Adriaan CGM van Es (Radiology, Erasmus MC University Medical Center); Charles BLM Majoie (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam); Yvo BWEM Roos (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 (Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam); Wouter J Schonewille (Department of Neurology, Sint Antonius Hospital, Nieuwegein); Jan Albert Vos (Radiology, Sint Antonius Hospital, Nieuwegein); Marieke JH Wermer; Marianne AA van Walderveen (Department of Neurology, 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 (Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht (CARIM)); Jeannette Hofmeijer; Jasper M Martens (Department of Neurology, Radiology, Rijnstate Hospital, Arnhem); Geert J Lycklama à Nijeholt (Department of Radiology, Haaglanden MC, the Hague); Jelis Boiten (Neurology, Haaglanden MC, the Hague); Sebastiaan F de Bruijn (Department of Neurology, HAGA Hospital, the Hague); Lukas C van Dijk (Radiology, HAGA Hospital, the Hague); H Bart van der Worp (Department of Neurology, University Medical Center Utrecht); Rob H Lo (Radiology, University Medical Center Utrecht); Ewoud J van Dijk (Department of Neurology, Radboud University Medical Center, Nijmegen); Hieronymus D Boogaarts (Neurosurgery, Radboud University Medical Center, Nijmegen); J de Vries (Department of Neurology, Isala Klinieken, Zwolle); Paul LM de Kort (Department of Neurology, Elisabeth-TweeSteden ziekenhuis, Tilburg); Julia van Tuijl (Department of Neurology, Elisabeth-TweeSteden ziekenhuis, Tilburg); Jo P Peluso (Radiology, Elisabeth-TweeSteden ziekenhuis, Tilburg); Puck Fransen (Department of Neurology, Isala Klinieken, Zwolle); Jan SP van den Berg (Department of Neurology, Isala Klinieken, Zwolle); Boudewijn AAM van Hasselt (Radiology, Isala Klinieken, Zwolle); Leo AM Aerden (Department of Neurology, Reinier de Graaf Gasthuis, Delft); René J Dallinga (Radiology, Reinier de Graaf Gasthuis, Delft); Maarten Uyttenboogaart (Department of Neurology, University Medical Center Groningen); Omid Eschgi (Radiology, University Medical Center Groningen); Reinoud PH Bokkers (Radiology, University Medical Center Groningen); Tobien HCML Schreuder (Department of Neurology, Atrium Medical Center, Heerlen); Roel JJ Heijboer (Radiology, Atrium Medical Center, Heerlen); Koos Keizer (Department of Neurology, Catharina Hospital, Eindhoven); Lonneke SF Yo (Radiology, Catharina Hospital, Eindhoven); Heleen M den Hertog (Department of Neurology, Isala Klinieken, Zwolle); Tomas Bulut (Radiology, Medisch Spectrum Twente, Enschede); Paul JAM Brouwers (Department of Neurology, Medisch Spectrum Twente, Enschede). Imaging assessment committee: Charles BLM Majoie (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam) (chair); Wim H van Zwam (Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht (CARIM)); Aad van der Lugt (Radiology, Erasmus MC University Medical Center); Geert J Lycklama à Nijeholt (Department of Radiology, Haaglanden MC, the Hague); Marianne AA van Walderveen (Radiology, Leiden University Medical Center); Marieke ES Sprengers (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam); Sjoerd FM Jenniskens (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, United States of America); Ludo FM Beenen (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam); Alida A Postma (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 FW van der Kallen (Department of Radiology, Haaglanden MC, the Hague); Ido R van den Wijngaard (Department of Radiology, Haaglanden MC, the Hague); Adriaan CGM van Es (Radiology, Erasmus MC University Medical Center); Bart J Emmer (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam); Jasper M. Martens (Radiology, Rijnstate Hospital, Arnhem); Lonneke SF Yo (Radiology, Catharina Hospital, Eindhoven); Jan Albert Vos (Radiology, Sint Antonius Hospital, Nieuwegein); Joost Bot (Department of Radiology, Amsterdam UMC, Vrije Universiteit van Amsterdam, Amsterdam); Pieter-Jan van Doormaal (Radiology, Erasmus MC University Medical Center); Anton Meijer (Radiology, Radboud University Medical Center, Nijmegen); Elyas Ghariq (Department of Radiology, Haaglanden MC, the Hague); Reinoud PH Bokkers (Radiology, University Medical Center Groningen); Marc P van Proosdij37; G Menno Krietemeijer (Radiology, Catharina Hospital, Eindhoven); Jo P Peluso (Radiology, Elisabeth-TweeSteden ziekenhuis, Tilburg); Hieronymus D Boogaarts (Neurosurgery, Radboud University Medical Center, Nijmegen); Rob Lo (Radiology, University Medical Center Utrecht); Wouter Dinkelaar (Radiology, Erasmus MC University Medical Center); Auke PA Appelman (Radiology, University Medical Center Groningen); Bas Hammer (Radiology, HAGA Hospital, the Hague); Sjoert Pegge (Radiology, Radboud University Medical Center, Nijmegen); Anouk van der Hoorn (Radiology, University Medical Center Groningen); Saman Vinke (Neurosurgery, Radboud University Medical Center, Nijmegen). Writing committee: Diederik WJ Dippel (Department of Neurology, Erasmus MC University Medical Center) (chair); Aad van der Lugt (Radiology, Erasmus MC University Medical Center); Charles BLM Majoie (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam); Yvo BWEM Roos (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 (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 (Neurology, Haaglanden MC, the Hague); Jan Albert Vos (Radiology, Sint Antonius Hospital, Nieuwegein); Wouter J Schonewille (Department of Neurology, Sint Antonius Hospital, Nieuwegein); Jeannette Hofmeijer (Department of Neurology, Rijnstate Hospital, Arnhem); Jasper M Martens (Radiology, Rijnstate Hospital, Arnhem); H Bart van der Worp (Department of Neurology, University Medical Center Utrecht); Rob H Lo (Radiology, University Medical Center Utrecht). Adverse event committee: Robert J van Oostenbrugge (Department of Neurology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht (CARIM)) (chair); Jeannette Hofmeijer (Department of Neurology, Rijnstate Hospital, Arnhem); H Zwenneke Flach (Radiology, Isala Klinieken, Zwolle) Trial methodologist: Hester F Lingsma (Public Health, Erasmus MC University Medical Center) Research nurses / local trial coordinators: Naziha el Ghannouti (Department of Neurology, Erasmus MC University Medical Center); Martin Sterrenberg (Department of Neurology, Erasmus MC University Medical Center); Wilma Pellikaan (Department of Neurology, Sint Antonius Hospital, Nieuwegein); Rita Sprengers (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 (Radiology, Rijnstate Hospital, Arnhem); Joke de Meris (Neurology, Haaglanden MC, the Hague); Tamara Vermeulen (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, Medisch Spectrum Twente, Enschede); Jasmijn Lodico (Department of Neurology, Medisch Spectrum Twente, Enschede); Hanneke Droste (Department of Neurology, Medisch 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 Jeurrissen (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); Jocova 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 (Radiology, Leiden University Medical Center). PhD / Medical students: Esmee Venema (Public Health, Erasmus MC University Medical Center); Vicky Chalos (Department of Neurology, Erasmus MC University Medical Center; 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 (Department of Neurology, Erasmus MC University Medical Center); Roger RM Harmsma (Department of Neurology, Erasmus MC University Medical Center); Daan Muijres (Department of Neurology, Erasmus MC University Medical Center); Anouk de Jong (Department of Neurology, Erasmus MC University Medical Center); Olvert A Berkhemer (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam; (Department of Neurology, Erasmus MC University Medical Center); Radiology, Maastricht University Medical Center and Cardiovascular Research Institute Maastricht (CARIM)); Anna MM Boers (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam; Biomedical Engineering & Physics, Amsterdam UMC, University of Amsterdam, Amsterdam); J Huguet (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam); PFC 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 Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam; Biomedical Engineering & Physics, 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 LF Kirkels (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam), Eva JHF Voogd (Department of Neurology, Rijnstate Hospital, Arnhem); Lieve M Schupp (Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam); Sabine L Collette (Department of Neurology, University Medical Center Groningen; Radiology, University Medical Center Groningen); Adrien ED Groot (Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam); Natalie E LeCouffe (Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam); Praneeta R Konduri (Biomedical Engineering & Physics, Amsterdam UMC, University of Amsterdam, Amsterdam); Haryadi Prasetya (Biomedical Engineering & Physics, Amsterdam UMC, University of Amsterdam, Amsterdam); Nerea Arrarte-Terreros (Biomedical Engineering & Physics, Amsterdam UMC, University of Amsterdam, Amsterdam); Lucas A Ramos (Biomedical Engineering & Physics, Amsterdam UMC, University of Amsterdam, Amsterdam).

