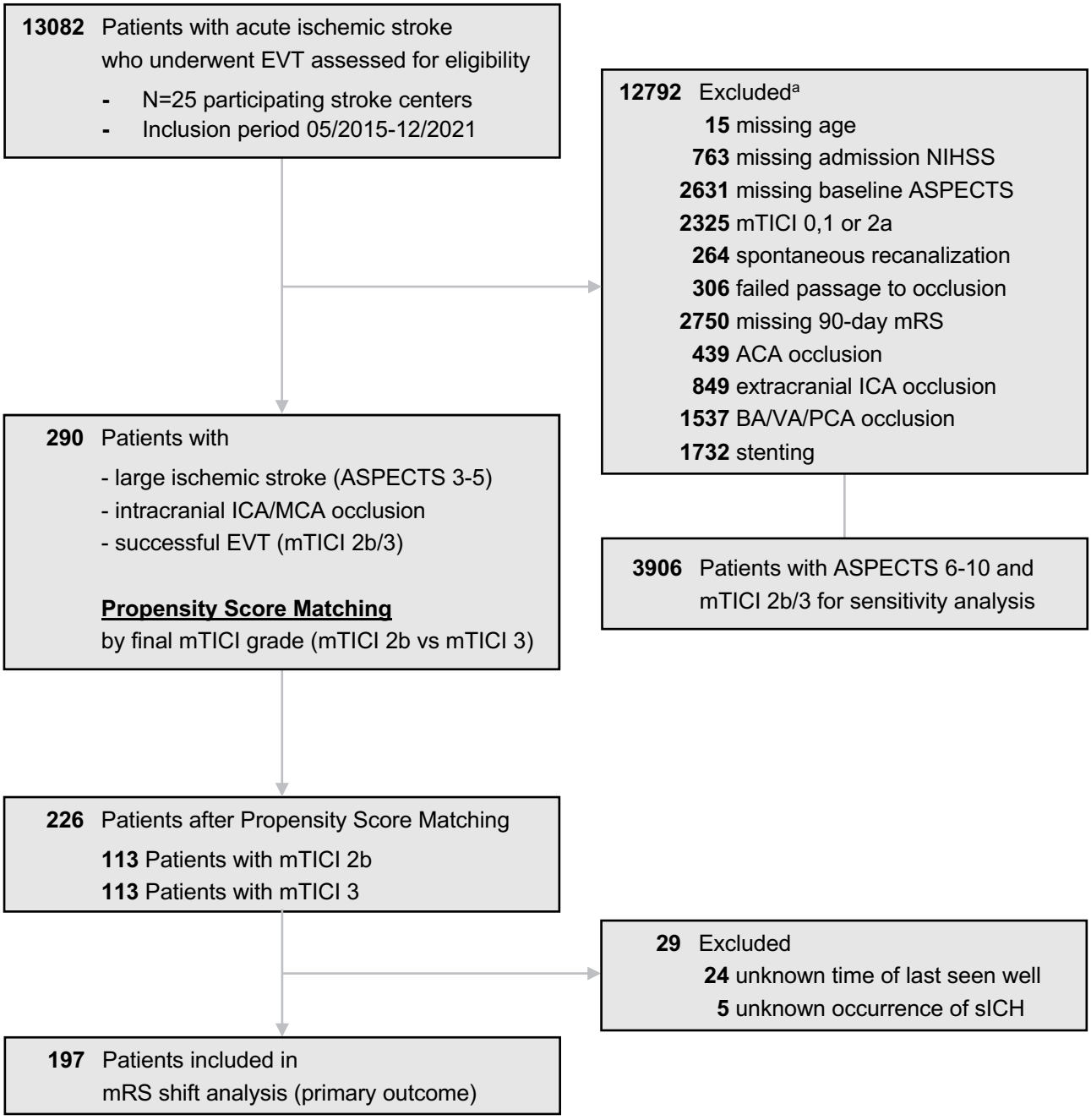
Supplementary Information for

Comparison of TICI 2b and TICI 3 Reperfusion in Endovascular Therapy for Large Ischemic Anterior Circulation Strokes

Figure S1. Flow chart of patient inclusion and exclusion criteria.



