Supplemental Online Content

Lapergue B, Blanc R, Costalat V, et al. Effect of thrombectomy with combined contact aspiration and stent retriever vs stent retriever alone on revascularization in patients with acute ischemic stroke and large vessel occlusion: the ASTER2 randomized clinical trial. *JAMA*. doi:10.1001/jama.2021.13827

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

eAppendix. Definitions of eTICI and mRankin Score

- **Expanded thrombolysis in cerebral infarction (eTICI): Liebeskind DS, et al. J NeuroIntervent Surg 2018;0:1–7.**

This 7-point compilation of TICI grades, termed the expanded TICI (eTICI), reflects all previously reported thresholds used to

define reperfusion after endovascular stroke therapy.

In brief, eTICI grade 0 is equivalent to no reperfusion or 0% filling of the downstream territory; eTICI 1 reflects thrombus reduction without any reperfusion of distal arteries; eTICI 2a is reperfusion in less than half or 1–49% of the territory; eTICI 2b50 is 50–66% reperfusion, exceeding the modified TICI (mTICI) 2B threshold but below the original TICI 2B cut-off point; eTICI 2b67 is 67–89% reperfusion, exceeding mTICI but below TICI2C; eTICI 2c is equivalent to TICI 2C or 90–99% reperfusion (near total); and eTICI 3 is total or 100% reperfusion, tantamount to TICI 3.

In the ASTER2 trial, we chose to combine the eTICI2b67 and eTICI2b50 levels into a single category named eTICI2b50.

- **modified Rankin Score: Bamford JM, et al. J. Stroke. 1989 Jun;20(6):828.**

0 No symptoms at all
1 No significant disability despite symptoms; able to carry out all usual duties and activities.

2 Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance.

3 Moderate disability; requiring some help, but able to walk without assistance.

4 Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance.

5 Severe disability; bedridden, incontinent and requiring constant nursing care and attention.

6 Dead.

eMethods. Interventions and Thrombectomy Procedure

Experimental group "Combined contact aspiration/stent retriever Technique" ([8-10,16])

The combined contact aspiration/stent retriever approach was performed, as in standard care, using a balloon-guide catheter. A 0.021-to-0.027-inch inner lumen microcatheter, with a 0.014-to-0.016-inch microwire inside, was introduced into a large-bore aspiration catheter and this construct was introduced into the balloon-guide catheter as a unit. The balloon-guide catheter was placed at the origin of the cervical intracranial carotid artery. The microcatheter was then advanced past the thrombus over the microwire to allow deployment of the stent-retriever as in the control group. The stent retriever (Any CE-marked device) was then deployed beyond the occlusion. After deployment of the stent retriever, the large bore distal access catheter was advanced to contact the proximal edge of the stent retriever. Then, the aspiration pump was connected to the large bore distal access catheter. After at least 90 sec of aspiration, the stent retriever and the large bore distal access catheter were pulled out as a unit from the balloon-guide catheter and from the patient. Manual aspiration was also applied to the balloon-guide catheter during the pull-out maneuver, which was performed after the temporary inflation of the balloon at the tip of the balloon-guide catheter to ensure carotid flow arrest.

This process was repeated until successful reperfusion (eTICI 2c/3) was achieved or the procedure terminated. At least three attempts were made before switching to another adjunctive device. A revascularization score was recorded after each device attempt.

Control group « standard stent retriever technique":

The technique used was in accordance with the device instruction for use. A large bore balloon guide catheter was placed at the origin of the cervical ICA. A suitable delivery microcatheter was navigated over a microwire into the occluded MCA and across the occlusion. A control super-selective angiogram was used to document the extent of occlusion and thrombus. The stent retriever (Any CE-marked device) was then deployed across the occlusion. After at least 90 seconds, withdrawal was performed with proximal occlusion by inflation of the balloon guide catheter. This process was repeated until successful reperfusion (eTICI 2c/3) was achieved, or the procedure terminated. At least three attempts were made before switching to another adjunctive device. A revascularization score was recorded after each device attempt.