Contributors NAT developed the study, performed the data analysis, wrote the manuscript, and is the guarantor of the study. AAEB, HvV, and PRK contributed to the study design. IGHJ, MK, MLT, and NB helped with data acquisition and interpretation. DWJD, AvdL, WHvZ, RJvO, BvdW, BJE, FJAM, and YBWEMR contributed to the clinical assessment of the data. EvB, HAM, and CBLMM contributed to the research development and project supervision. All authors contributed to the final version of the manuscript.

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Patient consent for publication Not applicable.

Ethics approval These patients are part of the MR CLEAN Registry, a multicenter prospective observational registry of all patients undergoing EVT for AIS in the Netherlands. This registry was approved by the central medical ethics committee of the Erasmus Medical Center Rotterdam, which served as the review board of all participating centers (MEC-2014–235). The requirement for written informed consent was waived, but all patients or legal representatives were provided with oral and written information on the registry, and had the opportunity to withdraw consent to use their data via an opt-out form, conforming to the European Union General Data Protection Regulation.

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ORCID iDs
Nerea Arrarte Terreros http://orcid.org/0000-0002-9912-7508
Agnetha A E Bruggeman http://orcid.org/0000-0002-6873-2545
Henk van Voorst http://orcid.org/0000-0002-2647-3557
Manon Kappelhof http://orcid.org/0000-0001-5250-8955
Manon L Tolhuisen http://orcid.org/0000-0002-2695-1117
Diederik W J Dippel http://orcid.org/0000-0002-9234-3515
Wim H van Zwam http://orcid.org/0000-0003-1631-7056

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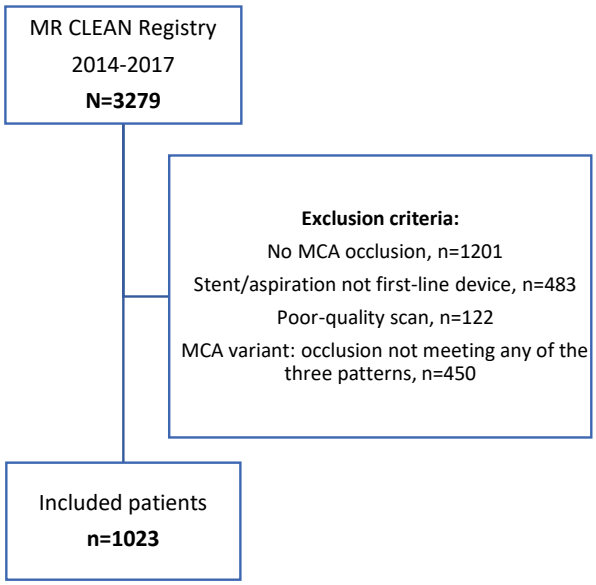
Supplementary material



Supplemental Material, Figure S1: Patient inclusion flow chart. In total, 3279 patients were presented in the hospital between 2014-2017. Among these, 1201 patients had an occlusion other than an MCA occlusion; 483 patients did not undergo EVT with a stent-retriever or aspiration device as a first-line approach; 122 had poor quality CTA scans; and 450 patients did not satisfy any of the three MCA occlusion patterns definitions. The abbreviations stand for: EVT, endovascular treatment; MCA, middle cerebral artery.

Supplemental Material, Table S1: MCA occlusion patterns for all 1023 patients. The occlusion patterns include MCA main stem, single branch, and double branch occlusions, as shown in Figure 1C.

Main stem occlusions, n=370				
Number of patients	Occluded segment			
	Proximal M1	Distal M1	Temporal M2	Frontoparietal M2
47	1	0	0	0
182	0	1	0	0
141	1	1	0	0
Single branch occlusions, n=151				
Number of patients	Occluded segment			
	Proximal M1	Distal M1	Temporal M2	Frontoparietal M2
36	0	1	1	0
69	0	1	0	1
27	1	1	1	0
19	1	1	0	1
Double branch occlusions, n=502				
Number of patients	Occluded segment			
	Proximal M1	Distal M1	Temporal M2	Frontoparietal M2
348	0	1	1	1
154	1	1	1	1

With 4 possible occlusion segments (proximal M1, distal M1, temporal M2 and frontoparietal M2), there are 16 possible combinations for the occlusion patterns. Some combinations are removed: 0000, non-occlusion; 1001, 1010 and 1011, non-continuous occlusions; 0010, 0001 and 0011, single and double branch occlusion patterns that do not include an M1 segment.

Supplemental Material, Table S2: Patient functional outcome.

