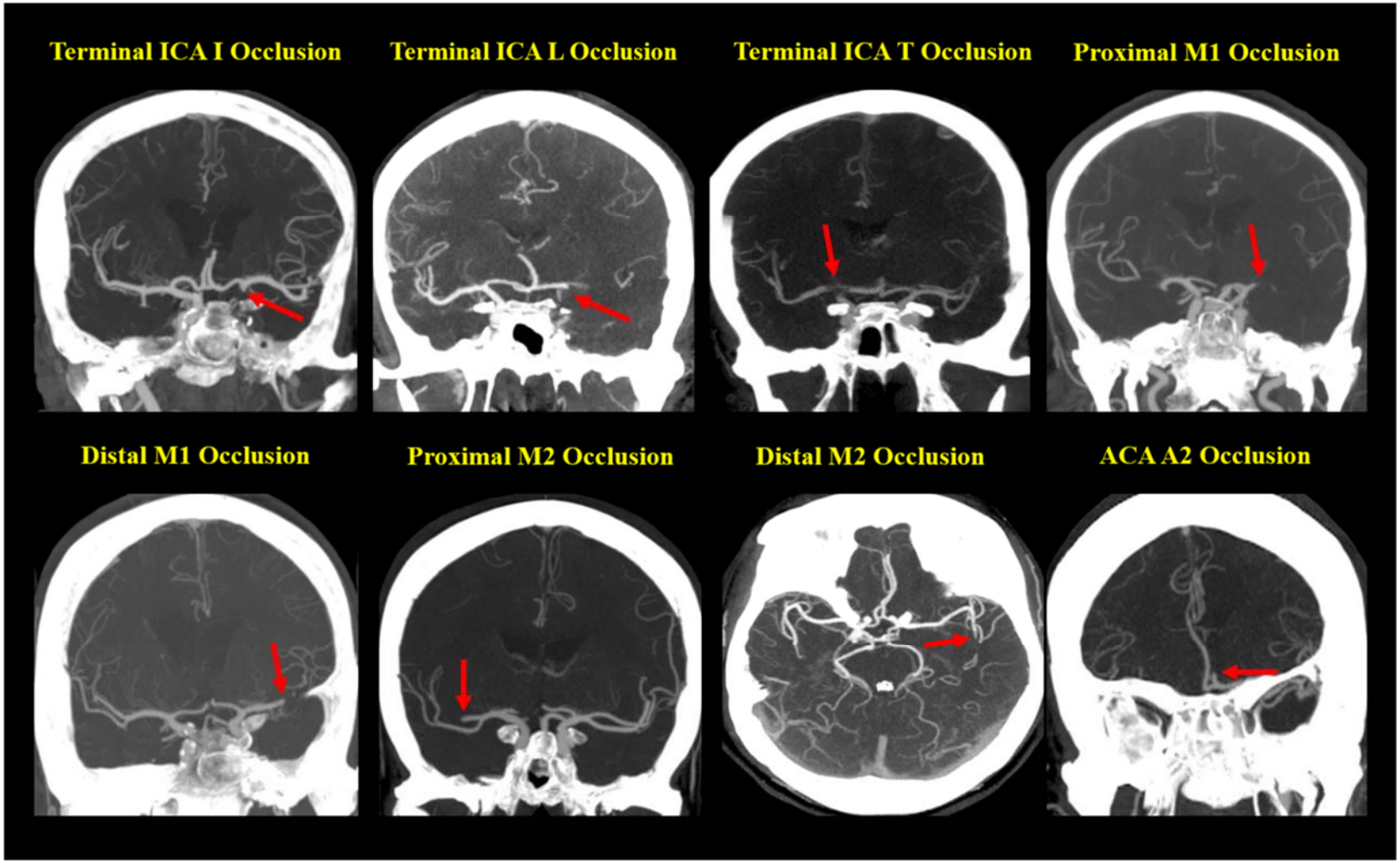
Supplementary Online Content

Menon BK, Al-Ajlan FS, Najm M, et al; for the INTERRSeCT Study Investigators. Association of clinical, imaging, and thrombus characteristics with recanalization of visible intracranial occlusion in patients with acute ischemic stroke. *JAMA*. doi:10.1001/jama.2018.12498

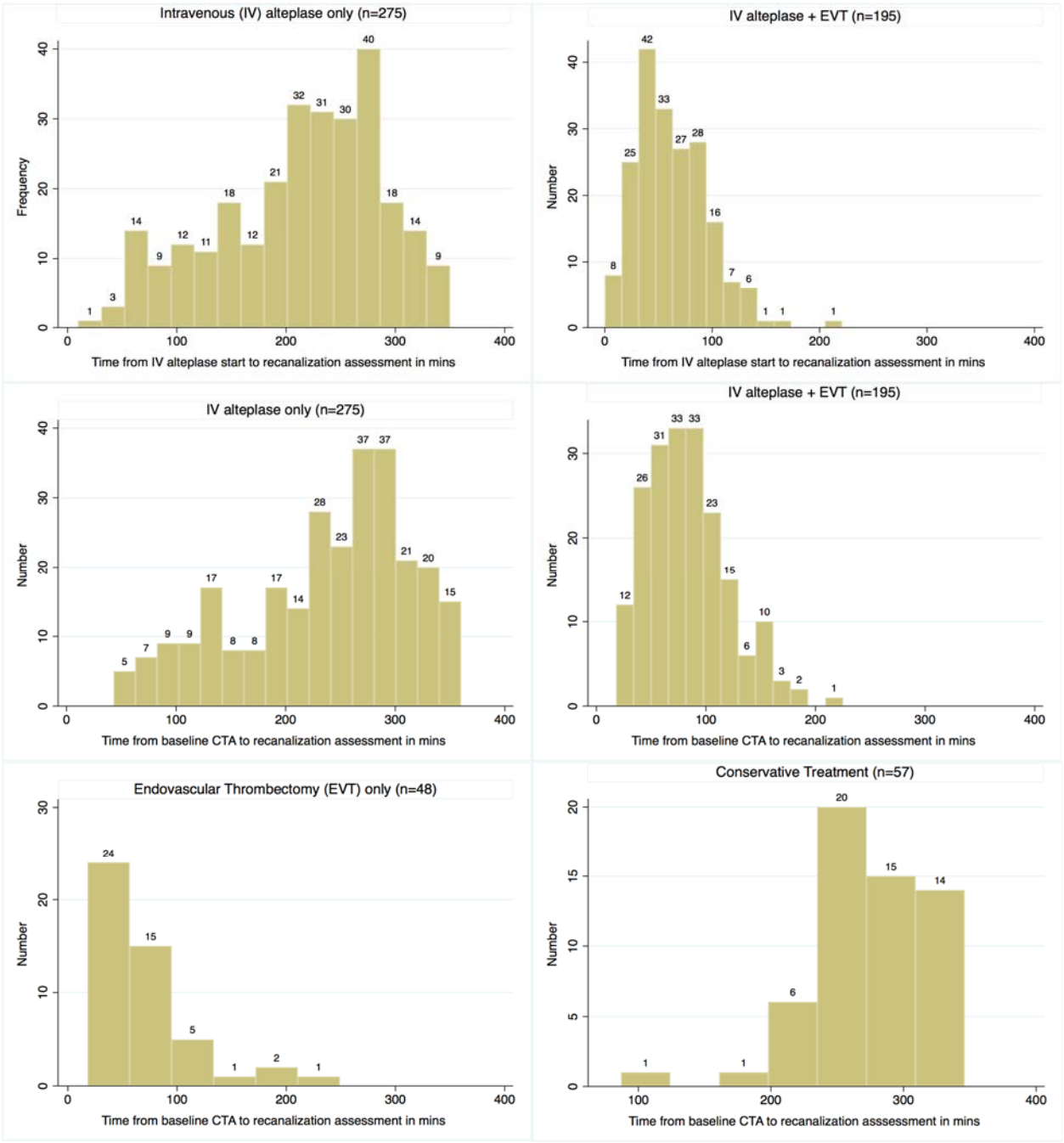
This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1: Location of intracranial thrombus identified using CT angiography.