eTable 1. Number of Patients Included Per Participating Center

	Overall	Date of first enrolled patient	First-line CA/SR thrombectomy	First-line SR alone thrombectomy
Center n°1	71	2017/10/16	36	35
Center n°2	120	2017/10/17	61	59
Center n°3	33	2017/11/28	17	16
Center n°4	54	2017/12/02	26	28
Center n°5	16	2017/11/24	8	8
Center n°6	30	2017/11/18	15	15
Center n°7	38	2017/12/01	20	18
Center n°8	16	2018/02/07	8	8
Center n°9	22	2018/02/09	11	11
Center n°10	5	2018/04/25	2	3
Center n°11	3	2018/02/06	1	2

Abbreviations: CA=contact aspiration; SR=stent retriever.

eTable 2. Procedural Details (in Analyzed Population After at Least 1 Device Pass [a])

Procedural characteristics	First allocated Contact aspiration /Stent retriever thrombectomy (N=185)	First allocated Stent retriever thrombectomy(N=181)
First-line strategy		
Allocated group	184/185 (99.5)	181/181 (100.0)
Balloon guide catheter use	176/185 (95.1)	164/181 (90.6)
Number of passes		
1	94/185 (50.8)	81/181 (44.8)
2	43/185 (23.2)	42/181 (23.2)
3	48/185 (26.0)	58/181 (32.0)
Second-line strategy	39/185 (21.1)	54/181 (29.8)
Contact aspiration alone	11/185 (6.0)	9/181 (5.0)
Stent retriever alone	3/185 (1.6)	2/181 (1.1)
Contact aspiration and Stent retriever	25/185 (13.5)	42/181 (23.2)
Others	0/185 (0.0)	1/181 (0.6) [b]
Number of passes		
1	15/185 (8.1)	15/181 (8.3)
2	13/185 (7.0)	21/181 (11.6)
3	4/185 (2.2)	7/181 (3.9)
4-5	4/185 (2.2)	7/181 (3.9)
6-13	3/185 (1.6)	4/181 (2.2)
Time from arterial puncture to clot contact	23 (17 to 34)	22 (17 to 32)
Time from arterial puncture to maximal recanalization (procedural time)	47 (30 to 72)	50 (32 to 77)

[a] data among randomized patients after at least one thrombectomy device pass (excluding patients with spontaneous clot revascularization (n=30), intracranial access failure (n=6) and the 3 cases who did not receive any device pass) and after exclusion for legal reasons of the 3 patients (see flow chart, one allocated to SR group but treated by combination first-line CA/SR) [b] Recanalization with a micro guidewire.

Abbreviations: CA=contact aspiration; SR=stent retriever.

eTable 3. Detail of Thrombectomy Devices Used in Frontline and Rescue Strategies According to the Assigned Groups

	Used in Stent Retriever Group		Used in Combination of Stent retriever and Contact aspiration Group	
Devices	**Initial strategy**	**Rescue strategy**	**Initial strategy**	**Rescue strategy**
Balloon guide catheters				
Merci 8F	4	1	3	0
Merci 9F	64	15	67	10
Floxgate 2 8F	26	10	28	6
Cello 8 F	11	2	3	0
Cello 9F	63	20	79	13
Stent Retrievers				
Trevo 4	31	10	43	7
Trevo 6	17	5	18	0
Solitaire 4*20	51	11	52	10
Solitaire 6*30	47	13	40	5
Eric	14	4	13	5
Embotrap	3	0	2	0
Preset	6	1	8	1
Solitaire4*40	1	2	3	0
Solitaire 6*40	3	1	2	0
Solitaire6*24	1	1	2	0
Solitaire 6*20	2	0	1	0
Trevo 3	2	0	0	1
Trevo 3*20	2	0	3	0
Trevo 4*20	1	0	0	0
Vesalio Neva	1	0	2	1
Catchmini	0	0	1	0
Catchmaxi6*30	0	1	1	1
Tigertriever	0	1	0	0
Contact Aspiration catheters				
ACE 64	0	1	1	0
ACE60	0	4	1	1
ACE 68	6	17	84	9
3 max	0	5	1	7
4 max	0	2	2	1
5 Max	0	0	2	0
Sofia 5F	2	17	37	12
Sofia 6Fplus	8	8	42	8
Arc	0	0	11	0
Navien 072	0	0	1	0
Catalyst 6F	0	2	8	3
Catalyst 5F	0	0	2	0

