Thrombus Imaging Characteristics and Outcomes in Acute Ischemic Stroke Patients Undergoing Endovascular Treatment

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Background and Purpose—Thrombus imaging characteristics have been reported to be useful to predict functional outcome and reperfusion in acute ischemic stroke. However, conflicting data about this subject exist in patients undergoing endovascular treatment. Therefore, we aimed to evaluate whether thrombus imaging characteristics assessed on computed tomography are associated with outcomes in patients with acute ischemic stroke treated by endovascular treatment.

Methods—The MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) Registry is an ongoing, prospective, and observational study in all centers performing endovascular treatment in the Netherlands. We evaluated associations of thrombus imaging characteristics with the functional outcome (modified Rankin Scale at 90 days), mortality, reperfusion, duration of endovascular treatment, and symptomatic intracranial hemorrhage using univariable and multivariable regression models. Thrombus characteristics included location, clot burden score (CBS), length, relative and absolute attenuation, perviousness, and distance from the internal carotid artery terminus to the thrombus. All characteristics were assessed on thin-slice (≤2.5 mm) noncontrast computed tomography and computed tomography angiography, acquired within 30 minutes from each other.

Results—In total, 408 patients were analyzed. Thrombus with distal location, higher CBS, and shorter length were associated with better functional outcome (adjusted common odds ratio, 3.3; 95% CI, 2.0–5.3 for distal M1 occlusion compared with internal carotid artery occlusion; adjusted common odds ratio, 1.15; 95% CI, 1.07–1.24 per CBS point; and adjusted common odds ratio, 0.96; 95% CI, 0.94–0.99 per mm, respectively) and reduced duration of endovascular procedure (adjusted coefficient B, −14.7; 95% CI, −24.2 to −5.1 for distal M1 occlusion compared with internal carotid artery occlusion; adjusted coefficient B, −8.5; 95% CI, −14.5 to −2.4 per CBS point; and adjusted coefficient B, 7.3; 95% CI, 2.9–11.8 per mm, respectively). Thrombus perviousness was associated with better functional outcome (adjusted common odds ratio, 1.01; 95% CI, 1.00–1.02 per Hounsfield units increase). Distal thrombi were associated with successful reperfusion (adjusted odds ratio, 2.6; 95% CI, 1.4–4.9 for proximal M1 occlusion compared with internal carotid artery occlusion).

Conclusions—Distal location, higher CBS, and shorter length are associated with better functional outcome and faster endovascular procedure. Distal thrombus is strongly associated with successful reperfusion, and a pervious thrombus is associated with better functional outcome. **(*Stroke*. 2019;50:2057-2064. DOI: 10.1161/STROKEAHA.118.024247.)**

Key Words: computed tomography angiography ■ endovascular procedure ■ reperfusion ■ stroke ■ thrombectomy ■ thrombus

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†A list of all MR CLEAN Registry Investigators is given in the online-only Data Supplement.

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Thrombus location is the only thrombus imaging characteristic currently evaluated in the assessment of patients with acute ischemic stroke (AIS) in daily practice.[1,2] However, recent studies have reported other thrombus imaging characteristics that may be useful for predicting functional outcome and reperfusion in AIS.[3–6] Associations between thrombus imaging characteristics and these outcomes have been evaluated primarily in patients undergoing intravenous thrombolysis (IVT).[3,6–9] Conflicting data exist about the associations between thrombus characteristics and outcomes after endovascular treatment (EVT) of AIS.

Because EVT has emerged as the mainstay of treatment for AIS because of proximal intracranial occlusions, identification of imaging biomarkers that predict EVT outcomes would be highly relevant to acute stroke management. The aim of the present study is to evaluate the associations between thrombus imaging characteristics and outcomes in patients undergoing EVT in the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) Registry.

Methods

Patient Selection

The MR CLEAN Registry is an ongoing, prospective, observational, multicenter study at 16 intervention hospitals in the Netherlands. It includes all patients with AIS who underwent EVT since the completion of the MR CLEAN trial in March 2014. Patients were treated with IVT before EVT if eligible. The central medical ethics committee of the Erasmus Medical Centre Rotterdam, the Netherlands, evaluated the study protocol and granted permission (MEC-2014–235) to perform the study as a registry.[10] For the purpose of this analysis, we used the following inclusion criteria: intracranial proximal occlusion in the anterior arterial circulation; age ≥18 years; groin puncture within 6.5 hours after stroke onset; and treatment in an MR CLEAN trial center. The current study reports on patients registered in the MR CLEAN Registry between March 2014 and June 2016. Source data of this study are available from the corresponding author on reasonable request.