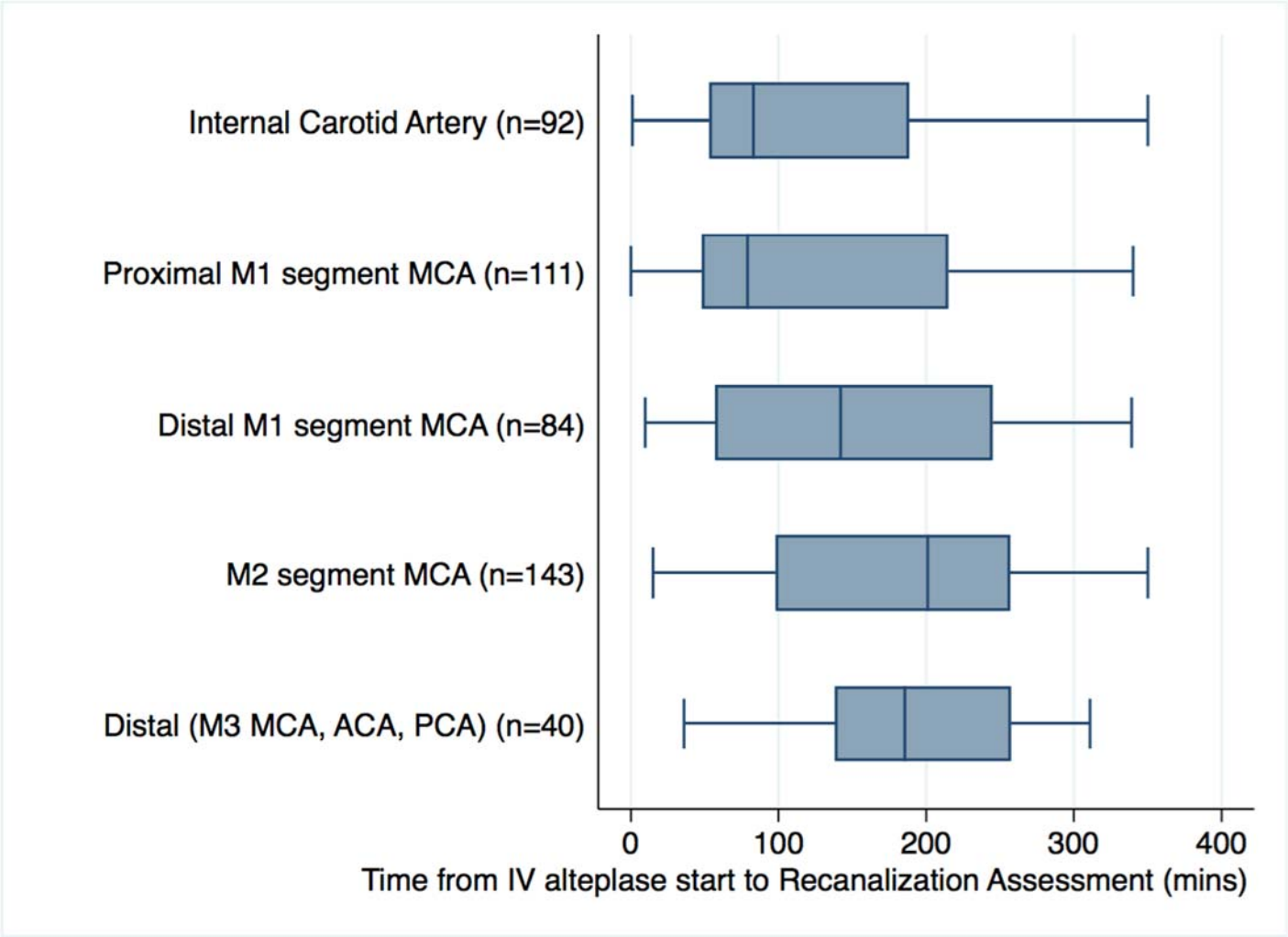
All images are coronal plane acquisitions except for the distal M2 segment occlusion identified on the axial plane. Arterial segments were identified as per template provided by Goyal et al (J Neurointerv Surg. 2016 Jan 11. doi: 10.1136/neurintsurg-2015-012191)



eFigure 2. Time from intravenous alteplase start or from baseline CTA to recanalization assessment in the different treatment groups in the study, namely intravenous alteplase only, endovascular thrombectomy only, intravenous alteplase + endovascular thrombectomy and conservative treatment.

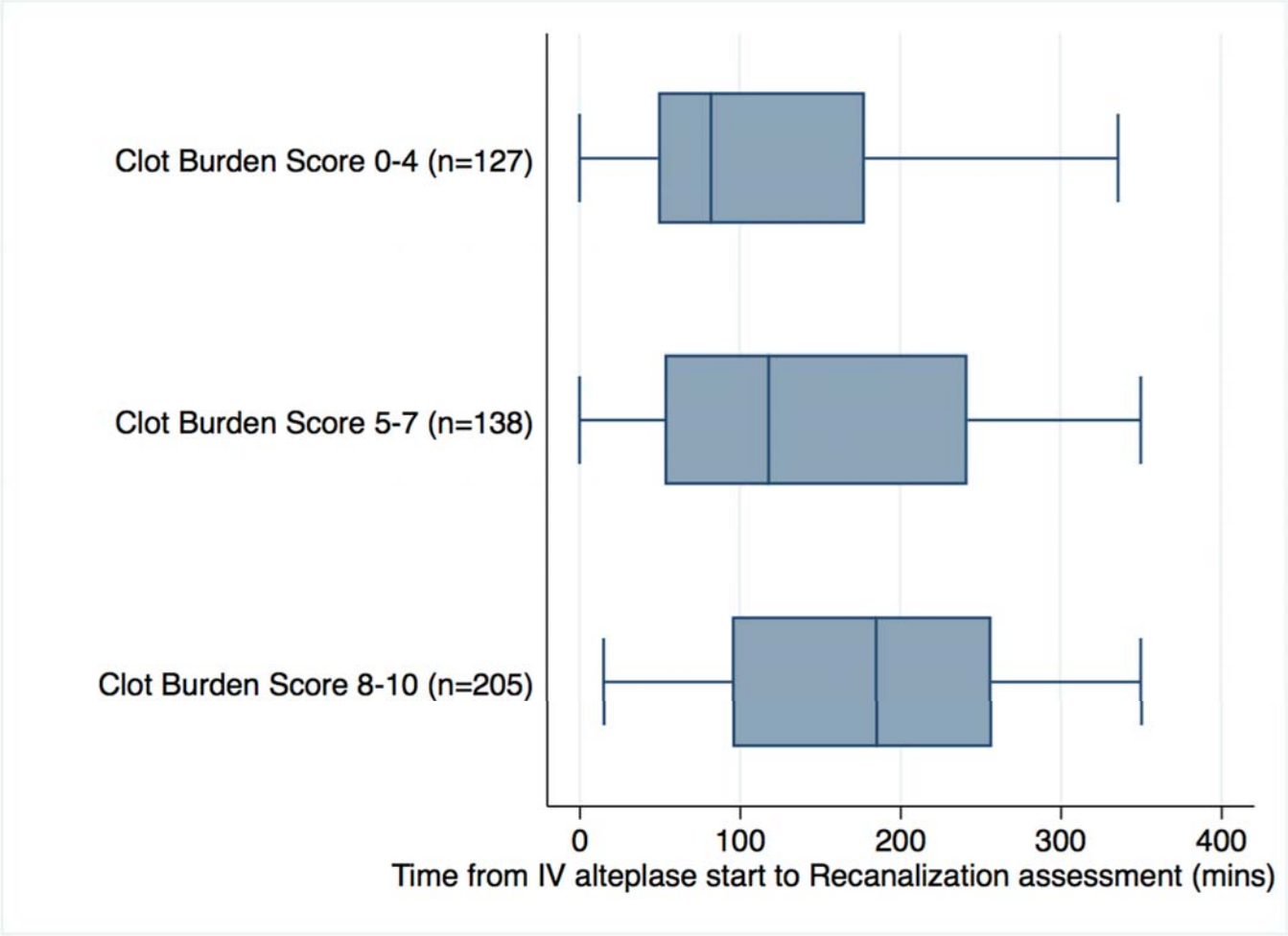


eFigure 3. Box plots showing time from IV alteplase start to recanalization assessment stratified by site of occlusion on baseline CT angiography.