eTable 4. Primary and Secondary Efficacy Outcomes in Per-Protocol Population

	First allocated contact aspiration/stent retriever thrombectomy (N=167)	**First allocated stent retriever thrombectomy** (N=146)	**Adjusted odds ratio (95%CI)**	**P-Value**
Primary efficacy outcome				
Reperfusion (eTICI 2c/3) at the end of procedures	110 (65.9)	88 (60.3)	1.26 (0.79 to 2.02)	0.32
Secondary angiographic efficacy outcomes				
Reperfusion outcomes at the end of procedures				
eTICI 2b50/2c/3	152 (91.0)	130 (89.0)	1.28 (0.59 to 2.76)	0.53
eTICI 3	47 (28.1)	36 (24.7)	1.20 (0.72 to 2.01)	0.48
Reperfusion outcomes after the assigned initial intervention alone				
eTICI 2b50/2c/3	144 (86.2)	111 (76.0)	2.07 (1.12 to 3.78)	0.019
eTICI 2c/3	104 (62.3)	76 (52.1)	1.51 (0.95 to 2.38)	0.078
eTICI 3	46 (27.5)	31 (21.3)	1.42 (0.83 to 2.40)	0.19
First pass effect (eTICI 2c/3 after first pass)	67 (40.1)	47 (32.2)	1.41 (0.88 to 2.26)	0.15
Modified First Pass Effect (eTICI 2b50/2c/3 after first pass)	88 (52.7)	64 (43.8)	1.44 (0.91 to 2.28)	0.11
eTICI 3 after first pass	33 (19.8)	18 (12.3)	1.77 (0.94 to 3.32)	0.075
Use of rescue treatment	31 (18.6)	45 (30.8)	0.49 (0.28 to 0.85)	0.011
Arterial puncture to eTICI 2c/3[a]				
Median (IQR)	42 (28 to 58) [n=110]	43 (28 to 59) [n=88]		
Mean (95%CI)[b]	3.80 (3.65 to 3.94)	3.75 (3.59 to 3.91)	0.044 (-0.10 to 0.19)[c]	0.54
Clot contact to maximal reperfusion[d]				
Median (IQR)	16 (8 to 37) [n=165]	20 (10 to 44) [n=143]		
Mean (95%CI)[b]	3.02 (2.81 to 3.23)	3.15 (2.93 to 3.37)	-0.13 (-0.35 to 0.09)[c]	0.23
Clinical efficacy outcomes				
Change in NIHSS score at 24 hours, mean (95%CI)[e]	-3.5 (-5.2 to -1.9) [n=159]	-3.3 (-4.8 to -1.7) [n=142]	-0.2 (-2.0 to 2.5)[c]	0.82
Functional independence [f]				
at 3 months	61/160 (38.1)	62/142 (43.7)	0.80 (0.49 to 1.30)	0.36

at 12 months	60/145 (41.4)	54/130 (41.5)	1.03 (0.61 to 1.72)	0.91
Modified Rankin Scale				
at 3 months, median (IQR)	3.5 (1 to 6) [n=160]	3 (2 to 5) [n=142]	0.97 (0.64 to 1.46)[g]	0.87
at 12 months, median (IQR)	4 (1 to 6) [n=145]	3 (1 to 6) [n=130]	0.95 (0.60 to 1.47)[g]	0.80
EQ-5D utility index score at 12 months[h]				
Median (IQR)	0 (0 to 0.75) [n=151]	0.27 (0 to 0.80) [n=132]		
Mean (95%CI)	0.33 (0.24 to 0.43)	0.37 (0.27 to 0.47)	-0.04 (-0.13 to 0.06)[c]	0.46
EQ-5D visual analogue scale at 12 months[i]	70 (64 to 77) [n=75]	64 (58 to 71) [n=78]	5.88 (-0.91 to 12.68)[c]	0.09

Values expressed as n (%), unless otherwise stated. Effect sizes were calculated after adjustment for randomization stratification variables (center, age (<70 vs. ≥70 years), intravenous thrombolysis and occlusion site (isolated MCA versus tandem MCA and /ICA)).