Imaging Analyses

Patients underwent the MR CLEAN Registry imaging protocol (Methods I in the online-only Data Supplement). We included patients with available thin-slice (≤2.5 mm) baseline noncontrast computed tomography (NCCT) and computed tomography angiography (CTA), acquired within 30 minutes from each other. All baseline NCCT and CTA scans were automatically aligned using rigid registration with Elastix software.[11] In case of suboptimal alignment, adjustments were performed by manual rigid registration, with Mevislab (by Dr Dutra). Scans with uncorrectable registration errors, artifacts, excessive noise, or poor contrast opacification on CTA were excluded. To prevent bone artifacts that might interfere with the thrombus attenuation measurements, we excluded patients with an intracranial arterial occlusion restricted to the petrous, cavernous, and clinoid segments of the internal carotid artery (ICA). Calcified thrombi were also excluded because of their higher attenuation values (related to calcium composition) compared with the attenuation values of noncalcified thrombi, and because calcification produces streak and partial volume artifacts, which can cause overestimation of the thrombus size.

We evaluated the following thrombus imaging characteristics: location, clot burden score (CBS), absolute and relative attenuation, perviousness, length, and distance from the ICA terminus to the thrombus (DT). The observers were blinded for all clinical data except for symptom side. The assessments of thrombus imaging characteristics are detailed in the online-only Data Supplement (Methods II and Figures I and II in the online-only Data Supplement).

Outcome Measures

The primary outcome was defined as the modified Rankin Scale (mRS) score at 90 days. The mRS is a 7-point scale ranging from 0 (no symptoms) to 6 (death). Secondary outcomes were good functional outcome (score of 0–2 on the mRS), mortality at 90 days, reperfusion status assessed on digital subtraction angiography according to the extended Thrombolysis in Cerebral Infarction (eTICI) score,[12] duration of EVT, and symptomatic intracranial hemorrhage (sICH). The eTICI score was assessed by the MR CLEAN Registry imaging core lab, based on the degree of reperfusion in the downstream territory of the original occlusion on digital subtraction angiography. The eTICI score ranges from 0 (no reperfusion or antegrade flow beyond occlusion site) to 3 (complete reperfusion), including a 2C category (90%–99% reperfusion).[12,13] Successful reperfusion status was defined as eTICI scores of 2b, 2c, or 3.

Duration of EVT was determined in patients who underwent an actual thrombectomy, and this outcome was measured from artery puncture (time zero) to the time that successful reperfusion was achieved or to the end of procedure if no successful reperfusion was achieved. The following patients were not considered in the assessments of duration of EVT: no target occlusion depicted on digital subtraction angiography (recanalization of primary occlusion on the first run), or unreachable target occlusion (ie, due to vascular tortuosity, stenosis, or occlusion of the carotid artery).

Statistical Analysis

Subject Characteristics

We present the baseline clinical and imaging characteristics of our study population and of the full published MR CLEAN Registry data set[10] using median and interquartile range (IQR) for continuous variables and frequencies and percentages for categorical variables. Correlation chart was performed to summarize the data about the distribution of each thrombus imaging characteristics, and to investigate whether thrombus imaging characteristics are correlated to each other, using the Spearman correlation coefficient for non-normally distributed data and the Pearson correlation coefficient for normally distributed data.

Associations Between Thrombus Imaging Characteristics and Outcomes

Univariable and multivariable regression models were used to evaluate the association between thrombus imaging characteristics and outcomes. Ordinal logistic regression was used to assess the associations between thrombus characteristics and mRS as primary outcome measurement, resulting in an unadjusted and adjusted common odds ratio (common OR and adjusted common OR, respectively) for a 1-step shift towards better functional outcome. Unadjusted and adjusted binary logistic regression models were used to assess the associations with good functional outcome, successful reperfusion, mortality, and sICH as secondary outcomes. Unadjusted and adjusted linear regressions were performed to evaluate the associations with a duration of EVT as a secondary outcome measurement. We adjusted for age, prestroke mRS, time from stroke onset to artery puncture, IVT, diabetes mellitus, previous myocardial infarction, previous stroke, hypertension, and atrial fibrillation. Use of anticoagulants and antiplatelet agents was added to the adjustments for the analyses with reperfusion status, duration of EVT, and sICH as outcome measurements. In developing the multivariable model, we did not consider Alberta Stroke Program Early CT Score, baseline National Institutes of Health Stroke Scale score, and collaterals as potential confounders because we assumed they were in the causal pathway between thrombus and outcomes, as the following: proximal arterial thrombi (low CBS, short DT, and longer thrombus length) are hypothesized to