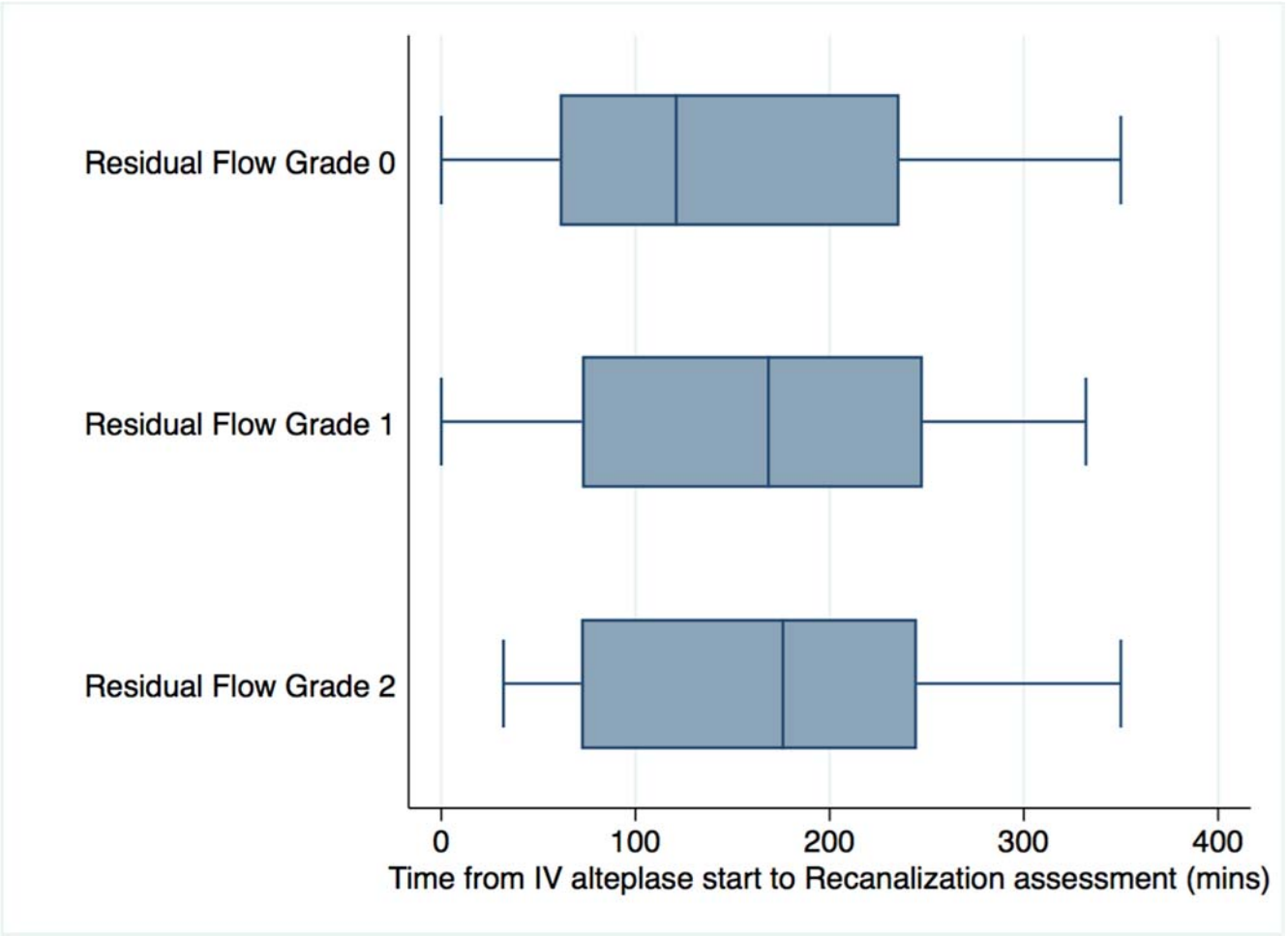
The line in the box is the median, the ends of the box represent 25th and 75th percentile data, the length of the box represents the inter-quartile range, the whiskers (adjacent values) are drawn to span all data points within 1.5 IQR of the nearer quartile.

eFigure 4. Box plots showing time from IV alteplase start to recanalization assessment stratified by clot burden score on baseline CT angiography.



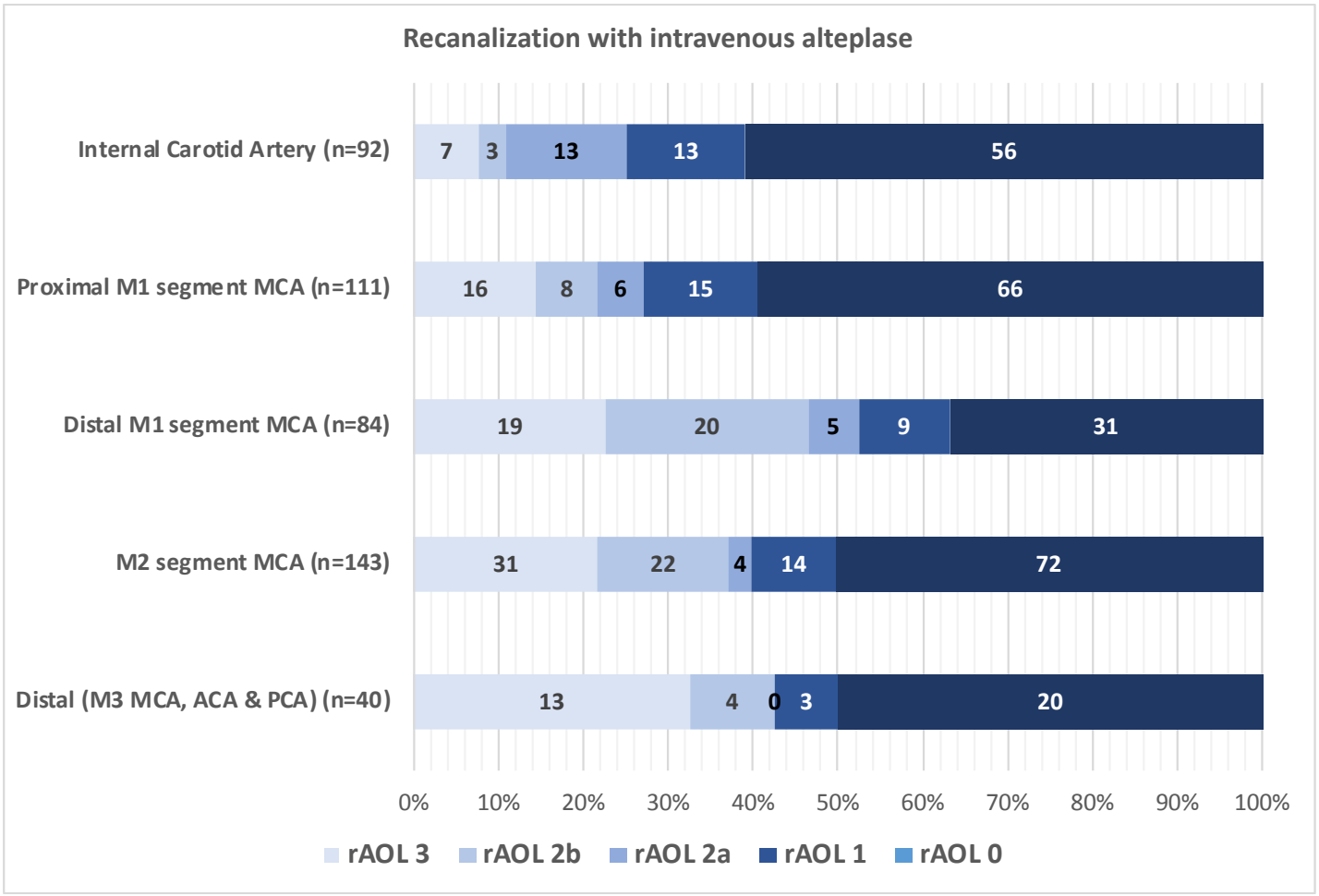
The line in the box is the median, the ends of the box represent 25th and 75th percentile data, the length of the box represents the inter-quartile range, the whiskers (adjacent values) are drawn to span all data points within 1.5 IQR of the nearer quartile. The Clot Burden Score is an ordinal score that measures extent of thrombus within anterior circulation arteries. A score of 0 implies complete occlusion of the ipsilateral anterior circulation vessels while a score of 10 implies no occlusion.

eFigure 5. Box plots showing time from IV alteplase start to recanalization assessment stratified by residual flow grade on baseline CT angiography.