[a] data among patients with near total/total reperfusion after at least one device pass, [b] calculated after log-transformation of values, [c] difference in means, [d] data among patients after at least one device pass, [e] additional adjustment on baseline NIHSS score, [f] modified Rankin scale score ≤2 (the modified Rankin Scale measures the degree of disability; score ranges from 0 (symptom free) to 6 (dead)), [g] common adjusted odds ratio of improvement of 1 point in Modified Rankin Scale score, [h] treating death with EQ-5D utility index score=0, [i] data among patients alive at 12-months.

Abbreviations: CI=confidence interval; ICA=internal carotid artery; IQR=interquartile range; MCA=middle cerebral artery; eTICI= Expanded Treatment in Cerebral Infarction Score; NIHSS=National Institutes of Health Stroke Scale.

eTable 5. Primary and Secondary Reperfusion Outcomes in Complete Case-Analysis

	First allocated contact aspiration/stent retriever thrombectomy	First allocated stent retriever thrombectomy	Adjusted odds ratio (95%CI)	P-Value
Primary efficacy outcome				
Reperfusion (eTICI 2c/3) at the end of procedures	114/180 (63.3)	102/174 (58.6)	1.21 (0.78 to 1.87)	0.38
Secondary angiographic efficacy outcomes				
Reperfusion outcomes at the end of procedures				
eTICI 2b50/2c/3	163/180 (90.6)	155/174 (89.1)	1.21 (0.59 to 2.46)	0.60
eTICI 3	49/190 (27.2)	41/174 (23.6)	1.21 (0.74 to 1.96)	0.44
Reperfusion outcomes after the assigned initial intervention alone				
eTICI 2b50/2c/3	159/185 (86.0)	130/175 (74.3)	2.17 (1.25 to 3.76)	0.006
eTICI 2c/3	105/185 (56.8)	85/175 (48.6)	1.38 (0.90 to 2.11)	0.13
eTICI 3	46/185 (24.9)	35/175 (20.0)	1.33 (0.80 to 2.20)	0.27
First pass effect (eTICI 2c/3 after first pass)	67/185 (36.2)	53/175 (30.3)	1.31 (0.84 to 2.04)	0.23
Modified First Pass Effect (eTICI 2b50/2c/3 after first pass)	93/185 (50.3)	75/175 (42.9)	1.36 (0.89 to 2.07)	0.15
eTICI 3 after first pass	33/185 (17.8)	21/175 (12.0)	1.60 (0.88 to 2.92)	0.12

Values expressed as n (%), unless otherwise stated. Effect sizes were calculated after adjustment for randomization stratification variables (center, age (<70 vs. ≥70 years), intravenous thrombolysis and occlusion site (isolated MCA versus tandem MCA and /ICA)) by restricting analysis to patients with post-baseline eTICI evaluation by the core-laboratory.

Abbreviations: CI=confidence interval; ICA=internal carotid artery; IQR=interquartile range; MCA=middle cerebral artery; eTICI= Expanded Treatment in Cerebral Infarction Score; NIHSS=National Institutes of Health Stroke Scale.

eTable 6. Primary and Secondary Reperfusion Outcomes in Multiple-Imputation Analysis