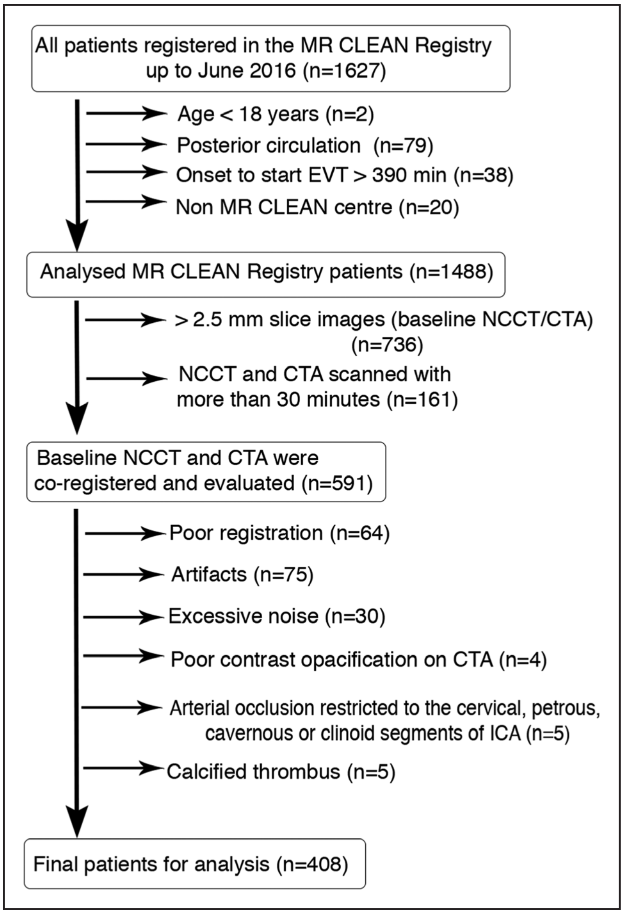

Figure. Flow chart of the patient selection process. CTA indicates computed angiography tomography; EVT, endovascular treatment; ICA, internal carotid artery; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; and NCCT, noncontrast computed tomography.

cause impaired collateral filling[14,15] and greater areas of hypodensity on NCCT, consequently leading to a lower Alberta Stroke Program Early CT Score, higher severity stroke score scale (National Institutes of Health Stroke Scale score),[16] poorer functional outcome and higher chances of sICH. Interaction terms between primary treatment modalities and thrombus burden (CBS and length) were performed for the achieved outcomes.

All statistical analyses were performed using R (R Foundation for Statistical Computing, version 3.5.1). For the regression analyses, missing data were imputed using multiple imputation.[17] Missing mRS scores at 90 days or mRS scores of 0–5 assessed at <30 days from stroke were imputed. We performed multiple imputation using the variables listed in the online-only Data Supplement (Table I in the online-only Data Supplement).

Results

Subject Characteristics

Overall, 408 patients were included in our analysis (Figure). The median age was 70 years (IQR, 59–80), 54% (n=222) were male, and the median National Institutes of Health Stroke Scale score was 16 (IQR, 11–20). Of all patients eligible for EVT, 87% (n=356/408) underwent EVT with thrombus retrieval, and the most used primary treatment modality was the stent retriever (75%). The median duration of EVT was 62 minutes (IQR, 44–90 minutes). Thrombus location was the most commonly distal M1 (36%) followed by ICA (25%), and proximal M1 (24%). CBS of 8 to 10 was observed in 29% of patients (n=102/353). Median values of thrombus length, DT, absolute attenuation, relative attenuation, and perviousness were 12.7 mm (IQR, 8.7–17.9 mm), 8.3 mm (IQR, 0–14.4 mm), 51.8 Hounsfield units (HU; IQR 45–58 HU), 1.33 (IQR, 1.19–1.52), and 5 HU (−0.2 to 12.3 HU). IVT was administered in 77% of patients (n=314). Baseline characteristics in our cohort were similar to the full MR CLEAN Registry data set[10] (Table 1).