Patient outcome	Main stem, n=370	Single branch, n=151	Double branch, n=502	p-value
$NIHSS_{FU}^{\alpha}$ – median (IQR)	**7 (2-15)**	**11 (4-17)**	**9 (4-16)**	**<0.01**
$\Delta NIHSS^{\beta}$ – median (IQR)	-6 (-11-(-1))	-4 (-9-0)	-5 (-10-0)	0.20
mRS at 90 days – no./total (%)				0.58
0	26/350 (7)	7/139 (5)	25/466 (5)	
1	69/350 (20)	22/139 (16)	79/466 (17)	
2	81/350 (23)	26/139 (19)	103/466 (22)	
3	37/350 (11)	17/139 (12)	66/466 (14)	
4	38/350 (11)	17/139 (12)	50/466 (11)	
5	18/350 (5)	14/139 (10)	28/466 (6)	
6	81/350 (23)	36/139 (26)	115/466 (25)	
sICH – no./total (%)	22/370 (6)	3/151 (2)	20/502 (4)	0.11

Missing values: $^{\alpha}$94, and $^{\beta}$96.

ΔNIHSS, change in NIHSS score at 24-48h compared to baseline; NIHSS, National Institute of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage.

Supplemental Material, Table S3: Subgroup analysis of $NIHSS_{FU}$, stratified by median age of the study population.

Subgroup I: age ≤ 72 years	**Main stem, n=213**	**Single branch, n=66**	**Double branch, n=241**	**p-value**
$NIHSS_{FU}^{\alpha}$ – median (IQR)	7 (2-12)	7 (3-15)	7 (3-13)	0.46
Subgroup II: age >72 years	**Main stem, n=157**	**Single branch, n=85**	**Double branch, n=261**	
$NIHSS_{FU}^{\beta}$ – median (IQR)	**8 (3-16)**	**13 (6-18)**	**11 (5-17)**	**0.03**

Missing values: $^{\alpha}45$, and $^{\beta}49$.
FU, follow-up; IQR, interquartile range; NIHSS, National Institute of Health Stroke Scale.

Subgroup analysis: first-line EVT approach

Supplemental Material, Table S4: Subgroup analysis: patients treated with a stent-retriever as first-line device (n=750). Baseline characteristics, EVT outcomes, and functional outcomes of the three occlusion pattern groups.

Baseline characteristics	Main stem, n=268	Single branch, n=114	Double branch, n=368	p-value
Age – median (IQR)	70 (59-79)	73 (62-82)	72 (63-80)	0.11
Sex, female – no./total (%)	123/268 (46)	52/114 (46)	181/368 (49)	0.65
Medical history – no./total (%)				
Previous stroke	45/268 (17)	22/113 (19)	72/366 (20)	0.63
Diabetes mellitus	48/267 (18)	11/113 (10)	62/366 (17)	0.12
Hypertension	130/264 (49)	61/111 (55)	203/362 (56)	0.23
Atrial fibrillation	62/267 (23)	31/112 (28)	104/366 (28)	0.33
Pre-stroke mRS – no./total (%)				0.35
0	182/265 (69)	69/113 (61)	235/360 (65)	
1	36/265 (14)	19/113 (17)	47/360 (13)	
2	20/265 (7)	5/113 (4)	27/360 (8)	
≥3	27/265 (10)	20/113 (18)	51/360 (14)	
Systolic blood pressure$^{\alpha}$ [mmHg] – median (IQR)	147 (128-164)	148 (130-165)	148 (130-162)	0.64
Diastolic blood pressure$^{\beta}$ [mmHg] – median (IQR)	80 (70-90)	80 (70-94)	80 (70-90)	0.96
$NIHSS_{BL}{}^{\gamma}$ – median (IQR)	15 (10-19)	15 (12-19)	15 (12-19)	0.32
$ASPECTS_{BL}{}^{\delta}$ – median (IQR)	9 (8-10)	9 (8-10)	9 (7-10)	0.89
CS – no./total (%)				**<0.01**
0	**5/257 (2)**	**0/113 (0)**	**18/361 (5)**	
1	**54/257 (21)**	**41/113 (36)**	**131/361 (36)**	
2	**100/257 (39)**	**61/113 (54)**	**164/361 (45)**	
3	**98/257 (38)**	**11/113 (10)**	**48/361 (13)**	
CBS	**8 (6-8)**	**7 (5-7)**	**6 (4-6)**	**<0.01**
Treatment and workflow				
IVT – no./total (%)	201/268 (75)	81/114 (71)	259/368 (70)	0.47
Transferred patients – no./total (%)	137/268 (51)	67/114 (59)	200/368 (54)	0.38
Stroke onset* to first	56 (38-108)	52 (40-105)	58 (40-103)	0.97

hospital presentation[ε] [min] – median (IQR)				
Hospital presentation to IVT [min][ζ] – median (IQR)	24 (19-30)	24 (19-35)	22 (17-33)	0.35
Stroke onset to groin puncture [min] – median (IQR)	197 (150-260)	217 (162-276)	195 (149-260)	0.12
EVT outcomes	**Main stem, n=268**	**Single branch, n=114**	**Double branch, n=368**	**p-value**
Procedural time[η] [min] – median (IQR)	58 (40-85)	60 (40-89)	62 (44-88)	0.54
Retrieval attempts – no./total (%)				0.36
1	104/253 (41)	49/109 (45)	126/351 (36)	
2	55/253 (22)	18/109 (17)	98/351 (28)	
3	46/253 (18)	20/109 (18)	60/351 (17)	
4	25/253 (10)	9/109 (8)	29/351 (8)	
≥5	23/253 (9)	13/109 (13)	38/351 (11)	
eTICI scores – no./total (%)				0.42
0	20/266 (8)	11/112 (10)	30/362 (8)	
1	12/266 (5)	7/112 (6)	8/362 (2)	
2A	47/266 (18)	22/112 (20)	82/362 (23)	
2B	59/266 (22)	21/112 (19)	80/362 (22)	
2C	30/266 (11)	10/112 (9)	47/362 (13)	
3	98/266 (37)	41/112 (36)	115/362 (32)	
ENT – no./total (%)	10/244 (4)	5/102 (5)	21/336 (6)	0.51
Patient outcome	**Main stem, n=268**	**Single branch, n=114**	**Double branch, n=368**	**p-value**
$NIHSS_{FU}$[θ]– median (IQR)	**7 (2-15)**	**10 (4-17)**	**9 (4-15)**	**0.02**
ΔNIHSS[ι] – median (IQR)	-6 (-11-(-2))	-4 (-9-0)	-5 (-10-0)	0.19
mRS at 90 days – no./total (%)				0.73
0	19/255 (8)	6/106 (6)	17/345 (5)	
1	53/255 (21)	13/106 (12)	60/345 (17)	

2	57/255 (22)	21/106 (20)	74/345 (21)	
3	29/255 (11)	15/106 (14)	49/345 (14)	
4	26/255 (10)	14/106 (13)	40/345 (12)	
5	14/255 (6)	10/106 (9)	23/345 (7)	
6	57/255 (22)	27/106 (26)	82/345 (24)	
sICH – no./total (%)	**17/268 (6)**	**2/114 (2)**	**10/368 (3)**	**0.04**

Missing values: $^{\alpha}$13, $^{\beta}$18, $^{\gamma}$8, $^{\delta}$1, $^{\varepsilon}$112, $^{\zeta}$305, $^{\eta}$59, $^{\theta}$59, and $^{\iota}$60.