Abbreviations:
EVT, Endovascular Therapy; NIHSS, National Institutes Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; mTICI, modified Thrombolysis in Cerebral Infarction; mRS, modified Rankin Scale; ACA, Anterior Cerebral Artery; ICA, Internal Carotid Artery, BA, Basilar Artery; VA, Vertebral Artery; PCA, Posterior Cerebral Artery; MCA, Middle Cerebral Artery, sICH, Symptomatic Intracranial Hemorrhage

[a] Multiple selection of patients possible.

Figure S2. Propensity score matching for final angiographic outcome.
(A) Distributions of propensity scores before and after propensity score matching for the treatment (mTICI 3) and control group (mTICI 2b). **(B)** Scatter plots showing the respective propensity scores before and after propensity score matching for the treatment and control group. **(C)** Standardized mean differences (SMD) before propensity score matching (red) and after propensity score matching (blue) for all selected baseline covariates. We assumed sufficient balancing for all selected covariates between the treatment and control group given an absolute SMD of <0.10 (dashed lines).

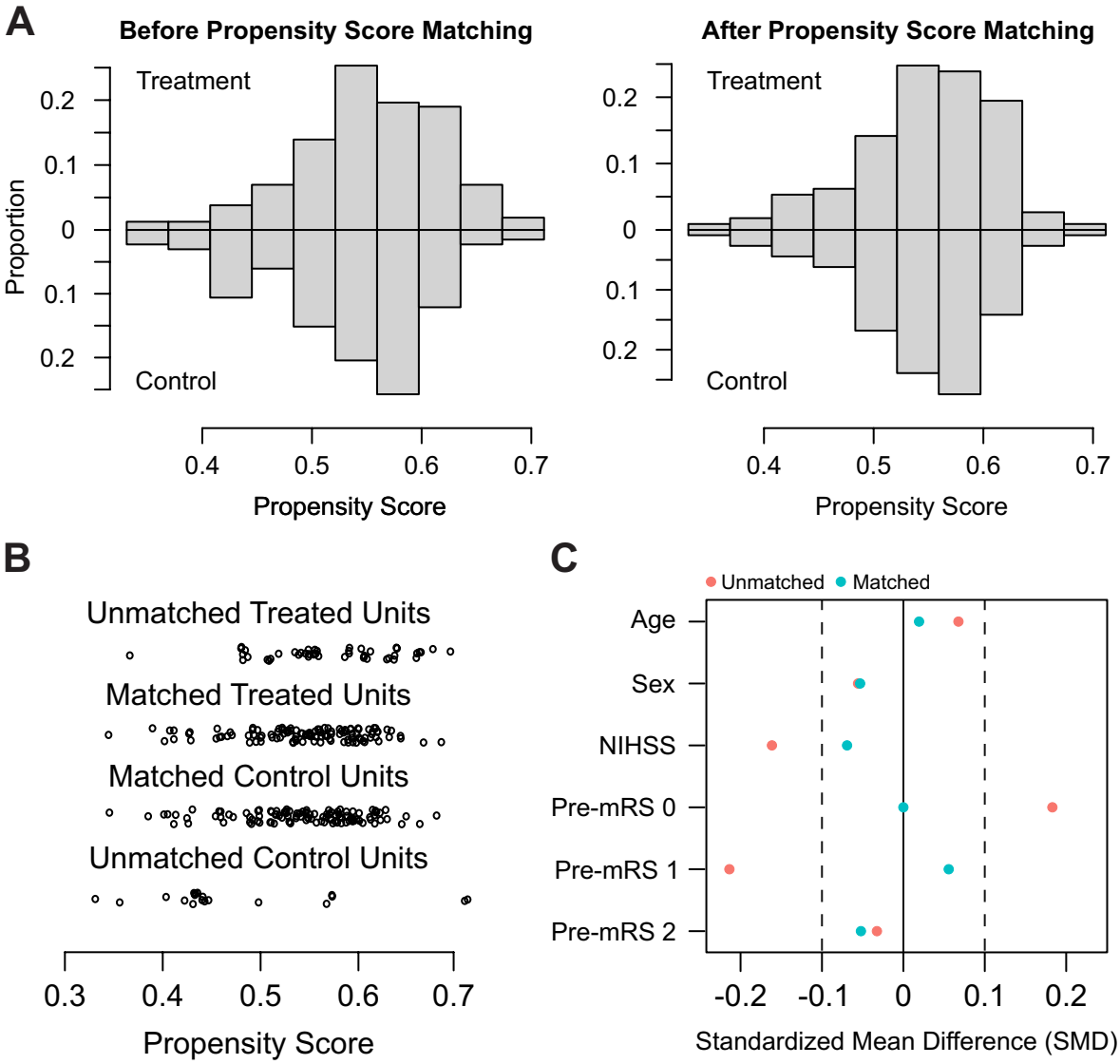
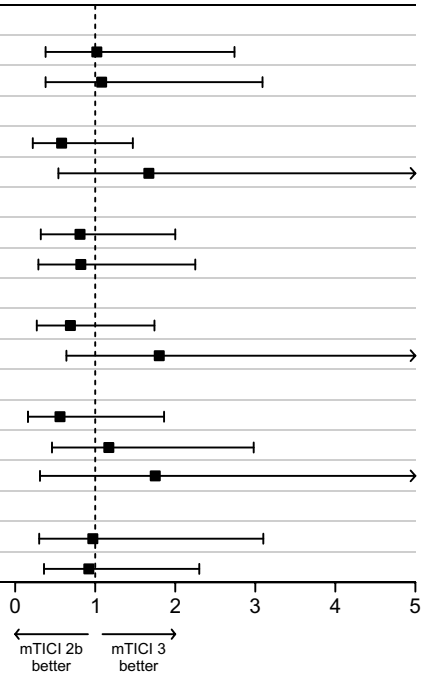