Results of data distribution and correlation analyses among thrombus characteristics are detailed in the online-only Data Supplement (Figure III in the online-only Data Supplement). Longer thrombi were statistically correlated with shorter DT, more proximal location, lower CBS, lower perviousness, and higher absolute attenuation (correlation coefficients of −0.44, −0.45, −0.53, −0.23, and +0.35, respectively).

Associations Between Thrombus Imaging Characteristics and Outcomes

Primary Outcome

More distal thrombus location and higher CBS values were significantly associated with improved functional outcome in the unadjusted and adjusted models. Thrombus located in the distal M1 segment had an increased odds of having improved functional outcome compare to ICA thrombus (adjusted common OR, 3.27; 95% CI, 2.03–5.29). Unadjusted and adjusted common ORs per point CBS were 1.12 (95% CI, 1.04–1.20) and 1.15 (95% CI, 1.07–1.24). A longer thrombus was associated with reduced likelihood of improved functional outcome (adjusted common OR, 0.96; 95% CI, 0.94–0.99 per mm). An increased chance of improved functional outcome was observed in a more pervious thrombus (adjusted common OR, 1.01; 95% CI, 1.00–1.02 per HU increase) in the adjusted analyses (Table 2).

Secondary Outcomes

Favorable Functional Outcome (mRS Score of 0–2)

Favorable functional outcome was observed in 38% of patients (n=155). Associations between thrombus imaging characteristics and dichotomized functional outcome (mRS score of 0–2) were similar to the primary functional outcome analyses, as listed in Table 2. A statistically significant interaction was observed between CBS and primary EVT modality. For higher CBS, patients treated with stent-retriever had increased chances of having favorable functional outcome compared with others EVT modalities (Figure IV in the online-only Data Supplement). No statistically significant interaction was observed between thrombus length and primary treatment modality.

Mortality at 90 Days

Death at 90 days was observed in 26.2% of patients (n=107). This outcome was significantly associated with more proximally located thrombi (adjusted OR [aOR], 0.29; 95% CI, 0.14–0.61 for proximal M1 thrombi compared with ICA occlusions), lower CBS (aOR, 0.85; 95% CI, 0.77–0.95), and longer thrombus length (aOR, 1.04; 95% CI, 1.01–1.07), as detailed in Table 2.

Table 1. Baseline Characteristics of the Registry Subgroup Included in Our Study and of the MR CLEAN Registry Database