*Time of stroke onset was defined as the time of witnessed symptom onset or, if unknown, as the time the patient was last seen well.

ΔNIHSS, change in NIHSS score at 24-48h compared to baseline; ASPECTS, Alberta Stroke Programme Early CT Score; BL, baseline; CBS, clot burden score; CS, collateral score; CT, computed tomography; ENT, embolization to new (previously unaffected) vascular territory; eTICI, expanded thrombolysis in cerebral infarction; EVT, endovascular treatment; IQR, interquartile range; IVT, intravenous treatment with alteplase; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage.

Supplemental Material, Table S5: Subgroup analysis: patients treated with aspiration as first-line device (n=273). Baseline characteristics, EVT outcomes, and functional outcomes of the three occlusion pattern groups.

Baseline characteristics	**Main stem, n=102**	**Single branch, n=37**	**Double branch, n=134**	**p-value**
Age – median (IQR)	69 (58-79)	76 (61-82)	74 (63-79)	0.28
Sex, female – no./total (%)	51/102 (50)	21/37 (57)	74/134 (55)	0.66
Medical history – no./total (%)				
Previous stroke	15/100 (15)	5/36 ()	21/134 (16)	0.96
Diabetes mellitus	15/102 ()	7/37 (19)	25/134 (19)	0.70
Hypertension	55/100 (55)	22/36 (61)	71/133 (53)	0.71
Atrial fibrillation	25/100 (25)	6/35 (17)	28/133 (21)	0.58
Pre-stroke mRS – no./total (%)				0.67
0	61/98 (62)	22/34 (65)	92/131 (70)	
1	21/98 (22)	6/34 (17)	16/131 (12)	
2	6/98 (6)	3/34 (9)	8/131 (6)	
≥3	10/98 (10)	3/34 (9)	15/131 (12)	
Systolic blood pressure$^{\alpha}$ [mmHg] – median (IQR)	**156 (136-178)**	**149 (131-160)**	**145 (127-164)**	**0.04**
Diastolic blood pressure$^{\alpha}$ [mmHg] – median (IQR)	**85 (77-95)**	**80 (70-88)**	**80 (70-90)**	**<0.01**
$NIHSS_{BL}$$^{\beta}$ – median (IQR)	15 (11-18)	16 (11-21)	16 (11-21)	0.31
$ASPECTS_{BL}$ – no./total (%)	9 (7-10)	9 (8-10)	9 (7-10)	0.52

CS – no./total (%)				**<0.01**
0	**3/101 (3)**	**0/37 (0)**	**10/131 (8)**	
1	**21/101 (21)**	**15/37 (41)**	**48/131 (37)**	
2	**43/101 (43)**	**19/37 (51)**	**45/131 (34)**	
3	**34/101 (34)**	**3/37 (8)**	**28/131 (21)**	
CBS	**8 (6-8)**	**7 (5-7)**	**6 (4-6)**	**<0.01**
Treatment and workflow				
IVT – no./total (%)	76/102 (75)	31/37 (84)	106/134 (79)	0.07
Transferred patients – no./total (%)	54/102 (53)	22/37 (59)	81/134 (60)	0.50
Stroke onset to first hospital presentation[γ] [min] – median (IQR)	52 (35-75)	62 (49-95)	55 (33-94)	0.45
Hospital presentation to IVT[δ] [min] – median (IQR)	**30 (20-37)**	**20 (17-27)**	**26 (20-34)**	**0.04**
Stroke onset to groin puncture [min] – median (IQR)	182 (145-244)	185 (148-235)	182 (139-246)	0.77
EVT outcomes	**Main stem, n=102**	**Single branch, n=37**	**Double branch, n=134**	**p-value**
Procedural time[ε] [min] – median (IQR)	50 (30-67)	46 (34-88)	42 (31-68)	0.53
Retrieval attempts – no./total (%)				0.23
1	42/90 (47)	18/35 (51)	68/125 (54)	
2	13/90 (14)	10/35 (29)	29/125 (23)	
3	15/90 (17)	4/35 (11)	12/125 (10)	
4	8/90 (9)	1/35 (3)	5/125 (4)	
≥5	12/90 (13)	2/35 (6)	11/125 (9)	
eTICI scores – no./total (%)				0.32
0	7/96 (7)	3/36 (8)	5/132 (4)	
1	2/96 (2)	0/36 (0)	0/132 (0)	
2A	25/96 (26)	8/36 (22)	23/132 (17)	
2B	14/96 (15)	10/36 (28)	27/132 (21)	

2C	13/96 (14)	4/36 (11)	20/132 (15)	
3	35/96 (36)	11/36 (31)	57/132 (43)	
ENT – no./total (%)	1/92 (1)	1/36 (3)	1/129 (1)	0.61
Patient outcome	**Main stem, n=102**	**Single branch, n=37**	**Double branch, n=134**	**p-value**
$NIHSS_{FU}$[ζ] – median (IQR)	8 (3-14)	11 (5-17)	9 (4-17)	0.45
ΔNIHSS[η] – median (IQR)	-6 (-9-(-1))	-4 (-10-1)	-4 (-11-0)	0.84
mRS at 90 days – no./total (%)				0.54
0	7/95 (8)	1/33 (3)	8/121 (7)	
1	16/95 (17)	9/33 (27)	19/121 (16)	
2	24/95 (25)	5/33 (16)	29/121 (24)	
3	8/95 (8)	2/33 (6)	17/121 (14)	
4	12/95 (13)	3/33 (9)	10/121 (8)	
5	4/95 (4)	4/33 (12)	5/121 (4)	
6	24/95 (25)	9/33 (27)	33/121 (27)	
sICH – no./total (%)	5/102 (5)	1/37 (3)	10/134 (7)	0.48

Missing values: [α]13, [β]5, [γ]73, [δ]124, [ε]12, [ζ]35, and [η]36.