	First allocated contact aspiration/stent retriever thrombectomy (N=203)	**First allocated stent retriever thrombectomy** (N=202)	**Adjusted odds ratio (95%CI)**	**P-Value**
Primary efficacy outcome				
Reperfusion (eTICI 2c/3) at the end of procedures	128 (63.2)	117 (57.9)	1.25 (0.80 to 1.95)	0.32
Secondary angiographic efficacy outcomes				
Reperfusion outcomes at the end of procedures				
eTICI 2b50/2c/3	182 (89.9)	179 (88.5)	1.18 (0.56 to 2.48)	0.66
eTICI 3	56 (27.6)	48 (23.7)	1.23 (0.76 to 1.99)	0.39
Reperfusion outcomes after the assigned initial intervention alone				
eTICI 2b50/2c/3	174 (85.6)	151 (74.8)	2.07 (1.18 to 3.62)	0.01
eTICI 2c/3	115 (56.8)	99 (48.9)	1.39 (0.91 to 2.13)	0.13
eTICI 3	52 (25.4)	41 (20.2)	1.34 (0.82 to 2.20)	0.24
First pass effect (eTICI 2c/3 after first pass)	76 (37.5)	62 (30.7)	1.38 (0.89 to 2.13)	0.15
Modified First Pass Effect (eTICI 2b50/2c/3 after first pass)	106 (52.3)	88 (43.4)	1.45 (0.96 to 2.18)	0.07
eTICI 3 after first pass	38 (18.9)	25 (12.4)	1.66 (0.93 to 2.96)	0.09

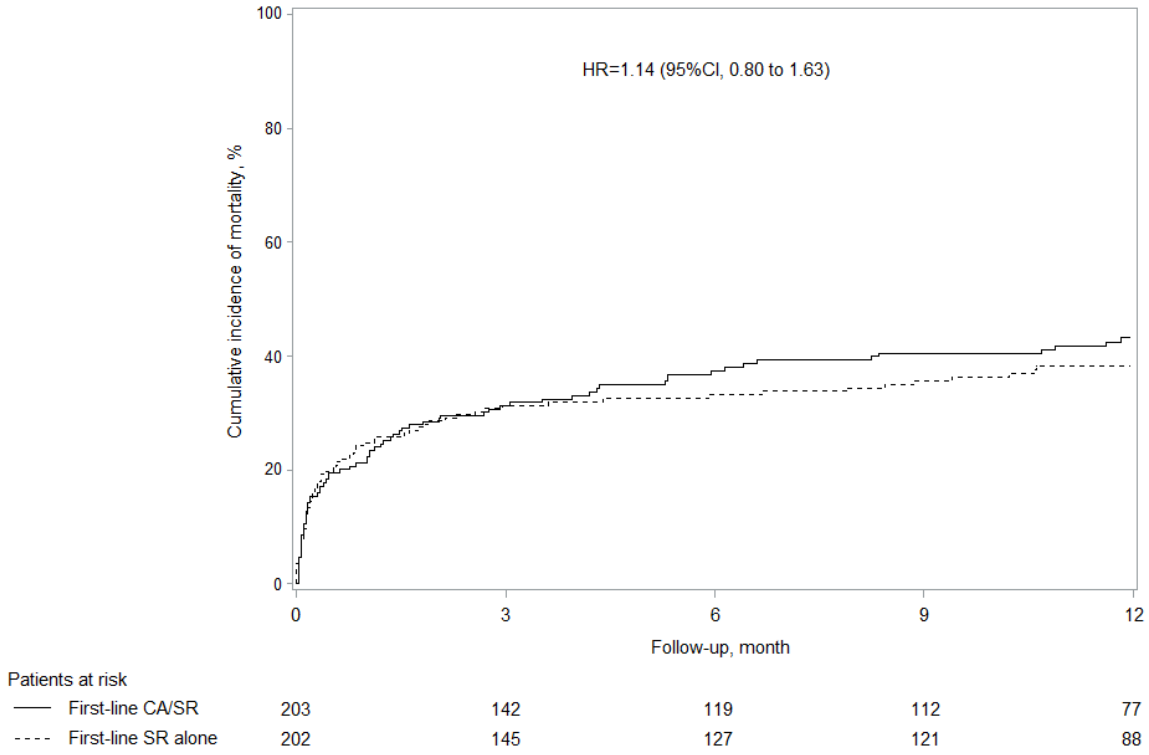
Values expressed as n (%), unless otherwise stated. Effect sizes were calculated after adjustment for randomization stratification variables (center, age (<70 vs. ≥70 years), intravenous thrombolysis and occlusion site (isolated MCA versus tandem MCA and /ICA)) after handling missing values in post-baseline eTICI evaluation by the core-laboratory using multiple imputation procedures (m=10). Missing data were imputed under the missing at random assumption (MAR), using the regression switching approach (chained equation) with a predictive mean matching method for quantitative variables, logistic regression models (binomial, ordinal or multinomial) for categorical variables. The imputation procedure was performed using all baseline characteristics (see Table 1) and the treatment group. Treatment effect estimates obtained in multiple imputed data sets were combined using the Rubin's rules.