	MR CLEAN Registry Subgroup Included (n=408)	Full MR CLEAN Registry Database (n=1488)
Baseline clinical variables		
Age, median (IQR)	70 (59 to 80); n=408	71 (60 to 80); n=1488
Sex (men), n (%)	222 (54.4); n=408	794 (53.3); n=1488
NIHSS baseline, median (IQR)	16 (11 to 20); n=398	16 (11 to 20); n=1458
SBP, mm Hg, median (IQR)	149 (131 to 163); n=397	150 (125 to 175); n=1446
DBP, mm Hg, median (IQR)	80 (70 to 90); n=396	80 (70 to 91); n=1439
Medical history, n (%)		
Diabetes mellitus	75 (18.6); n=404	255 (17.2); n=1479
Hypertension	202 (50.4); n=401	745 (50.7); n=1469
Dyslipidemia	116 (29.1); n=398	431 (29.9); n=1441
Current smoking	97 (24); n=404	338 (22.9); n=1474
Previous stroke	63 (15.6); n=404	249 (16.8); n=1479
Previous myocardial infarction	73 (18.4); n=397	228 (15.6); n=1459
Previous atrial fibrillation	84 (20.9); n=401	327 (22.3); n=1466
Anticoagulation	131 (33.2); n=395	493 (33.6); n=1469
Prestroke modified Rankin Scale score, n (%)		
0	253/397 (63.7)	991/1461 (67.8)
1	52/397 (13.1)	189/1461 (12.9)
2	36/397 (9.1)	110/1461 (7.5)
≥3	56/397 (14.1)	171/1461 (11.7)
Imaging variables		
ASPECTS subgroups, n (%)		
0–4	23/408 (5.6)	93/1423 (6.5)
5–7	101/408 (24.7)	341/1423 (24)
8–10	284/408 (69.6)	989/1423 (69.5)
Collateral score, n (%)		
0% filling of the occluded territory	32/397 (8.1)	97/1381 (7)
>0% and ≤50% filling of the occluded territory	127/397 (32.0)	461/1381 (33.3)
>50% and <100% filling of the occluded territory	158/397 (39.8)	535/1381 (38.7)
100% filling of the occluded territory	80/397 (20.2)	282/1381 (20.9)
Thrombus location, n (%)		
ICA	101/407 (24.8)	395/1422 (27.8)
Proximal M1	97/407 (23.8)	364/1422 (25.6)
Distal M1	148/407 (36.4)	462/1422 (32.4)
M2	51/407 (12.5)	175/1422 (12.3)
M3	4/407 (1.0)	9/1422 (0.6)
A1/A2	6/407 (1.4)	6/1422 (0.4)
Clot burden score, n (%)		
0–4	97/353 (27.5)	371/1238 (30)
5–7	154/353 (43.6)	510/1238 (41.2)
8–10	102/353 (28.9)	357/1238 (28.8)
DT, median (IQR)	8.3 (0 to 14.4)	NA
Thrombus length, mm, median (IQR)	12.75 (8.7 to 17.9); n=408	NA
Thrombus absolute attenuation (HU), median (IQR)	51.8 (45 to 58); n=408	NA
Thrombus relative attenuation, median (IQR)	1.33 (1.19 to 1.52); n=408	NA
Thrombus perviousness (HU), median (IQR)	5.02 (−0.2 to 12.3); n=408	NA
Treatment variables		
Intravenous thrombolysis, n (%)	314/408 (77)	1161/1488 (78.0)
Time to artery puncture (minutes), median (IQR)	195 (150 to 251); n=408	208 (160 to 265); n=1488
Performed procedure, n (%)		
EVT with thrombus retrieval	356/408 (87.3)	1280/1488 (86)
Target occlusion not accessible	21/408 (5.1)	80/1488 (5.4)
No target occlusion depicted on DSA	27/408 (6.6)	119/1488 (8)
Other (procedure ended before attempt)	4/408 (1)	80/1488 (5.4)
Primary treatment modality, n (%)	334/356 (93.8)	1220/1280 (95.3)
Stent retriever	252/334 (75.4)	969/1220 (79.4)
Aspiration device	65/334 (19.4)	207/1220 (17)
Local delivery of the thrombolytic agent	4/334 (1.2)	10/1220 (0.8)
Different approach	13/334 (3.8)	34/1220 (2.8)
Duration of EVT (minutes), median (IQR)	62 (44 to 90); n=319	64 (40 to 90); n=1331

(*Continued*)

A1/A2 indicates occlusions in segment A1 or A2 of the anterior cerebral artery; ASPECTS, Alberta Stroke Program Early CT Score; DBP, diastolic blood pressure; DSA, digital subtraction angiography; DT, distance from the internal carotid artery terminus to the thrombus; EVT, endovascular treatment; HU, Hounsfield units; ICA, internal carotid artery; IQR, interquartile range; M1, segment M1 of the middle cerebral artery; M2, segment M2 of the middle cerebral artery; M3, segment M3 of the middle cerebral artery; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; NA, not available; NIHSS, National Institutes of Health Stroke Scale; and SBP, systolic blood pressure.

Table 2. Associations of Thrombus Imaging Characteristics With Functional Outcome (Modified Rankin Scale) and Mortality at 90 Days

	Functional Outcome (mRS)								Mortality at 90 Days			
	Ordinal Regression (Shift to Better Outcome)				Binary Regression (Good Outcome, mRS Score of 0–2)				Binary Regression (Death)			
	Unadjusted Model		Adjusted Model*		Unadjusted Model		Adjusted Model*		Unadjusted Model		Adjusted Model*	
	cOR	95% CI	acOR	95% CI	OR	95% CI	aOR	95% CI	OR	95% CI	aOR	95% CI
Site of occlusion												
ICA	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Proximal M1	1.97†	1.20–3.24†	2.44†	1.44–4.13†	1.88†	1.03–3.41†	2.35†	1.21–4.57†	0.44†	0.24–0.84†	0.29†	0.14–0.61†
Distal M1	2.44†	1.55–3.86†	3.27†	2.03–5.29†	2.26†	1.30–3.89†	3.17†	1.72–5.85†	0.35†	0.19–0.61†	0.19†	0.09–0.38†
M2	1.52	0.82–2.82	2.13†	1.11–4.09†	1.49	0.72–3.08	2.29†	1.02–5.14†	0.79	0.38–1.59	0.52	0.21–1.23
Other‡	2.01	0.52–7.81	3.91	0.96–15.84	2.05	0.43–9.78	2.98	0.47–18.85	0.63	0.08–3.11	0.21	0.01–2.30
CBS	1.12†	1.04–1.20†	1.15†	1.07–1.24†	1.12†	1.03–1.21†	1.16†	1.06–1.28†	0.91†	0.83–0.99†	0.85†	0.77–0.95†
DT	1.00	0.98–1.02	1.01	0.99–1.03	1.00	0.98–1.02	1.01	0.99–1.04	1.00	0.98–1.02	0.98	0.95–1.01
Length	0.98	0.96–1.00	0.96†	0.94–0.99†	0.98	0.96–1.01	0.96†	0.93–0.99†	1.01	0.98–1.04	1.04†	1.01–1.07†
Perviousness	1.01	0.99–1.02	1.01†	1.00–1.02†	1.01	0.99–1.02	1.01	0.99–1.02	1.00	0.99–1.01	0.99	0.98–1.01
Absolute attenuation	1.02	0.99–1.03	1.01	0.98–1.02	1.02	1.00–1.04	1.01	0.98–1.04	0.98	0.96–1.01	1.00	0.97–1.03
Relative attenuation	1.01	0.99–1.03	1.00	0.98–1.02	1.66	0.85–3.24	1.72	0.82–3.60	1.27	0.62–2.62	1.64	0.72–3.73