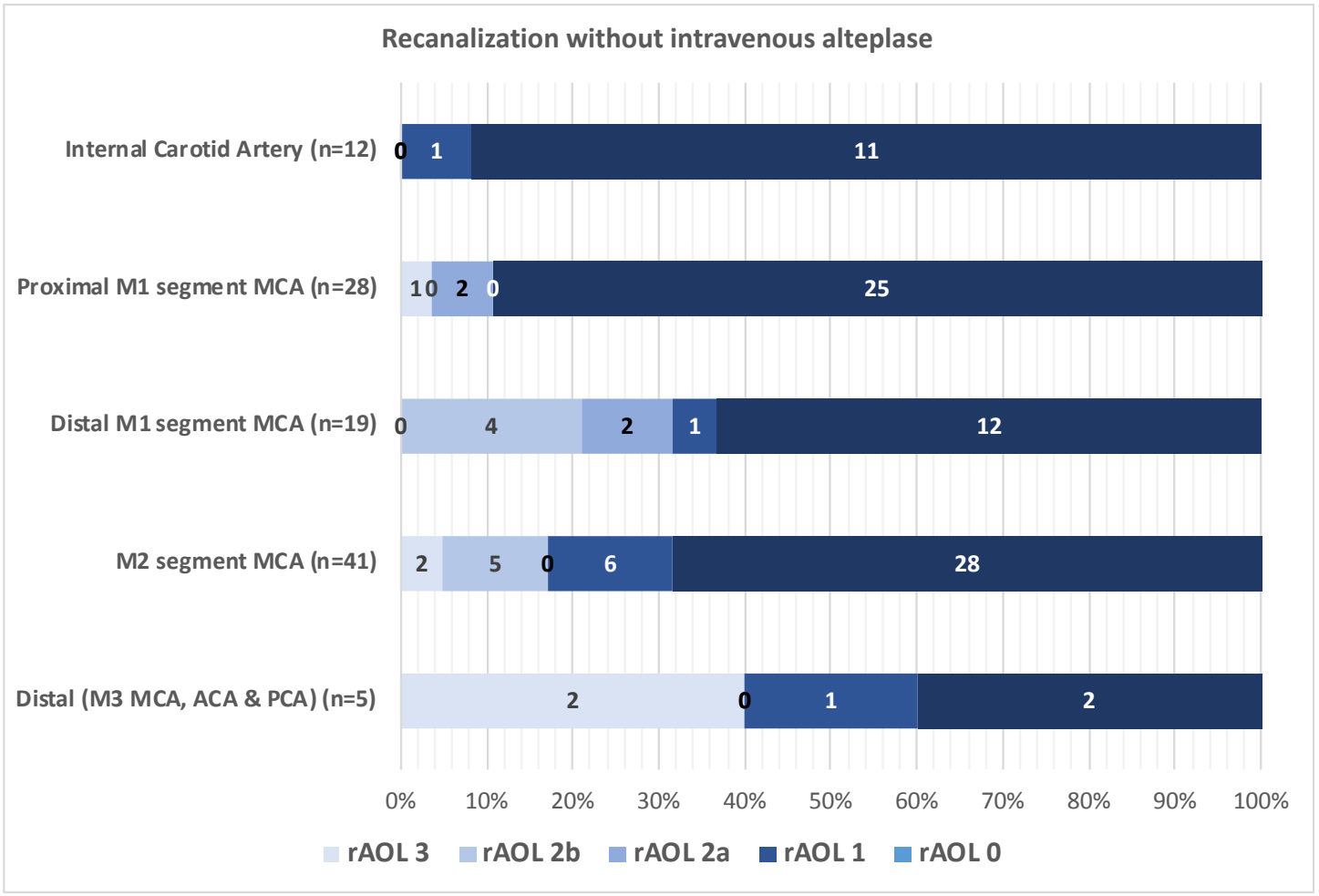
The line in the box is the median, the ends of the box represent 25th and 75th percentile data, the length of the box represents the inter-quartile range, the whiskers (adjacent values) are drawn to span all data points within 1.5 IQR of the nearer quartile.
Residual Flow Grade is graded on the CTA source images (3 mm MIP preferred) as follows—grade 0: no contrast permeation of thrombus; grade 1: contrast permeating diffusely through thrombus; grade 2: tiny hairline lumen or streak of well-defined contrast within the thrombus extending either through its entire length part or of thrombus.

eFigure 6a. The revised Arterial Occlusive Lesion (rAOL) score assessing recanalization with intravenous alteplase stratified by site of occlusion on baseline CT angiography.



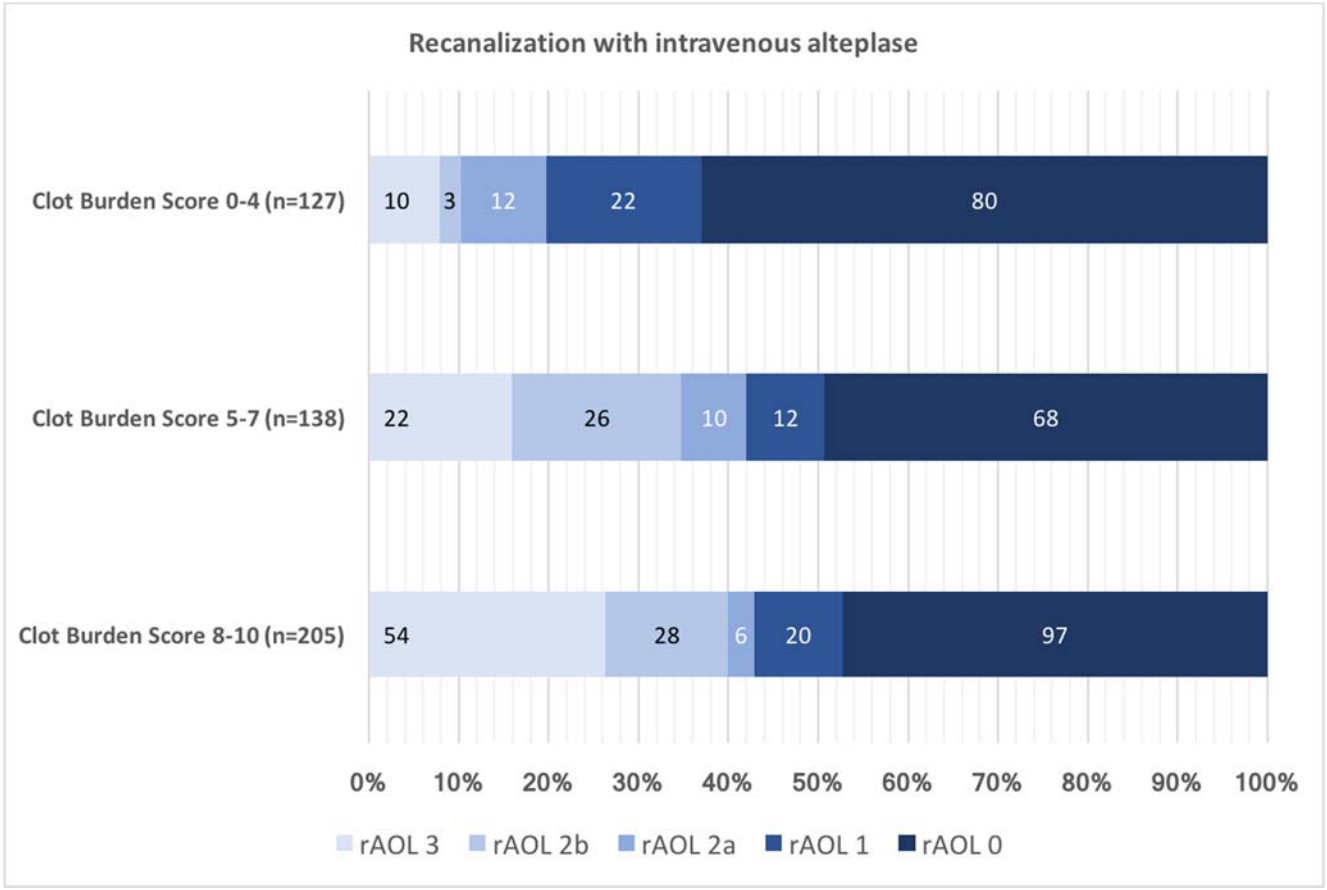
The rAOL score categories are 0: Primary occlusive thrombus remains same. 1: Debulking of proximal part of the thrombus but without any recanalization. 2a: Partial or complete recanalization of the primary thrombus with occlusion in major distal vascular branch. 2b: Partial or complete recanalization of the primary thrombus with occlusion in minor distal vascular branch, or partial recanalization of the primary thrombus with no thrombus in the vascular tree at or beyond the primary occlusive thrombus. 3: Complete recanalization of the primary occlusive thrombus with no clot in the vascular tree beyond.

eFigure 6b. The revised Arterial Occlusive Lesion (rAOL) score assessing recanalization without intravenous alteplase stratified by site of occlusion on baseline CT angiography.