Figure S3. Subgroup analyses for independent ambulation.
Shown are the subgroup analyses indicating the odds of achieving independent ambulation (defined as modified Rankin Scale score of 0 to 3 at 90 days) depending on the final angiographic outcome (mTICI 2b vs mTICI 3). Compared with mTICI 2b reperfusion, mTICI 3 reperfusion was not associated with the frequency of independent ambulation in patients of older and younger age, different sex, shorter and longer time between symptom onset or last known well and hospital admission, lower and higher NIHSS scores on admission and various sites of vessel occlusion. Unless otherwise indicated, results are adjusted for significant parameters from the mRS shift analysis (Table S1).

Subgroup	No. of patients	mTICI 2b	mTICI 3	Adjusted Odds Ratio for 90-d mRS 0-3 (95% CI)[a]
		90-d mRS 0-3 (%)		
Age				
≥70 years	136	19.7%	22.9%	1.02 (0.38 to 2.74)
<70 years	90	68.1%	65.1%	1.08 (0.38 to 3.09)
Sex				
male	117	52.6%	43.3%	0.58 (0.22 to 1.47)
female	109	26.8%	34.0%	1.67 (0.54 to 5.40)
Onset/LSW to admission				
≤360 minutes	124	41.0%	41.2%	0.81 (0.32 to 2.00)
>360 minutes or unknown	102	38.5%	34.0%	0.82 (0.29 to 2.25)
Baseline NIHSS score				
>15 points	141	30.6%	23.2%	0.69 (0.27 to 1.74)
≤15 points	85	56.1%	63.6%	1.80 (0.64 to 5.31)
Occlusion site				
ICA	78	36.8%	27.5%	0.56 (0.16 to 1.86)
MCA M1	148	41.3%	40.3%	1.29 (0.52 to 3.22)
MCA M2	21	44.4%	58.3%	1.75 (0.31 to 10.69)[b]
ASPECTS				
3-4	93	36.2%	37.0%	0.97 (0.30 to 3.10)
5	133	42.4%	40.3%	0.92 (0.36 to 2.30)



[a] Adjusted odds ratios of the predefined subgroups. Results were adjusted for age, baseline NIHSS, and the occurrence of symptomatic intracranial hemorrhage. No adjustments were made for the respective stratification variable.

[a] Unadjusted results to avoid overfitting given the small number of cases.