*Time of stroke onset was defined as the time of witnessed symptom onset or, if unknown, as the time the patient was last seen well.

ΔNIHSS, change in NIHSS score at 24-48h compared to baseline; ASPECTS, Alberta Stroke Programme Early CT Score; BL, baseline; CBS, clot burden score; CS, collateral score; CT, computed tomography; ENT, embolization to new (previously unaffected) vascular territory; eTICI, expanded thrombolysis in cerebral infarction; EVT, endovascular treatment; IQR, interquartile range; IVT, intravenous treatment with alteplase; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage.

Impact of proximal M1 occlusions

Supplemental Material, Table S6: Subgroup analysis: impact of proximal M1 segments on main stem occlusions (n=370). Baseline characteristics, EVT outcomes, and functional outcomes for patients with an occluded vs. non-occluded proximal M1 segment.

Main stem Baseline characteristics	**Occluded proximal M1, n=188**	**Non-occluded proximal M1, n=182**	**p-value**
Age – median (IQR)	70 (59-81)	69 (59-79)	0.37
Sex, female – no./total (%)	83/188 (44)	91/182 (50)	0.26
Medical history – no./total (%)			
Previous stroke	30/187 (16)	30/181 (17)	0.89
Diabetes mellitus	32/187 (17)	31/182 (17)	0.98
Hypertension	98/187 (52)	87/177 (49)	0.54
Atrial fibrillation	44/187 (24)	43/180 (24)	0.94
Pre-stroke mRS – no./total (%)			0.09
0	122/184 (66)	121/179 (68)	
1	31/184 (17)	26/179 (14)	
2	8/184 (4)	18/179 (10)	
≥3	23/184 (13)	14/179 (8)	
Systolic blood pressure$^{\alpha}$ [mmHg] – median (IQR)	150 (131-170)	149 (129-164)	0.20
Diastolic blood pressure$^{\beta}$ [mmHg] – median (IQR)	**83 (75-93)**	**80 (70-90)**	**0.05**
$NIHSS_{BL}{}^{\gamma}$ – median (IQR)	**16 (12-20)**	**14 (10-17)**	**<0.01**
$ASPECTS_{BL}{}^{\delta}$ – median (IQR)	**9 (7-10)**	**9 (8-10)**	**<0.01**
CS – no./total (%)			0.47
0	5/181 (3)	3/177 (2)	
1	41/181 (23)	34/177 (19)	
2	75/181 (41)	68/177 (38)	
3	60/181 (33)	72/177 (41)	
Treatment and workflow			
IVT – no./total (%)	143/188 (76)	134/182 (74)	0.59
Transferred patients – no./total (%)	105/188 (56)	86/182 (47)	0.10
Stroke onset* to first hospital presentation$^{\varepsilon}$ [min] – median (IQR)	55 (39-104)	54 (37-105)	0.65
Hospital presentation to IVT [min]$^{\zeta}$ – median (IQR)	24 (18-30)	25 (20-35)	0.07
Stroke onset to groin puncture [min] – median (IQR)	200 (151-255)	190 (145-256)	0.58
Main stem EVT outcomes	**Occluded proximal M1, n=188**	**Non-occluded proximal M1, n=182**	**p-value**
Procedural time$^{\eta}$ [min] – median (IQR)	59 (40-78)	50 (35-80)	0.46

Retrieval attempts – no./total (%)			0.48
1	72/174 (41)	74/169 (44)	
2	31/174 (18)	37/169 (22)	
3	36/174 (21)	25/169 (15)	
4	19/174 (11)	14/169 (8)	
≥5	16/174 (9)	19/169 (11)	
eTICI scores – no./total (%)			0.23
0	14/186 (8)	13/176 (8)	
1	9/186 (5)	5/176 (3)	
2A	28/186 (15)	44/176 (25)	
2B	41/186 (22)	32/176 (18)	
2C	25/186 (13)	18/176 (10)	
3	69/186 (37)	64/176 (36)	
ENT – no./total (%)	6/173 (4)	5/163 (3)	0.84
Main stem Patient outcome	**Occluded proximal M1, n=188**	**Non-occluded proximal M1, n=182**	**p-value**
$NIHSS_{FU}^{\theta}$– median (IQR)	8 (2-15)	6 (2-14)	0.17
$\Delta NIHSS^{\theta}$ – median (IQR)	-6 (-11-(-2))	-5 (-10-(-1))	0.20
mRS at 90 days – no./total (%)			0.25
0	14/176 (8)	12/174 (7)	
1	28/176 (16)	41/174 (24)	
2	37/176 (21)	44/174 (25)	
3	22/176 (12)	15/174 (9)	
4	22/176 (13)	16/174 (9)	
5	7/176 (4)	11/174 (6)	
6	46/176 (26)	35/174 (20)	
sICH – no./total (%)	14/188 (7)	8/182 (4)	0.22

Missing values: $^{\alpha}10$, $^{\beta}12$, $^{\gamma}4$, $^{\delta}1$, $^{\varepsilon}58$, $^{\zeta}143$, $^{\eta}30$, and $^{\theta}40$.
*Time of stroke onset was defined as the time of witnessed symptom onset or, if unknown, as the time the patient was last seen well.
ΔNIHSS, change in NIHSS score at 24-48h compared to baseline; ASPECTS, Alberta Stroke Programme Early CT Score; BL, baseline; CS, collateral score; CT, computed tomography; ENT, embolization to new (previously unaffected) vascular territory; eTICI, expanded thrombolysis in cerebral infarction; EVT, endovascular treatment; IQR, interquartile range; IVT, intravenous treatment with alteplase; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage.

Supplemental Material, Table S7: Subgroup analysis: impact of proximal M1 segments on single branch occlusions (n=151). Baseline characteristics, EVT outcomes, and functional outcomes for patients with an occluded vs. non-occluded proximal M1 segment.