Abbreviations: CI=confidence interval; ICA=internal carotid artery; IQR=interquartile range; MCA=middle cerebral artery; eTICI= Expanded Treatment in Cerebral Infarction Score; NIHSS=National Institutes of Health Stroke Scale.

eTable 7. Data on Angiographic and Clinical Outcomes on the Rescue Therapy Group

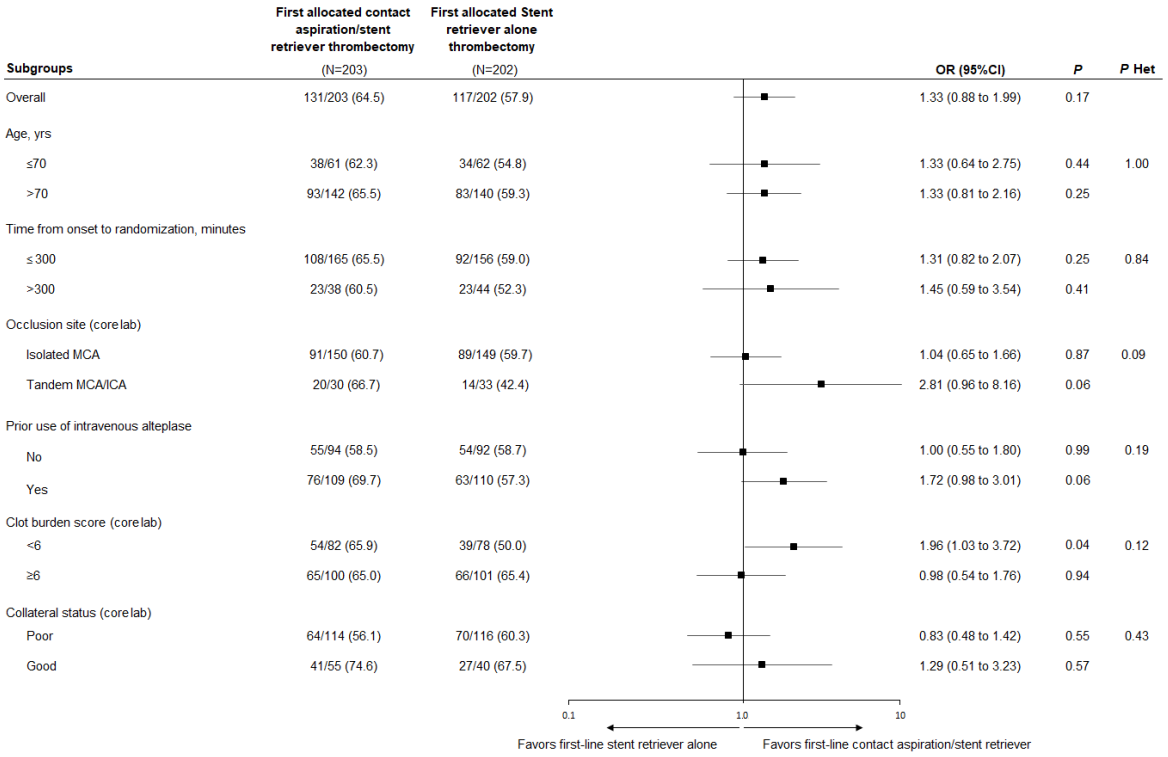
	First allocated Contact aspiration /Stent retriever thrombectomy	**First allocated Stent retriever thrombectomy**
Rescue therapy	39/185 (21.1)	54/181 (29.8)
Contact aspiration alone	11/185 (6.0)	9/181 (5.0)
Stent retriever alone	3/185 (1.6)	2/181 (1.1)
Contact aspiration and Stent retriever	25/185 (13.5)	42/181 (23.2)
Per procedural complications,	3 (7.69)	4 (7.41)
eTICI 3 at end of procedure	4(10.26)	6(11.11)
eTICI 2c/3 at end of procedure	13(33.33)	18(33.33)
eTICI 2b50/2c/3 at end of procedure	25(64.10)	37(68.52)
modified Rankin Score 0-2 (3 months)	10(25.64)	17(32.08)
Death (3 months)	15(38.46)	19(35.85)

eFigure 1. Cumulative Incidence of All-Cause Mortality During the 12-Month Follow-up Period