acOR indicates adjusted common odds ratio; aOR, adjusted odds ratio; CBS, clot burden score; cOR, common odds ratio; distal M1, distal M1 segment of middle cerebral artery; DT, distance from the internal carotid artery terminus to the thrombus; ICA, internal carotid artery; M2, M2 segment of middle cerebral artery; mRS, modified Rankin Scale at 90 d; proximal M1, proximal M1 segment of middle cerebral artery; and OR, odds ratio.

*Adjusted for: age; prestroke mRS; intravenous thrombolysis; time from onset to groin puncture; previous history of stroke, atrial fibrillation, hypertension, diabetes mellitus, and myocardial infarction.

†*P* value <0.05.

‡M3 segment of middle cerebral artery or anterior cerebral artery.

Reperfusion Status

In patients who underwent thrombectomy, successful reperfusion was achieved in 60% (n=215/356). Only site of occlusion was significantly associated with successful reperfusion (Table 3). Proximal and distal M1 thrombi were associated with an increased likelihood of successful reperfusion compared with ICA thrombi (aOR, 2.60; 95% CI, 1.42–4.97 for proximal M1 thrombi and aOR, 1.96; 95% CI, 1.14–3.44 for distal M1 thrombi). No significant associations were observed between reperfusion and thrombus location in M2 or other segments. However, a trend towards an increased chance of successful reperfusion with a more distal thrombus location was observed.

Duration of Endovascular Procedure

Duration of EVT was significantly associated with thrombus location, CBS, and thrombus length (Table 3). Endovascular procedure was 14 to 15 minutes faster for distal M1 occlusions compared with ICA occlusions (adjusted coefficient B, −14.7; 95% CI, −24.2 to −5.1). For each 1 mm increase in thrombus length, there was an increase of ≈7 to 8 minutes in EVT duration (adjusted coefficient B, 7.3; 95% CI, 2.9–11.8). An increase of 1 point in CBS was associated with a reduction of ≈8 to 9 minutes of the duration of EVT (adjusted coefficient B, −8.5; 95% CI, −14.5 to −2.4).

Symptomatic Intracranial Hemorrhage

No significant associations were observed between thrombus imaging characteristics and sICH (Table 3).

Discussion

In the MR CLEAN Registry, thrombus imaging characteristics are associated with outcomes after EVT. A lower thrombus burden (ie, distal occlusion, shorter thrombus length, and higher CBS value) was associated with better functional outcome and faster endovascular procedure. A more pervious thrombus was also associated with favorable functional outcome. Only site of thrombus occlusion was significantly associated with reperfusion, in which a distal thrombus had a higher chance of successful reperfusion. We also demonstrated that a shorter thrombus is more likely to have a distal location, higher CBS, increased perviousness, and lower attenuation.