Single branch Baseline characteristics	**Occluded proximal M1, n=46**	**Non-occluded proximal M1, n=105**	**p-value**
Age – median (IQR)	73 (60-80)	74 (64-83)	0.31
Sex, female – no./total (%)	20/46 (44)	53/105 (51)	0.43
Medical history – no./total (%)			

Previous stroke	10/44 (23)	17/105 (16)	0.35
Diabetes mellitus	4/45 (9)	14/105 (13)	0.44
Hypertension	23/43 (54)	60/104 (58)	0.64
Atrial fibrillation	**6/44 (14)**	**31/103 (30)**	**0.04**
Pre-stroke mRS – no./total (%)			0.28
0	31/46 (67)	60/101 (59)	
1	7/46 (15)	18/101 (18)	
2	4/46 (9)	4/101 (4)	
≥3	4/46 (9)	19/101 (19)	
Systolic blood pressure$^{\alpha}$ [mmHg] – median (IQR)	146 (130-165)	149 (131-164)	0.85
Diastolic blood pressure$^{\alpha}$ [mmHg] – median (IQR)	80 (70-90)	80 (70-90)	0.99
$NIHSS_{BL}{}^{\beta}$– median (IQR)	**17 (14-20)**	**15 (12-18)**	**0.03**
$ASPECTS_{BL}$– median (IQR)	9 (7-10)	9 (8-10)	0.51
CS – no./total (%)			0.54
0	0/45 (0)	0/105 (0)	
1	16/45 (36)	40/105 (38)	
2	23/45 (51)	57/105 (54)	
3	6/45 (13)	8/105 (8)	
Treatment and workflow			
IVT – no./total (%)	34/46 (74)	78/105 (74)	0.79
Transferred patients – no./total (%)	29/46 (63)	60/105 (57)	0.50
Stroke onset* to first hospital presentation$^{\gamma}$ [min] – median (IQR)	59 (45-95)	55 (40-110)	0.83
Hospital presentation to IVT [min]$^{\delta}$ – median (IQR)	23 (16-33)	24 (18-33)	0.81
Stroke onset to groin puncture [min] – median (IQR)	195 (155-263)	210 (161-283)	0.25
Single branch EVT outcomes	**Occluded proximal M1, n=46**	**Non-occluded proximal M1, n=105**	**p-value**
Procedural time$^{\varepsilon}$ [min] – median (IQR)	60 (35-85)	56 (40-90)	0.69
Retrieval attempts – no./total (%)			0.92
1	18/43 (42)	49/101 (49)	
2	10/43 (23)	18/101 (18)	
3	8/43 (19)	16/101 (16)	
4	3/43 (7)	7/101 (7)	
≥5	4/43 (9)	11/101 (11)	
eTICI scores – no./total (%)			**0.05**
0	**5/44 (12)**	**9/104 (9)**	
1	**5/44 (11)**	**2/104 (2)**	
2A	**4/44 (9)**	**26/104 (25)**	

2B	**11/44 (25)**	**20/104 (19)**	
2C	**5/44 (11)**	**9/104 (9)**	
3	**14/44 (32)**	**38/104 (36)**	
ENT – no./total (%)	1/42 (2)	5/96 (5)	0.45
Single branch Patient outcome	**Occluded proximal M1, n=46**	**Non-occluded proximal M1, n=105**	**p-value**
$NIHSS_{FU}^{\zeta}$ – median (IQR)	10 (5-16)	11 (4-17)	0.77
$\Delta NIHSS^{\eta}$ – median (IQR)	-7 (-11-(-1))	-4 (-9-0)	0.07
mRS at 90 days – no./total (%)			0.80
0	2/42 (5)	5/97 (5)	
1	8/42 (19)	14/97 (14)	
2	8/42 (19)	18/97 (19)	
3	4/42 (10)	13/97 (14)	
4	3/42 (7)	14/97 (14)	
5	6/42 (14)	8/97 (8)	
6	11/42 (26)	25/97 (26)	
sICH – no./total (%)	1/146 (2)	2/105 (2)	0.91

Missing values: $^{\alpha}2$, $^{\beta}5$, $^{\gamma}30$, $^{\delta}68$, $^{\varepsilon}4$, $^{\zeta}13$, and $^{\eta}14$.

*Time of stroke onset was defined as the time of witnessed symptom onset or, if unknown, as the time the patient was last seen well.

ΔNIHSS, change in NIHSS score at 24-48h compared to baseline; ASPECTS, Alberta Stroke Programme Early CT Score; BL, baseline; CS, collateral score; CT, computed tomography; ENT, embolization to new (previously unaffected) vascular territory; eTICI, expanded thrombolysis in cerebral infarction; EVT, endovascular treatment; IQR, interquartile range; IVT, intravenous treatment with alteplase; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage.

Supplemental Material, Table S8: Subgroup analysis: impact of proximal M1 segments on double branch occlusions (n=502). Baseline characteristics, EVT outcomes, and functional outcomes for patients with an occluded vs. non-occluded proximal M1 segment.

Double branch Baseline characteristics	**Occluded proximal M1, n=154**	**Non-occluded proximal M1, n=348**	**p-value**
Age – median (IQR)	72 (64-80)	73 (62-80)	0.52
Sex, female – no./total (%)	82/154 (53)	173/348 (50)	0.47
Medical history – no./total (%)			
Previous stroke	31/154 (20)	62/346 (18)	0.56
Diabetes mellitus	28/154 (18)	59/346 (17)	0.76
Hypertension	88/152 (58)	186/343 (54)	0.45
Atrial fibrillation	36/153 (24)	96/346 (28)	0.33
Pre-stroke mRS – no./total (%)			0.16
0	107/149 (72)	220/342 (64)	
1	12/149 (8)	51/342 (15)	
2	12/149 (8)	23/342 (7)	
≥3	18/149 (12)	48/342 (14)	

Systolic blood pressure$^{\alpha}$ [mmHg] – median (IQR)	**150 (135-165)**	**144 (127-160)**	**0.02**
Diastolic blood pressure$^{\beta}$ [mmHg] – median (IQR)	81 (70-90)	80 (72-90)	0.38
$NIHSS_{BL}{}^{\gamma}$– median (IQR)	**17 (13-20)**	**15 (11-19)**	**<0.01**
$ASPECTS_{BL}$– median (IQR)	**9 (7-10)**	**9 (8-10)**	**<0.01**
CS – no./total (%)			0.13
0	9/148 (6)	19/344 (6)	
1	65/148 (44)	114/344 (33)	
2	54/148 (37)	155/344 (45)	
3	20/148 (13)	56/344 (16)	
Treatment and workflow			
IVT – no./total (%)	117/154 (76)	248/348 (71)	0.43
Transferred patients – no./total (%)	86/154 (56)	195/348 (56)	0.97
Stroke onset* to first hospital presentation$^{\delta}$ [min] – median (IQR)	59 (40-110)	56 (37-99)	0.45
Hospital presentation to IVT [min]$^{\varepsilon}$ – median (IQR)	22 (19-34)	24 (17-33)	0.87
Stroke onset to groin puncture [min] – median (IQR)	193 (147-246)	192 (147-260)	0.69
Double branch EVT outcomes	**Occluded proximal M1, n=154**	**Non-occluded proximal M1, n=348**	**p-value**
Procedural time$^{\zeta}$ [min] – median (IQR)	55 (35-85)	57 (40-83)	0.59
Retrieval attempts – no./total (%)			0.72
1	64/148 (43)	130/328 (40)	
2	37/148 (25)	90/328 (27)	
3	19/148 (13)	53/328 (16)	
4	10/148 (7)	24/328 (7)	
≥5	18/148 (12)	31/328 (10)	
eTICI scores – no./total (%)			**0.04**
0	**13/153 (9)**	**22/341 (7)**	
1	**4/153 (3)**	**4/341 (1)**	
2A	**19/153 (12)**	**86/341 (25)**	
2B	**34/153 (22)**	**73/341 (21)**	
2C	**24/153 (16)**	**43/341 (13)**	
3	**59/153 (39)**	**113/341 (33)**	
ENT – no./total (%)	7/145 (5)	15/320 (5)	0.95
Double branch Patient outcome	**Occluded proximal M1, n=154**	**Non-occluded proximal M1, n=348**	**p-value**
$NIHSS_{FU}{}^{\eta}$ – median (IQR)	**11 (5-17)**	**8 (3-15)**	**0.01**
$\Delta NIHSS^{\theta}$ – median (IQR)	-5 (-10-0)	-5 (-10-(-1))	0.90