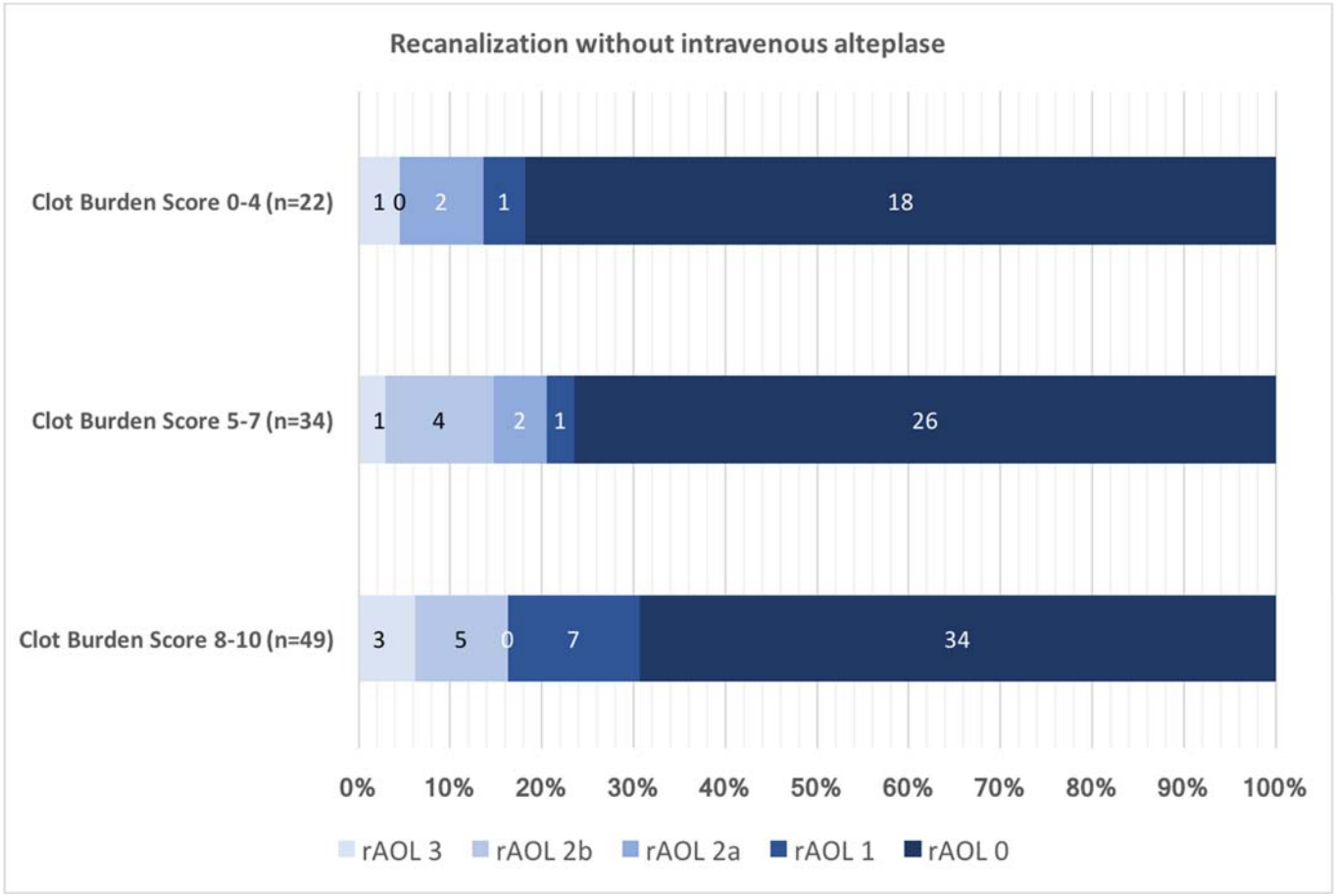
The rAOL score categories are 0: Primary occlusive thrombus remains same. 1: Debulking of proximal part of the thrombus but without any recanalization. 2a: Partial or complete recanalization of the primary thrombus with occlusion in major distal vascular branch. 2b: Partial or complete recanalization of the primary thrombus with occlusion in minor distal vascular branch, or partial recanalization of the primary thrombus with no thrombus in the vascular tree at or beyond the primary occlusive thrombus. 3: Complete recanalization of the primary occlusive thrombus with no clot in the vascular tree beyond.

eFigure 7a: The revised Arterial Occlusive Lesion (rAOL) score assessing recanalization with intravenous alteplase stratified by Clot Burden Score on baseline CT angiography.



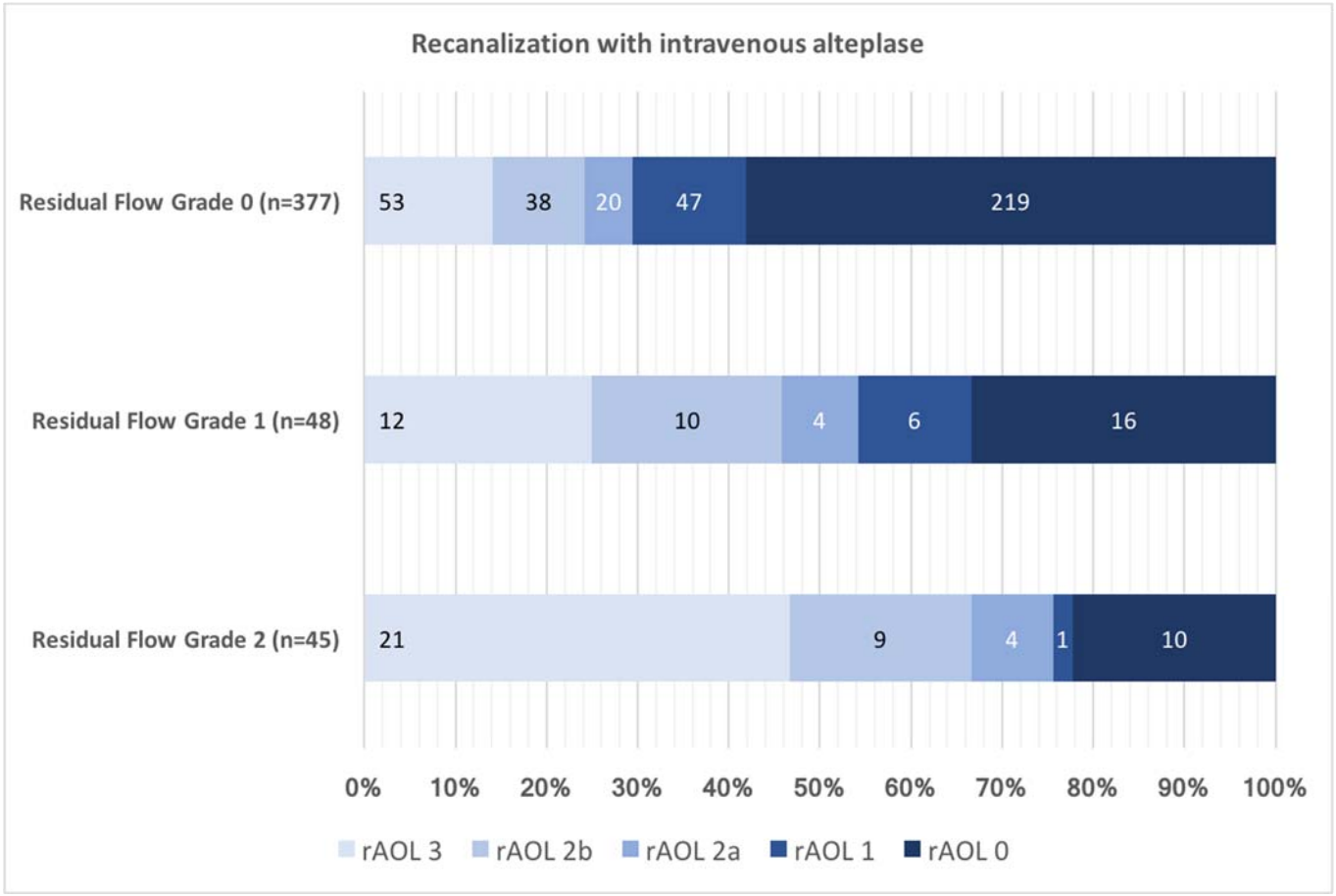
The rAOL score categories are 0: Primary occlusive thrombus remains same. 1: Debulking of proximal part of the thrombus but without any recanalization. 2a: Partial or complete recanalization of the primary thrombus with occlusion in major distal vascular branch. 2b: Partial or complete recanalization of the primary thrombus with occlusion in minor distal vascular branch, or partial recanalization of the primary thrombus with no thrombus in the vascular tree at or beyond the primary occlusive thrombus. 3: Complete recanalization of the primary occlusive thrombus with no clot in the vascular tree beyond.
The Clot Burden Score is an ordinal score that measures extent of thrombus within anterior circulation arteries. A score of 0 implies complete occlusion of the ipsilateral anterior circulation vessels while a score of 10 implies no occlusion.