Associations of thrombus imaging characteristics with functional outcome and recanalization are well-described in patients treated with IVT, in whom failed recanalization and worse functional outcome were associated with low CBS, proximal thrombus location, longer thrombus length, and lower perviousness.[3,6,8,9] However, conflicting data about thrombus imaging characteristics and outcomes are observed in EVT. In accordance with our study, thrombi with a more distal location, shorter length, and higher CBS have been reported to be associated with improved functional outcome in patients who underwent EVT.[6,18–20] Conversely, some studies reported no association between functional outcome and thrombus length after EVT, however, they included only MCA thrombi.[21,22] In accordance with our study, longer endovascular procedural time has been associated with longer thrombus length.[18] The associations of thrombus characteristics with

Table 3. Associations of Thrombus Imaging Characteristics With Successful Reperfusion, Duration of EVT, and sICH

	Successful Reperfusion				Duration of EVT				sICH			
	Binary Regression				Linear Regression				Binary Regression			
	Unadjusted Model		Adjusted Model*		Unadjusted Model		Adjusted Model*		Unadjusted Model		Adjusted Model*	
	OR	95% CI	aOR	95% CI	B	95% CI	B	95% CI	OR	95% CI	aOR	95% CI
Site of occlusion												
ICA	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
Proximal M1	2.37†	1.35 to 4.25†	2.60†	1.42 to 4.97†	−14.58†	−19.9 to −4.3†	−14.62†	−25.1 to −4.1†	0.45	0.13 to 1.43	0.33	0.09 to 1.20
Distal M1	1.87†	1.12 to 3.13†	1.96†	1.14 to 3.44†	−15.17†	−24.6 to −6.3†	−14.68†	−24.2 to −5.1†	0.43	0.15 to 1.25	0.32	0.10 to 1.02
M2	1.34	0.68 to 2.65	1.55	0.74 to 3.32	−16.58†	−29.9 to −3.2†	−10.86	−24.3 to 2.6	0.42	0.08 to 2.00	0.38	0.07 to 1.98
Other‡	1.47	0.30 to 7.79	0.87	0.13 to 5.63	−31.58†	−60.6 to −2.6†	−21.32	−52.8 to 10.18	0.00	NA	0.00	NA
CBS	1.05	0.97 to 1.13	1.05	0.97 to 1.14	−9.18†	−15.0 to −3.3†	−8.47†	−14.5 to −2.4†	0.95	0.79 to 1.13	0.92	0.76 to 1.12
DT	0.98	0.96 to 1.01	0.98	0.95 to 1.01	−4.57	−10.3 to 1.2	−3.17	−9.0 to 2.7	0.98	0.91 to 1.06	0.99	0.90 to 1.08
Length	0.98	0.95 to 1.01	0.97	0.94 to 1.01	8.20†	3.7 to 12.7†	7.33†	2.9 to 11.8†	1.03	0.98 to 1.09	1.04	0.98 to 1.10
Perviousness	0.99	0.98 to 1.01	0.99	0.98 to 1.01	−1.22	−4.1 to 1.7	−0.61	−3.6 to 2.4	1.13	0.92 to 1.39	1.16	0.94 to 1.43
Absolute attenuation	1.01	0.98 to 1.03	1.00	0.98 to 1.02	4.62	−0.2 to 9.6	3.25	−1.8 to 8.3	1.01	0.99 to 1.03	1.01	0.99 to 1.03
Relative attenuation	1.31	0.67 to 2.57	1.35	0.65 to 2.79	0.27	−4.0 to 4.6	0.86	−3.6 to 5.3	0.91	0.21 to 4.04	0.84	0.16 to 4.25

aOR indicates adjusted odds ratio; B, regression coefficient B; CBS, clot burden score; distal M1, distal M1 segment of middle cerebral artery; DT, distance from the internal carotid artery terminus to the thrombus; EVT, endovascular treatment; ICA, internal carotid artery; M2, M2 segment of middle cerebral artery; proximal M1, proximal M1 segment of middle cerebral artery; OR, odds ratio; and sICH, symptomatic intracerebral hemorrhage.

*Adjusted for: age; prestroke mRS; intravenous thrombolysis; time from onset to groin puncture; use of anticoagulants and antiplatelet agents; previous history of stroke, atrial fibrillation, hypertension, diabetes mellitus, and myocardial infarction.

†*P* value <0.05.