mRS at 90 days – no./total (%)			0.17
0	2/144 (1)	23/322(7)	
1	24/144 (17)	55/322 (17)	
2	28/144 (19)	75/322 (23)	
3	21/144 (15)	45/322 (14)	
4	19/144 (13)	31/322 (10)	
5	10/144 (7)	18/322 (6)	
6	40/144 (28)	75/322 (23)	
sICH – no./total (%)	9/154 (6)	11/348 (3)	0.16

Missing values: $^{\alpha}$14, $^{\beta}$17, $^{\gamma}$4, $^{\delta}$97, $^{\varepsilon}$218, $^{\zeta}$37, $^{\eta}$41, and $^{\theta}$42.

*Time of stroke onset was defined as the time of witnessed symptom onset or, if unknown, as the time the patient was last seen well.

ΔNIHSS, change in NIHSS score at 24-48h compared to baseline; ASPECTS, Alberta Stroke Programme Early CT Score; BL, baseline; CS, collateral score; CT, computed tomography; ENT, embolization to new (previously unaffected) vascular territory; eTICI, expanded thrombolysis in cerebral infarction; EVT, endovascular treatment; IQR, interquartile range; IVT, intravenous treatment with alteplase; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage.

MR CLEAN Registry investigators – Group author

Executive committee
Diederik W.J. Dippel[1]; Aad van der Lugt[2]; Charles B.L.M. Majoie[3]; Yvo B.W.E.M. Roos[4]; Robert J. van Oostenbrugge[5]; Wim H. van Zwam[6]; Jelis Boiten[14]; Jan Albert Vos[8].

Study coordinators
Ivo G.H. Jansen[3]; Maxim J.H.L. Mulder[1,2]; Robert- Jan B. Goldhoorn[5,6]; Kars C.J. Compagne[2]; Manon Kappelhof[3]; Josje Brouwer[4]; Sanne J. den Hartog[1,2,40]; Wouter H. Hinsenveld [5,6].

Local principal investigators
Diederik W.J. Dippel[1]; Bob Roozenbeek[1]; Aad van der Lugt[2]; Adriaan C.G.M. van Es[2]; Charles B.L.M. Majoie[3]; Yvo B.W.E.M. Roos[4]; Bart J. Emmer[3]; Jonathan M. Coutinho[4]; Wouter J. Schonewille[7]; Jan Albert Vos[8]; Marieke J.H. Wermer[9]; Marianne A.A. van Walderveen[10]; Julie Staals[5]; Robert J. van Oostenbrugge[5]; Wim H. van Zwam[6]; Jeannette Hofmeijer[11]; Jasper M. Martens[12]; Geert J. Lycklama à Nijeholt[13]; Jelis Boiten[14]; Sebastiaan F. de Bruijn[15]; Lukas C. van Dijk[16]; H. Bart van der Worp[17]; Rob H. Lo[18]; Ewoud J. van Dijk[19]; Hieronymus D. Boogaarts[20]; J. de Vries[22]; Paul L.M. de Kort[21]; Julia van Tuijl[21]; Jo P. Peluso[26]; Puck Fransen[22]; Jan S.P. van den Berg[22]; Boudewijn A.A.M. van Hasselt[23]; Leo A.M. Aerden[24]; René J. Dallinga[25]; Maarten Uyttenboogaart[28]; Omid Eschgi[29]; Reinoud P.H. Bokkers[29]; Tobien H.C.M.L. Schreuder[30]; Roel J.J. Heijboer[31]; Koos Keizer[32]; Lonneke S.F. Yo[33]; Heleen M. den Hertog[22]; Tomas Bulut[35]; Paul J.A.M. Brouwers[34].

Imaging assessment committee
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Writing committee
Diederik W.J. Dippel[1] (chair); Aad van der Lugt[2]; Charles B.L.M. Majoie[3]; Yvo B.W.E.M. Roos[4]; Robert J. van Oostenbrugge[5]; Wim H. van Zwam[6]; Geert J. Lycklama à Nijeholt[13]; Jelis Boiten[14]; Jan Albert Vos[8]; Wouter J. Schonewille[7]; Jeannette Hofmeijer[11]; Jasper M. Martens[12]; H. Bart van der Worp[17]; Rob H. Lo[18].

Adverse event committee
Robert J. van Oostenbrugge[5] (chair); Jeannette Hofmeijer[11]; H. Zwenneke Flach[23].

Trial methodologist
Hester F. Lingsma[40].

Research nurses / local trial coordinators

Naziha el Ghannouti[1]; Martin Sterrenberg[1]; Wilma Pellikaan[7]; Rita Sprengers[4]; Marjan Elfrink[11]; Michelle Simons[11]; Marjolein Vossers[12]; Joke de Meris[14]; Tamara Vermeulen[14]; Annet Geerlings[19]; Gina van Vemde[22]; Tiny Simons[30]; Gert Messchendorp[28]; Nynke Nicolaij[28]; Hester Bongenaar[32]; Karin Bodde[24]; Sandra Kleijn[34]; Jasmijn Lodico[34]; Hanneke Droste[34]; Maureen Wollaert[5]; Sabrina Verheesen[5]; D. Jeurrissen[5]; Erna Bos[9]; Yvonne Drabbe[15]; Michelle Sandiman[15]; Nicoline Aaldering[11]; Berber Zweedijk[17]; Jocova Vervoort[21]; Eva Ponjee[22]; Sharon Romviel[19]; Karin Kanselaar[19]; Denn Barning[10].