Abbreviations:
mTICI, modified Treatment in Cerebral Infarction; mRS, modified Rankin Scale; CI, Confidence Interval; LSW, Last Seen Well; NIHSS, National Institutes Health Stroke Scale; ICA, Internal Carotid Artery; MCA, Middle Cerebral Artery; ASPECTS, Alberta Stroke Program Early CT Score

Figure S4. Independent ambulation stratified for mTICI and recanalization attempts.
Shown are the rates of independent ambulation defined as 90-day mRS scores of 0-3 stratified for the final mTICI grade and the number of recanalization attempts. The results do neither indicate superior functional outcomes when mTICI 3 reperfusion is achieved after multiple attempts (mTICI 2b at attempt 1 vs mTICI 3 at attempt ≥2, Whitney U test, *P*=.74) nor a relevant first pass effect of immediate mTICI 3 compared with mTICI 2b after multiple attempts (mTICI 3 at attempt 1 vs mTICI 2b at attempt ≥2, Whitney U test, *P*=.92).

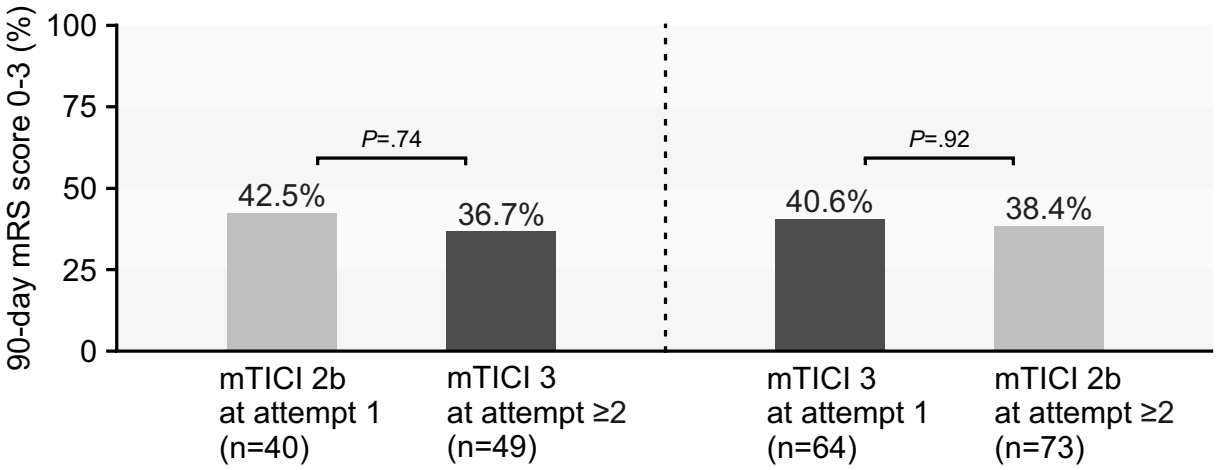


Table S1. Multivariable ordinal logistic regression (shift analysis).
Multivariable ordinal logistic regression to investigate the relationship between the distribution of modified Rankin Scale (mRS) scores at 90 days and selected independent variables (mRS shift analysis).

	90-day mRS score		
	β Coefficient	**Adjusted Common Odds Ratio (95% CI)**	***P***
Independent Variables			
Age (per 10 years)	-0.73	0.48 (0.38-0.61)	<.001
Female sex (yes)	-0.15	0.86 (0.50-1.49)	.59
Last known well/symptom onset to hospital admission (per 30 minutes)	-0.03	0.97 (0.95-0.99)	.01
Admission NIHSS score (per 1 point)	-0.15	0.86 (0.81-0.92)	<.001
Administration of IVT (yes)	-0.19	0.83 (0.45-1.51)	.54
Final mTICI 2b	Reference		
Final mTICI 3	0.11	1.12 (0.64-1.94)	.70
Number of recanalization attempts (per 1 additional attempt)	-0.07	0.93 (0.79-1.09)	.37
sICH (yes)	-1.94	0.14 (0.04-0.42)	<.001

n = 197 patients included. A *P* value of less than 0.05 was considered significant.