eFigure 7b. The revised Arterial Occlusive Lesion (rAOL) score assessing recanalization without intravenous alteplase stratified by Clot Burden Score on baseline CT angiography.



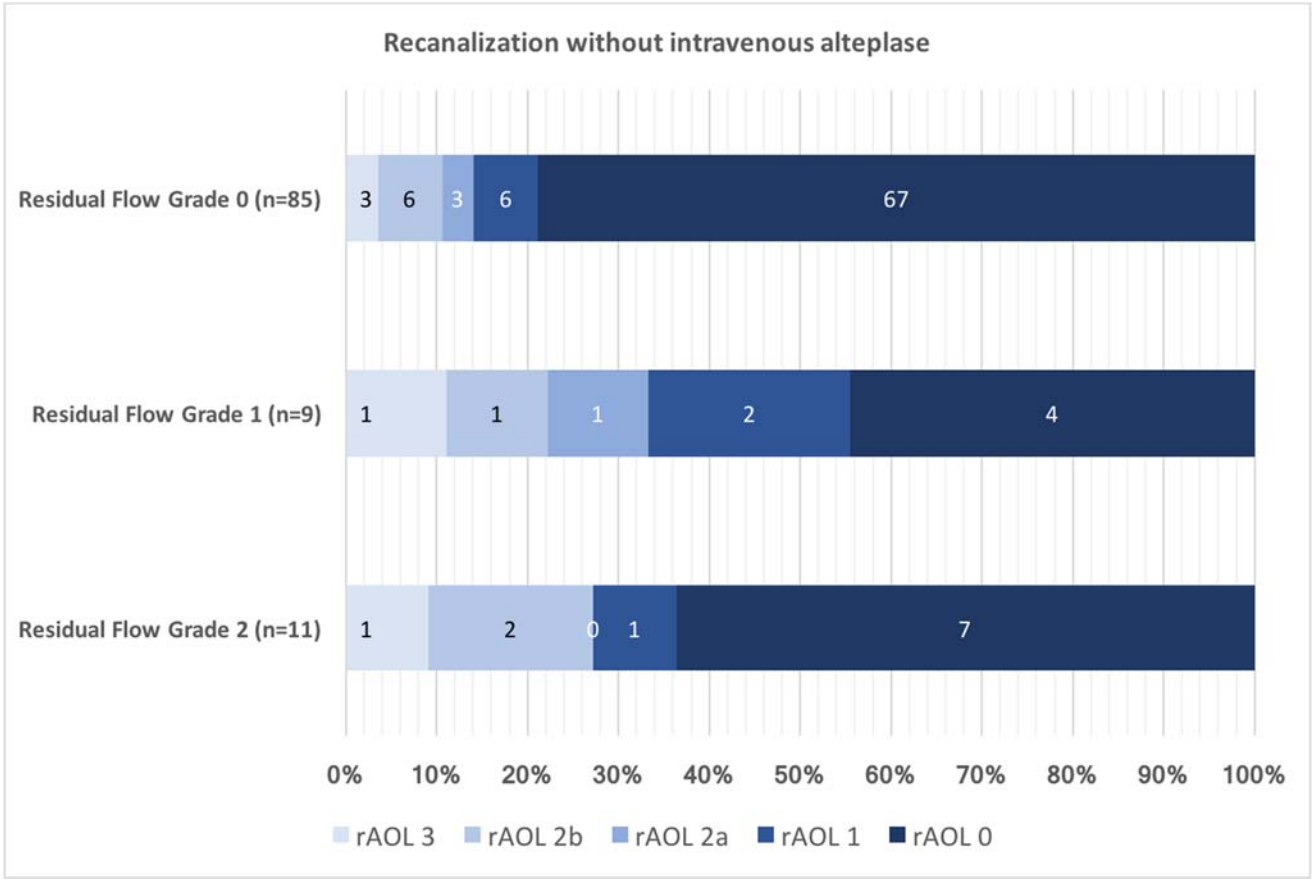
The rAOL score categories are 0: Primary occlusive thrombus remains same. 1: Debulking of proximal part of the thrombus but without any recanalization. 2a: Partial or complete recanalization of the primary thrombus with occlusion in major distal vascular branch. 2b: Partial or complete recanalization of the primary thrombus with occlusion in minor distal vascular branch, or partial recanalization of the primary thrombus with no thrombus in the vascular tree at or beyond the primary occlusive thrombus. 3: Complete recanalization of the primary occlusive thrombus with no clot in the vascular tree beyond.
The Clot Burden Score is an ordinal score that measures extent of thrombus within anterior circulation arteries. A score of 0 implies complete occlusion of the ipsilateral anterior circulation vessels while a score of 10 implies no occlusion.

eFigure 8a. The revised Arterial Occlusive Lesion (rAOL) score assessing recanalization with intravenous alteplase stratified by presence or absence of residual flow on baseline CT angiography.



The rAOL score categories are 0: Primary occlusive thrombus remains same. 1: Debulking of proximal part of the thrombus but without any recanalization. 2a: Partial or complete recanalization of the primary thrombus with occlusion in major distal vascular branch. 2b: Partial or complete recanalization of the primary thrombus with occlusion in minor distal vascular branch, or partial recanalization of the primary thrombus with no thrombus in the vascular tree at or beyond the primary occlusive thrombus. 3: Complete recanalization of the primary occlusive thrombus with no clot in the vascular tree beyond.
Residual Flow Grade is graded on the CTA source images (3 mm MIP preferred) as follows—grade 0: no contrast permeation of thrombus; grade 1: contrast permeating diffusely through thrombus; grade 2: tiny hairline lumen or streak of well-defined contrast within the thrombus extending either through its entire length part or of thrombus.

eFigure 8b. The revised Arterial Occlusive Lesion (rAOL) score assessing recanalization without intravenous alteplase stratified by presence or absence of residual flow on baseline CT angiography.



The rAOL score categories are 0: Primary occlusive thrombus remains same. 1: Debulking of proximal part of the thrombus but without any recanalization. 2a: Partial or complete recanalization of the primary thrombus with occlusion in major distal vascular branch. 2b: Partial or complete recanalization of the primary thrombus with occlusion in minor distal vascular branch, or partial recanalization of the primary thrombus with no thrombus in the vascular tree at or beyond the primary occlusive thrombus. 3: Complete recanalization of the primary occlusive thrombus with no clot in the vascular tree beyond.
Residual Flow Grade is graded on the CTA source images (3 mm MIP preferred) as follows—grade 0: no contrast permeation of thrombus; grade 1: contrast permeating diffusely through thrombus; grade 2: tiny hairline lumen or streak of well-defined contrast within the thrombus extending either through its entire length part or of thrombus.

eTable 1. The revised Arterial Occlusive Lesion (rAOL) score.

rAOL score	Definition
0	Primary occlusive lesion remains same
1	Debulking of thrombus without recanalization
2a	Partial or complete recanalization of the primary lesion with thrombus /occlusion in major vascular branch*
2b	Partial or complete recanalization of the primary lesion with thrombus /occlusion in minor vascular branch**, or partial recanalization of the primary lesion with no thrombus in the vascular tree at or beyond the primary occlusive lesion
3	Complete recanalization of the primary occlusion with no clot in the vascular tree at or beyond the primary occlusive lesion

***Major vascular branch:** ICA, M1 segment of MCA, Functional M1 "thrombus in both proximal M2s of MCA", A1 segment of ACA, Basilar artery, P1 segment of PCA.
****Minor vascular branch:** other distal vessels.
** When conventional angiography used for recanalization assessment, the rAOL score was based on the arterial phase of the first angiographic run.

eTable 2. Clinical and imaging characteristics in different treatment sub-groups, namely, Group 1 (intravenous alteplase only), Group 2 (Endovascular Thrombectomy only), Group 3 (intravenous alteplase + Endovascular Thrombectomy) and Group 4 (Conservative treatment). Groups 1 and 3 received intravenous alteplase and had recanalization with alteplase assessed using the revised Arterial Occlusion Scale (rAOL) scale on repeat CTA Head or on first angiographic acquisition of the affected intracranial circulation for EVT. Groups 2 and 4 did not receive intravenous alteplase and had recanalization assessed using the revised Arterial Occlusion Scale (rAOL) scale on repeat CTA Head or on first angiographic acquisition of the affected intracranial circulation for EVT.