PhD / Medical students:
Esmee Venema[40]; Vicky Chalos[1,40]; Ralph R. Geuskens[3]; Tim van Straaten[19]; Saliha Ergezen[1]; Roger R.M. Harmsma[1]; Daan Muijres[1]; Anouk de Jong[1]; Olvert A. Berkhemer[1,3,6]; Anna M.M. Boers[3,39]; J. Huguet[3]; P.F.C. Groot[3]; Marieke A. Mens[3]; Katinka R. van Kranendonk[3]; Kilian M. Treurniet[3]; Manon L. Tolhuisen[3,39]; Heitor Alves[3]; Annick J. Weterings[3], Eleonora L.F. Kirkels[3], Eva J.H.F. Voogd[11]; Lieve M. Schupp[3]; Sabine L. Collette[28,29]; Adrien E.D. Groot[4]; Natalie E. LeCouffe[4]; Praneeta R. Konduri[39]; Haryadi Prasetya[39]; Nerea Arrarte-Terreros[39]; Lucas A. Ramos[39].

List of affiliations
Department of Neurology[1], Radiology[2], Public Health[40], Erasmus MC University Medical Center;
Department of Radiology and Nuclear Medicine[3], Neurology[4], Biomedical Engineering & Physics[39], Amsterdam UMC, University of Amsterdam, Amsterdam;
Department of Neurology[5], Radiology[6], Maastricht University Medical Center and Cardiovascular Research Institute Maastricht (CARIM);
Department of Neurology[7], Radiology[8], Sint Antonius Hospital, Nieuwegein;
Department of Neurology[9], Radiology[10], Leiden University Medical Center;
Department of Neurology[11], Radiology[12], Rijnstate Hospital, Arnhem;
Department of Radiology[13], Neurology[14], Haaglanden MC, the Hague;
Department of Neurology[15], Radiology[16], HAGA Hospital, the Hague;
Department of Neurology[17], Radiology[18], University Medical Center Utrecht;
Department of Neurology[19], Neurosurgery[20], Radiology[27], Radboud University Medical Center, Nijmegen;
Department of Neurology[21], Radiology[26], Elisabeth-TweeSteden ziekenhuis, Tilburg;
Department of Neurology[22], Radiology[23], Isala Klinieken, Zwolle;
Department of Neurology[24], Radiology[25], Reinier de Graaf Gasthuis, Delft;
Department of Neurology[28], Radiology[29], University Medical Center Groningen;
Department of Neurology[30], Radiology[31], Atrium Medical Center, Heerlen;
Department of Neurology[32], Radiology[33], Catharina Hospital, Eindhoven;
Department of Neurology[34], Radiology[35], Medisch Spectrum Twente, Enschede;
Department of Radiology[36], Amsterdam UMC, Vrije Universiteit van Amsterdam, Amsterdam;
Department of Radiology[37], Noordwest Ziekenhuisgroep, Alkmaar;
Department of Radiology[38], Texas Stroke Institute, Texas, United States of America.

ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Bart J. Emmer

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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Date: 2/26/2022

Your Name: H.B. van der Worp

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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		HB van der Worp received funds from Bayer and LivaNova for consultancy, paid to his institution, and grants from the Dutch Heart Foundation, the Horizon 2020 programme, and Stryker, paid to his institution (all outside the work submitted).	

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ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Robert J. van Oostenbrugge

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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Date: 2/26/2022

Your Name: Wim H. van Zwam

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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Date: 2/26/2022

Your Name: Aad van der Lugt

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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Date: 2/26/2022

Your Name: Diederik W.J. Dippel

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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6	Payment for expert testimony	☒ **None**	
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8	Patents planned, issued or pending	☒ **None**	
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13	Other financial or non-financial interests	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Nikki Boodt

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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11	Stock or stock options	☒ **None**	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

Please place an "X" next to the following statement to indicate your agreement:

☒ I certify that I have answered every question and have not altered the wording of any of the questions on this form.

ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Manon L. Tolhuisen

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The author's relationships/activities/interests should be defined broadly. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

In item #1 below, report all support for the work reported in this manuscript without time limit. For all other items, the time frame for disclosure is the past 36 months.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) **No time limit for this item.**	☒ **None**	
			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
11	Stock or stock options	☒ **None**	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Manon Kappelhof

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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3	Royalties or licenses	☒ **None**	

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4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
11	Stock or stock options	☒ **None**	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Ivo G.H. Jansen

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	

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5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
11	Stock or stock options	☐ **None**	
		I.G.H. Jansen reports shareholder of Nicolab.	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

Please place an "X" next to the following statement to indicate your agreement:

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ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Praneeta R. Konduri

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) **No time limit for this item.**	☐ **None**	
		PR Konduri received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No 777072 (INSIST project).	
			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

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11	Stock or stock options	☒ **None**	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Henk van Voorst

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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Time frame: past 36 months			
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3	Royalties or licenses	☒ **None**	

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5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

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11	Stock or stock options	☒ **None**	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Agnetha A.E. Bruggeman

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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Time frame: past 36 months			
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3	Royalties or licenses	☒ **None**	

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5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
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12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
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ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Nerea Arrarte Terreros

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) **No time limit for this item.**	☐ **None**	
		N Arrarte Terreros has received funding from the AMC medical Research BV, Amsterdam UMC, location AMC, under project No 21937.	
			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated in item #1 above).	☒ **None**	
3	Royalties or licenses	☒ **None**	

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4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

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11	Stock or stock options	☒ **None**	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Charles B.L.M. Majoie

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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3	Royalties or licenses	☒ **None**	

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5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
11	Stock or stock options	☐ **None**	
		C.B.L.M. Majoie reports shareholder of Nicolab.	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

Please place an "X" next to the following statement to indicate your agreement:

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ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Henk A. Marquering

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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3	Royalties or licenses	☒ **None**	

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5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support for attending meetings and/or travel	☒ **None**	
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
11	Stock or stock options	☐ **None**	
		H.A. Marquering reports co-founder and shareholder of Nicolab (a company that focuses on the use of artificial intelligence for medical image analysis).	
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

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☒ I certify that I have answered every question and have not altered the wording of any of the questions on this form.

ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Ed van Bavel

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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Time frame: past 36 months			
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3	Royalties or licenses	☒ **None**	

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ICMJE DISCLOSURE FORM

Date: 2/26/2022

Your Name: Yvo B.W.E.M. Roos

Manuscript Title: Bifurcation occlusions and endovascular treatment outcome in acute ischemic stroke

Manuscript Number (if known): neurintsurg-2021-018560.R1

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☒ I certify that I have answered every question and have not altered the wording of any of the questions on this form.

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Date: 2/26/2022

Your Name: F.J.A. Meijer

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