Adjusted common odds ratios greater than 1 indicate a shift in the distribution of 90-day mRS scores toward lower values (better functional outcomes).

Abbreviations:
mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; IVT, Intravenous Thrombolysis; ASPECTS, Alberta Stroke Program Early CT Score; mTICI, modified Thrombolysis in Cerebral Infarction; sICH, Symptomatic Intracranial Hemorrhage

Table S2. Functional and safety outcomes before propensity score matching.

	Before Propensity Score Matching							
	Patients, No.(%)				Odds Ratio (95% CI)			
	All (n=290)	mTICI 2b (n=132)	mTICI 3 (n=158)	*P* [a]	Unadjusted [b]	*P*	Adjusted [c]	*P*
Primary Outcome								
90-day mRS score, median (IQR)	4 (2-6)	4 (3-6)	4 (2-6)	.32[1]	1.23 (0.82-1.86)	.32	1.27 (0.79-2.06)	.32
Secondary Outcomes								
Independent ambulation (90-day mRS score 0-3)	118/290 (40.7)	52/132 (39.4)	66/158 (41.8)	.68[2]	1.10 (0.69-1.77)	.68	1.00 (0.52-1.90)	.99
Functional independence (90-day mRS score 0-2)	76/290 (26.2)	30/132 (22.7)	46/158 (29.1)	.22[2]	1.40 (0.82-2.39)	.22	1.46 (0.72-3.02)[e]	.29
Safety Outcomes								
Symptomatic ICH within 24 hours	22/285 (7.7)	15/130 (11.5)	7/155 (4.5)	.03[2]	0.36 (0.13-0.89)	.03	NA[f]	NA[f]
Mortality within 90 days	96/290 (33.1)	47/132 (35.6)	49/158 (31.0)	.41[2]	0.81 (0.50-1.33)	.41	0.75 (0.40-1.41)	.37

[a] Characteristics were compared between mTICI 2b and mTICI 3 patients with the use of either Mann-Whitney U test (1) for continuous variables or a chi-square test (2) for categorical variables.

[b] Univariable regression analysis with final mTICI grade (mTICI 2b vs mTICI 3) as independent variable. mTICI 2b was used as reference level.

[c] Results were adjusted for age, sex, interval from last known well/symptom onset to hospital admission, admission NIHSS, ASPECTS, number of recanalization attempts, and occurrence of symptomatic intracranial hemorrhage within 24 hours.

[d] Common odds ratios derived from ordinal logistic regression analysis. Values greater than 1 indicate a shift in the distribution of 90-day mRS scores towards lower values (better functional outcomes) favoring mTICI 3 compared with mTICI 2b.

[e] All patients with symptomatic intracranial hemorrhage did not achieve functional independence at 90 days (perfect predictor). Thus, the occurrence of symptomatic intracranial hemorrhage was not considered as covariate for this model.

[f] A multivariable regression analysis for symptomatic intracranial hemorrhage was not performed given the small number of cases (n=22).

Abbreviations:
mTICI, modified Thrombolysis in Cerebral Infarction; CI, Confidence Interval; IQR, Interquartile Range; mRS, modified Rankin Scale; ICH, Intracranial Hemorrhage

Table S3. Sensitivity analysis after exclusion of patients with M2 occlusion.
Functional and safety outcomes after exclusion of patients with M2 occlusions (after propensity score matching). Results were comparable with the main analyses shown in Table 2.

	After Exclusion of M2 occlusion							
	Patients, No.(%)				Odds Ratio (95% CI)			
	All (n=205)	mTICI 2b (n=104)	mTICI 3 (n=101)	*P* [a]	Unadjusted [b]	*P*	Adjusted [c]	*P*
Primary Outcome								
90-day mRS score, median (IQR)	4 (3-6)	4 (3-6)	4 (3-6)	.93[1]	0.98 (0.60-1.60)[d]	.93	0.91 (0.51-1.61)[d]	.74
Secondary Outcomes								
Independent ambulation (90-day mRS score 0-3)	78/205 (38.0)	41/104 (39.4)	37/101 (36.6)	.68[2]	0.89 (0.50-1.56)	.68	0.79 (0.37-1.68)	.54
Functional independence (90-day mRS score 0-2)	47/205 (22.9)	23/104 (22.1)	24/101 (23.8)	.78[2]	1.10 (0.57-2.11)	.78	1.02 (0.44-2.34)[e]	.97
Safety Outcomes								
Symptomatic ICH within 24 hours	17/200 (8.5)	12/102 (11.8)	5/98 (5.1)	.09[2]	0.40 (0.12-1.13)	.10	NA[f]	NA[f]
Mortality within 90 days	73/205 (35.6)	37/104 (35.6)	36/101 (35.6)	.99[2]	1.00 (0.57-1.78)	.99	0.89 (0.41-1.96)	.78