Variable	**All patients (N=575)**	**Intravenous alteplase only (n=275)**	**Endovascular Thrombectomy only (n=48)**	**Intravenous alteplase + Endovascular Thrombectomy (n=195)**	**Conservative treatment (n=57)**
Clinical					
Age in years (Median, Q1-Q3)	72 (63-80)	74 (65-81)	70 (64-77)	70 (59-79)	73 (65-81)
Male Sex (n, %)	296 (51.5%)	137 (49.8%)	24 (50%)	100 (51.3%)	35 (61.4%)
Baseline NIHSS (Median, Q1-Q3)	14 (8-19)	12 (7-18)	16 (11-20)	17 (13-20)	6 (3-11)
History of Coronary Arterial Disease (n, %)	118 (20.5%)	50 (18.2%)	15 (31.2%)	36 (18.5%)	17 (29.8%)
History of Stroke/TIA (n, %)	93 (16.2%)	39 (14.2%)	13 (27.1%)%	31 (15.9%)	10 (17.5%)
History of Hypertension (n, %)	356 (61.9%)	178 (64.7%)	28 (58.3%)	113 (57.9%)	37 (64.9%)
History of Dyslipidemia (n, %) (N=572)	189 (33%)	103 (37.4%)	15 (31.2%)	58 (30.2%)	13 (22.8%)
History of Antiplatelet use (n, %)	201 (35%)	101 (36.7%)	18 (37.5%)	66 (33.8%)	16 (28.1%)
History of Atrial Fibrillation (n, %)	177 (30.8%)	74 (26.9%)	22 (45.8%)	55 (28.2%)	26 (45.6%)
Anticoagulation (n, %)	76 (13.2%)	26 (9.4%)	14 (29.2%)	23 (11.8%)	13 (22.8%)
History of Diabetes (n, %)	86 (15%)	16 (11.2%)	59 (18%)	27 (13.8%)	4 (7%)
History of Smoking (n, %) (N=562)	233 (41.5%)	101 (37.7%)	22 (45.8%)	85 (44.7%)	25 (44.6%)
Heart Rate per min (Median, Q1-Q3) (N=544)	76 (66.5-88)	78 (69-90)	76 (65-90)	75.5 (66-85)	73 (65-88)
Systolic Blood Pressure in mm Hg (Median, Q1-Q3)	147 (132-167)	150 (136-170)	134 (125-146)	146 (130-163)	145 (130-170)

Variable	All patients (N=575)	Intravenous alteplase only (n=275)	Endovascular Thrombectomy only (n=48)	Intravenous alteplase + Endovascular Thrombectomy (n=195)	Conservative treatment (n=57)
(N=572)					
Diastolic Blood Pressure in mm Hg (Median, Q1-Q3) (N=572)	81 (71-90)	82 (72-92)	80 (65-87)	80 (70-90)	85 (72-95)
Blood Glucose (millimol/L[#]) (Median, Q1-Q3) (N=574)	6.4 (5.8-7.3)	6.4 (5.8-7.8)	6.1 (5.3-6.9)	6.4 (5.7-7.5)	6.5 (5.7-7.2)
Serum Creatinine (micromol/L[#]) (Median, Q1-Q3)	78 (66.3-94)	77.8 (66-94)	80 (67-96)	76 (66-91)	85 (76-98)
Hematocrit % (Median, Q1-Q3)	41 (38-44)	41 (38-44)	41 (36-43.5)	41 (37-43)	42 (39-45)
Platelet count 10*9/L (Median, Q1-Q3) (N=574)	208.5 (170-254)	213 (177-256)	215.5 (169-249.5)	198 (164-256)	206 (170-244)
International Normalized Ratio (Median, Q1-Q3) (N=573)	1 (1-1.1)	1 (1-1.1)	1.1 (1-1.4)	1 (1 -1.1)	1 (1-1.2)
PTT in seconds (Median, Q1-Q3) (N=569)	27.9 (25-30)	27.9 (25.3-30.3)	28.5 (26.3-33.1)	27.2 (24.2-29.5)	27.9 (25.6-29.6)
Total Cholesterol (millimol/L[#]) (Median, Q1-Q3) (N=545)	4.2 (3.5-5)	4.5 (3.6-5.3)	3.8 (3.2-4.6)	4.1 (3.4-4.7)	4.1 (3.6-4.8)
Aetiology of Ischemic Stroke					
Extra-cranial Large Artery Disease (n, %)	86 (15%)	44 (16%)	10 (20.8%)	30 (15.4%)	2 (3.5%)
Intracranial Artery Disease (n, %)	15 (2.6%)	7 (2.6%)	0 (0%)	5 (2.6%)	3 (5.3%)
Cardio-embolic (n, %)	309 (53.7%)	140 (50.9%)	31 (64.6%)	98 (50.3%)	40 (70.2%)
Other causes (n, %)	12 (2.1%)	6 (2.2%)	1 (2.1%)	4 (2.1%)	1 (1.8%)
Undetermined (n, %)	153 (26.6%)	78 (28.4%)	6 (12.5%)	58 (29.7%)	11 (19.3%)
Imaging					
Baseline ASPECTS on NCCT (Median, Q1-Q3) (N=540)	9 (7-10)	9 (7-10)	9 (8-10)	9 (8-9)	9 (7-10)
Site of Intracranial Occlusion at Baseline					
Internal Carotid Artery (n, %)	104 (18.1%	35 (12.7%)	7 (14.6%)	57 (29.2%)	5 (8.8%)
Proximal M1 segment MCA (n, %)	139 (24.2%)	45 (16.4%)	20 (41.7%)	66 (33.8%)	8 (14%)

Variable	All patients (N=575)	Intravenous alteplase only (n=275)	Endovascular Thrombectomy only (n=48)	Intravenous alteplase + Endovascular Thrombectomy (n=195)	Conservative treatment (n=57)
Distal M1 segment MCA (n, %)	103 (17.9%)	50 (18.2%)	10 (20.8%)	34 (17.4%)	9 (15.8%)
M2 segment MCA (n, %)	184 (32%)	110 (40%)	11 (22.9%)	33 (16.9%)	30 (52.6%)
Distal (M3 MCA, ACA & PCA) (n, %)	45 (7.8%)	35 (12.7%)	0 (0%)	5 (2.6%)	5 (8.8%)
Residual Flow within intracranial thrombus					
Grade 0 (n, %)	462 (80.3%)	213 (77.5%)	39 (81.3%)	164 (84.1%)	46 (80.7%)
Grade 1 (n, %)	57 (9.9%)	31 (11.3%)	2 (4.2%)	17 (8.7%)	7 (12.3%)
Grade 2 (n, %)	56 (9.7%)	31 (11.3%)	7 (14.5%)	14 (7.2%)	4 (7%)
Clot Burden Score					
Score 0-4 (n, %)	149 (25.9%)	46 (16.7%)	13 (27.1%)	81 (41.5%)	9 (15.8%)
Score 5-7 (n, %)	172 (29.9%)	73 (26.6%)	22 (45.8%)	65 (33.3%)	12 (21%)
Score 8-10 (n, %)	254 (44.2%)	156 (56.7%)	13 (27.1%)	49 (25.1%)	36 (63.2%)
Stroke Workflow Interval Times					
Time from Onset (last known well) to baseline CT Angiography in mins (Median, Q1-Q3)	114 (74-180)	115 (76-171)	140.5 (66.5-308)	97 (67-143)	206 (134-390)
Time from Baseline CT Angiography to IV alteplase start in mins, Median (Q1-Q3)	19 (11-28)	19 (11-30)	N/A	19 (12-26)	N/A
Time from Baseline CT Angiography to Recanalization Assessment in mins, Median (Q1-Q3)	158 (79-268)	254 (185-295)	59 (44-88.5)	79 (55-106)	272 (245-307)
Time from intravenous alteplase to Recanalization	132.5 (62-238)	225 (164-273)	N/A	57 (38-85)	N/A