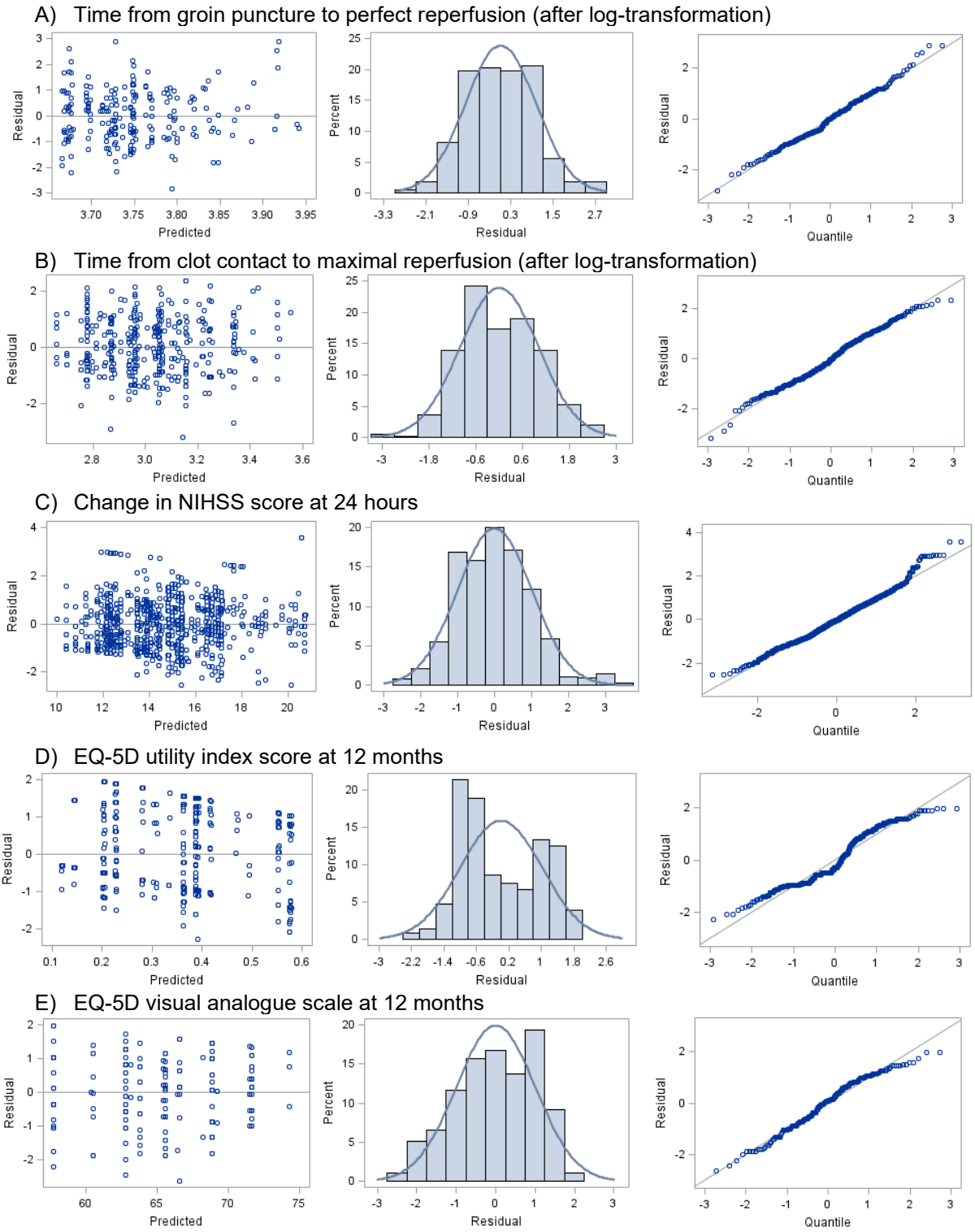
Hazard ratio (95% Confidence interval) for first allocated CA/SR vs. R-alone calculated using Cox's proportional hazard model adjusted for randomization stratification variables (center, age (<70 vs. ≥70 years), IV thrombolysis and occlusion site (isolated MCA versus tandem MCA and /ICA)) is reported.
Abbreviations: CA=contact aspiration, ICA=internal carotid artery; IV=intravenous; MCA=middle cerebral artery; SR=stent retriever