[a] Characteristics were compared between mTICI 2b and mTICI 3 patients with the use of either Mann-Whitney U test (1) for continuous variables or a chi-square test (2) for categorical variables.

[b] Univariable regression analysis with final mTICI grade (mTICI 2b vs mTICI 3) as independent variable. mTICI 2b was used as reference level.

[c] Results were adjusted for age, sex, interval from last known well/symptom onset to hospital admission, admission NIHSS, ASPECTS, number of recanalization attempts, and occurrence of symptomatic intracranial hemorrhage within 24 hours.

[d] Common odds ratios derived from ordinal logistic regression analysis. Values greater than 1 indicate a shift in the distribution of 90-day mRS scores towards lower values (better functional outcomes) favoring mTICI 3 compared with mTICI 2b.

[e] All patients with symptomatic intracranial hemorrhage did not achieve functional independence at 90 days (perfect predictor). Thus, the occurrence of symptomatic intracranial hemorrhage was not considered as covariate for this model.

[f] A multivariable regression analysis for symptomatic intracranial hemorrhage was not performed given the small number of cases (n=17).

Abbreviations:
mTICI, modified Thrombolysis in Cerebral Infarction; CI, Confidence Interval; IQR, Interquartile Range; mRS, modified Rankin Scale; ICH, Intracranial Hemorrhage

Table S4. Comparison of mTICI 2b and mTICI 3 for ASPECTS 6-8 and 9-10.
Functional and safety outcomes in patients with moderate baseline infarction (ASPECTS 6-8) and small baseline infarction (ASPECTS 9-10). Please note that in contrast to extensive baseline infarction (ASPECTS 3-5), there were superior 90-day mRS scores in patients with mTICI 3 compared with mTICI 2b in small and moderate baseline infarction.

	ASPECTS 6-8			ASPECTS 9-10		
	Patients, No. (%)			Patients, No. (%)		
	mTICI 2b (n=643)	mTICI 3 (n=845)	*P* [a]	mTICI 2b (n=844)	mTICI 3 (n=1574)	*P* [a]
Primary Outcome						
90-day mRS score, median (IQR)	4 (2-5)	3 (1-5)	.03[1]	3 (1-5)	2 (1-4)	<.001[2]
Secondary Outcomes						
Independent ambulation (90-day mRS score 0-3)	319 (49.6)	468 (55.4)	.03[2]	523 (62.0)	1109 (70.5)	<.001[2]
Functional independence (90-day mRS score 0-2)	225 (35.0)	338 (40.0)	.048[2]	401. (47.5)	888 (56.4)	<.001[2]
Safety Outcomes						
sICH within 24 hours	31 (4.9)	29 (3.5)	.18[2]	28 (3.3)	31 (2.0)	.04[2]
Mortality within 90 days	160 (24.9)	194 (23.0)	.39[2]	176 (20.9)	259(16.5)	.007[2]

[a] Characteristics were compared between mTICI 2b and mTICI 3 patients with the use of either Mann-Whitney U test (1) for continuous variables or a chi-square test (2) for categorical variables.

Abbreviations: mTICI, modified Thrombolysis in Cerebral Infarction; IQR, Interquartile Range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; ICA, Internal Carotid Artery, MCA, Middle Cerebral Artery; ASPECTS, Alberta Stroke Program Early CT Score; IVT, Intravenous Thrombolysis; EVT, Endovascular Therapy; sICH, Symptomatic Intracranial Hemorrhage.