Variable	All patients (N=575)	Intravenous alteplase only (n=275)	Endovascular Thrombectomy only (n=48)	Intravenous alteplase + Endovascular Thrombectomy (n=195)	Conservative treatment (n=57)
Assessment in mins (Median, Q1-Q3)					

Q1 - 25th percentile, Q3 – 75th percentile; mm Hg – millimeter mercury; millimol/L – millimols per liter; micromol/L – micromoles per liter; NCCT – Non-contrast Computed Tomography; NIHSS – National Institute of Health Stroke Scale (score ranges from 0-42 with higher scores indicate greater stroke severity); ASPECTS –Alberta Stroke Program Early CT Score. This ordinal score measures extent of early ischemic change in the middle cerebral artery territory on a 0-10 scale. Higher scores indicate smaller extent of early ischemic changes.

conversion factor for Blood Glucose: 1 millimol/L = 18.018 mg/dL; conversion factor for Serum Creatinine: 1 micromol/L = 0.01131 mg/dL; conversion factor for serum cholesterol: 1 millimol/L = 38.67 mg/dL.

eTable 3. Post hoc analysis of variables independently associated with successful recanalization with intravenous alteplase when accounting for differences by geographic region of patient enrolled. Results are reported as Odds Ratios with 95% confidence intervals. Only variables statistically significant (p<0.05) in bivariable tests in Table 1 and deemed clinically relevant were included in multivariable modeling.

			Model 1[#]		Model 2[#]	
Variable		**No. % of patients achieving successful recanalization with intravenous alteplase**	**Odds Ratio (95% CI)**	**p value**	**Odds Ratio (95% CI)**	**p value**
Site of Intracranial Occlusion at Baseline						
	Internal Carotid Artery (Reference)	10/92; 10.9%	1		N/A	N/A
	Proximal M1 segment MCA	24/111; 21.6%	2.00 (0.83-4.79)	0.12	N/A	N/A
	Distal M1 segment MCA	39/84; 46.4%	5.65 (2.39-13.35)	<0.001	N/A	N/A
	M2 segment MCA	53/143; 37.1%	3.64 (1.64-8.11)	0.002	N/A	N/A
	Distal (M3 MCA, ACA & PCA)	17/40; 42.5%	5.17 (1.94-13.75)	0.001	N/A	N/A
Clot Burden Score						
	0-4 (Reference)	13/127; 10.2%	N/A	N/A	1	
	5 to 7	48/138; 34.8%	N/A	N/A	3.31 (1.61-6.84)	0.001
	8 to 10	82/205; 40%	N/A	N/A	3.85 (1.93-7.64)	<0.001
Residual Flow						
	Grade 0 (Reference)	91/377; 24.1%	1			
	Grade 1	22/48; 45.8%	2.56 (1.26-5.20)	0.009	2.71 (1.36-5.39)	0.004
	Grade 2	(30/45; 66.7%)	7.02 (3.31-14.86)	<0.001	6.04 (2.91-12.51)	<0.001
Time from intravenous alteplase start to Recanalization Assessment (every 30 mins)		*N/A*	1.28 (1.18-1.38)	<0.001	1.27 (1.17-1.37)	<0.001
Geographic Region						
	North America (Reference)	95/303 (31.4%)	1		1	
	Europe	38/116 (32.8%)	0.90 (0.53-1.52)	0.698	0.94 (0.56-1.58)	0.817
	East Asia	10/51 (19.6%)	0.95 (0.42-2.17)	0.904	0.91 (0.40-2.08)	0.832

Models 1 and 2 are similar except for the variables “Site of Intracranial Occlusion at baseline” and “Clot Burden Score”. These variables both measure thrombus extent and therefore were not included in the same model. Other variables included in multivariable modeling included baseline NIHSS, residual flow grade and time from intravenous alteplase start to recanalization assessment. Only variables with p < 0.05 are reported in models above. Recanalization of intracranial thrombus with intravenous alteplase was assessed using the rAOL (revised Arterial Occlusive Lesion) score on repeat CTA Head or on first angiographic acquisition of the affected intracranial circulation. Successful recanalization was defined by a rAOL score of 2b or 3. The rAOL score is described in detail in Methods and in eTable 1.

eTable 4. Logistic regression model in patients not treated with intravenous alteplase with successful recanalization (rAOL score 2b or 3) as the dependent variable and variables that were statistically significant in univariate analysis as dependent variables (see Table 1). Results are reported as Odds Ratios with 95% confidence intervals. The final parsimonious model (after backwards elimination) only includes sex significantly associated with spontaneous recanalization.

Variable		Odds Ratio (95% CI)	p value
Male Sex		6.41 (1.02-40.37)	0.048
Baseline NIHSS		0.85 (0.71-1.00)	0.06
Serum Creatinine (mg/dL)[#]		7.99 (0.83-76.71)	0.07
Site of Intracranial Occlusion at Baseline			
	Distal (M3 MCA, ACA & PCA) (Reference)	1	
	M2 segment MCA	0.33 (0.03-3.19)	0.34
	Distal M1 segment MCA	0.28 (0.02-3.62)	0.33
	Proximal M1 segment MCA	0.11 (0.01-2.33)	0.16
	Internal Carotid Artery*	–	–
Residual Flow	Grade 0 (Reference)	1	
	Grade 1	3.14 (0.28-34.71)	0.35
	Grade 2	10.73 (1.30-88.54)	0.03
Time from intravenous alteplase start to Recanalization Assessment (every 30 mins)		0.99 (0.75-1.30)	0.94
Final Parsimonious Model			
Male Sex		5.61 (1.19-26.53)	0.029

*No patient with Intracranial Internal Carotid Artery Occlusion achieved recanalization.

conversion factor for Serum Creatinine: 1 mg/dL = 88.4 micromol/L;

eTable 5. Final logistic regression models for each individual intracranial occlusion site (models 1 to 5) showing variables associated with successful recanalization in patients treated with intravenous alteplase. Results are reported as Odds Ratios with 95% confidence intervals. Residual flow is categorized as Yes (grade 1 and 2) vs. No (Grade 0).

Variable	Successful Recanalization (n/N) (%)	Odds Ratio (95% CI)	p value
Intracranial Internal Carotid Artery Thrombus			
Residual Flow Yes	2/11 (18.2%)	2.04 (0.35-12.04)	0.43
Residual Flow No	8/81 (9.9%)		
Time from intravenous alteplase start to Recanalization Assessment (every 30 mins)		1.27 (1.04-1.56)	0.02
Proximal M1 segment MCA Thrombus			
Residual Flow Yes	13/28 (46.4%)	4.86 (1.72-13.76)	0.003
Residual Flow No	11/83 (13.3%)		
Time from intravenous alteplase start to Recanalization Assessment (every 30 mins)		1.26 (1.08-1.47)	0.003
Distal M1 segment MCA Thrombus			
Residual Flow Yes	20/29 (70%)	4.72 (1.61-13.86)	0.005
Residual Flow No	19/55 (34.5%)		
Time from intravenous alteplase start to Recanalization Assessment (every 30 mins)		1.33 (1.14-1.56)	<0.001
M2 segment MCA Thrombus			
Residual Flow Yes	15/22 (68.2%)	4.55 (1.65-12.58)	0.003
Residual Flow No	38/121 (31.4%)		
Time from intravenous alteplase start to Recanalization Assessment (every 30 mins)		1.26 (1.10-1.44)	0.001
Distal (M3 MCA, ACA & PCA) Thrombus			
Residual Flow Yes	2/3 (66.7%)	2.92 (0.24-35.70)	0.402
Residual Flow No	15/37 (40.5%)		
Time from intravenous alteplase start to Recanalization Assessment (every 30 mins)		1.21 (0.94-1.56)	0.136