eFigure 2. Treatment Effect Size (First Allocated Contact Aspiration and Stent Retriever Thrombectomy vs First Allocated Stent Retriever Alone Thrombectomy) on Primary Outcome According to Key Subgroups

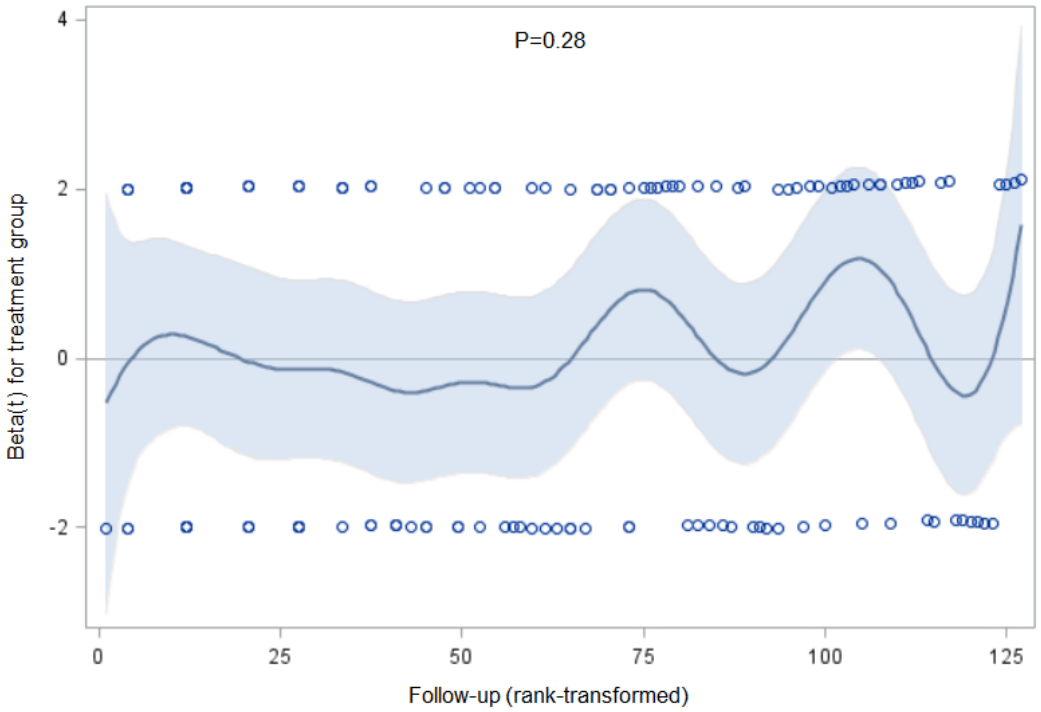


P het indicates *P-V*alues for heterogeneity test.
Abbreviations: CI=confidence interval; ICA=internal carotid artery; MCA=middle cerebral artery; OR=adjusted odds ratio.

eFigure 3. Conditional Studentized Residuals of Linear Mixed Models (Including the Constrained Longitudinal Data Analysis) for Secondary Quantitative Outcomes



eFigure 4. Schoenfeld Residuals Plot for Treatment Group Derived From the Cox Regression Model of 12-Month All-Cause Mortality



Solid line indicates the fitted penalized B-spline curves with 95% confidence interval (bands). The Schoenfeld residuals are shown to have mean zero under the proportional hazard assumption; P-value from the correlation test is reported and did not reject the proportional hazard assumption.