‡M3 segment of middle cerebral artery or anterior cerebral artery.

functional outcome and duration of EVT could be related to 2 possible mechanisms: (1) As demonstrated in our study, longer thrombi had a lower CBS and a more proximal location, and by virtue of their larger thrombus volume may simply be more difficult to retrieve, requiring more attempts and prolonging the procedural time, as shown previously[18,23] and (2) ICA and proximal M1 occlusions may result in decreased collateral flow via the anterior cerebral artery pial vessels[14,15] or lead to greater stroke volume because of the involvement of the lenticulostriate vessels, consequently leading to a higher NIHHS score and poor functional outcome.[16,24]

Conflicting data about the association of thrombus attenuation and perviousness with outcomes have been reported. Some studies have reported that successful reperfusion after EVT is more likely in hyperdense thrombi.[25,26] However, other reports, as well as the 2 largest published cohorts of thrombus attenuation assessments, are in line with our findings, showing that thrombus attenuation was not associated with reperfusion,[6,21,27,28] functional outcome, duration of EVT and sICH.[21] Different results about thrombus attenuation assessment might be because of variability in hematocrit levels, vessel calcification, and time of CT scan acquisition.[29] Further studies need to be performed before concluding that thrombus density is a not predictor of successful reperfusion and to evaluate the utility of this parameter in thrombectomy planning.

Thrombus perviousness has been associated with successful recanalization and improved functional outcome after IVT.[3,5,19] We observed an association between improved functional outcome and more pervious thrombi, yet no significant association was observed between thrombus perviousness and reperfusion after EVT. Likewise, despite a trend towards an increased chance of successful reperfusion with a more distal thrombus location, we observed no significant association between reperfusion and thrombus located in M2 or more distal segment. The absence of a significant effect of both thrombus perviousness and thrombus located in M2 or more distal segment on reperfusion may share an explanation since pervious thrombus, and more distal thrombus location was reported to be associated to one another,[3] as demonstrated in our study. Thrombi located in the M2 or M3 segments, and therefore, more pervious thrombi, are technically more difficult to reach during EVT because of their distal location and to the smaller diameter of these MCA segments.[30,31] Moreover, the use of IVT before EVT might increase the chance of thrombus fragility and thrombus migration especially in more pervious thrombi, leading to a higher frequency of clot inaccessibility by EVT, or thrombus fragmentation and thereby decreased eTICI scores.[32] Conversely, some studies have reported that IVT softens thrombi and thereby facilitates EVT.[33] Given that more pervious thrombi may be more sensitive to IVT, this effect may increase the chance of reperfusion after EVT.[19] All these together might provide an explanation for the neutral effect of thrombus perviousness or distal location on reperfusion after EVT. However, further research is needed on this topic.

Our study has limitations. Many patients were excluded because of the absence of thin-section NCCT or CTA, prolonged time between the scanned NCCT and CTA (>30 minutes), poorly co-registered scans and poorly image quality. This might be explained by the fact the MRCLEAN Registry is a multicenter study, and not all centers saved or performed thin-slice NCCT/CTA, especially primary stroke centers. However, despite excluding a considerable number of patients, our study population is the largest sample to date about thrombus imaging characteristics in AIS treated by EVT, and it was a reliable sample of the entire MR CLEAN Registry, demonstrating similar baseline characteristics. An additional limitation is the use of CTA to assess CBS and thrombus length, which may be influenced by the backflow of a poor collateral circulation. However, overestimated CBS and length may strengthen the prognostic value of these thrombus characteristics because poor collaterals are known to be associated with poor outcomes.[4,18] For a more reliable measurement, dynamic CTA imaging might be a valuable alternative. Furthermore, accurate measurements of thrombus length are limited in curved or branched arteries. Although thrombus volume has been described to be a more accurate measure for thrombus burden, irrespective of angioarchitecture and collaterals, we think thrombus length and CBS are reasonable quantitative parameters for thrombus burden, and they might be more feasible in clinical practice in terms of rapidity and ease of use.[18,22] Differences in operator techniques, thrombectomy devices,[10] imaging parameters across institutions, may have led to distinct clot-retriever interactions and might have interfere with thrombus imaging assessments. However, this aspect of the study makes it more generalizable to real-world clinical practice. In our population, stent-retriever was by far the most performed modality, which may be a bias in the statistical analyses because of the unbalanced variation of EVT modalities. Our study does not account for operator differences. Further studies need to be done analyzing this operator and device variables. Finally, our data were gathered in routine clinical practice. Registries, in general, are prone to missing and incorrect values. However, all data were verified by our study coordinators and missing values were imputed.

Conclusions

Imaging characteristics related to thrombus burden are associated with functional outcome and duration of endovascular procedure after thrombectomy for AIS. Distal site of occlusion, shorter thrombi, and higher CBS is associated with better functional outcome and faster endovascular procedure. Site of occlusion is strongly associated with reperfusion status, and pervious thrombus is associated with favorable functional outcome.

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