

## SUPPLEMENTAL MATERIAL

**Supplemental table 1. Baseline characteristics and outcomes of late window patients with EVT  $\geq 6.5$  hours after known time of stroke onset versus late window patients with EVT  $\geq 6.5$  hours after unknown time of stroke onset.**

	Late window patients with EVT $\geq 6.5$ hours after known time of stroke onset (n=13)	Late window patients with EVT $\geq 6.5$ hours after unknown time of stroke onset (LSW) (n=93)	p value*
<b>Baseline characteristics</b>			
Age (years); mean (SD)	67.7 (17.4)	67.0 (14.3)	0.87
Sex (male)	3/13 (23.1%)	44/93 (47.3%)	0.10
Pre-stroke mRS 0-1	11/13 (84.6%)	75/93 (80.6%)	0.73
Pre-stroke mRS 0-2	0	83/93 (89.2%)	0.21
NIHSS at presentation; median [IQR]	15 [9-19] (n=12)	16 [11-20] (n=91)	0.47
ASPECTS at presentation; median [IQR]	9 [7-10] (n=13)	8 [6-10] (n=89)	0.24
Location of occlusion			0.68
ICA	2/13 (15.4%)	27/89 (30.3%)	
MCA M1-segment	9/13 (69.2%)	48/89 (53.9%)	
MCA M2-segment	2/13 (15.4%)	13/89 (14.6%)	
Other (M3, ACA)	0	1/89 (1.1%)	
Collateral status			0.61
Absent collaterals	0	2/88 (2.3%)	
Filling $\leq 50\%$ of occluded area	3/13 (23.1%)	27/88 (30.7%)	
Filling 51-100% of occluded area	7/13 (53.8%)	31/88 (35.2%)	
Filling 100% of occluded area	3/13 (23.1%)	28/88 (31.8%)	
CT perfusion performed	2/13 (15.4%)	19/93 (20.4%)	0.67
Transfer from primary hospital to intervention center	9/13 (69.2%)	25/93 (26.9%)	<b>&lt;0.01</b>
Treated with IVT	6/13 (46.2%)	18/92 (19.6%)	<b>0.03</b>

Time between onset/LSW and groin puncture in minutes; mean (SD); median [IQR]	516 (172) (n=13) 449 [405-553]	565 (175) (n=93) 518 [420-654]	0.34
Time between onset/LSW and sheath from groin in minutes; mean (SD); median [IQR]	501 (63) (n=9) 481 [455-548]	628 (189) (n=86) 578 [469-733]	<b>0.05</b>
Performed procedure			0.91
Attempt for thrombectomy	12/13 (92.3%)	85/93 (91.4%)	
Catheterization/DSA only	1/13 (7.7%)	8/93 (8.6%)	
<b>Outcomes</b>			<i>p</i> value†
Primary outcome			
Median 3-month mRS score [IQR]	2 [1-5] (n=13)	3 [2-5] (n=91)	0.52
Secondary outcomes			
Functional independence (3-month mRS 0-2)	61.5% (8/13)	40.7% (37/91)	0.16
Successful reperfusion (eTICI ≥2B)	46.2% (6/13)	58.4% (52/89)	0.40
Significant early clinical improvement (≥4 points decrease on NIHSS or NIHSS 0)	45.5% (5/11)	46.6% (41/88)	0.94
Safety outcomes			
Peri-interventional complications	7.7% (1/13)	9.7% (9/93)	0.82
Symptomatic intracranial hemorrhage	7.7% (1/13)	4.3% (4/93)	0.59
Mortality at 3 months	23.1% (3/13)	24.2% (22/91)	0.93

\*Chi-square tests for categorical variables and independent t-tests or Mann-Whitney U tests for continuous variables with complete data

†Mann-Whitney U test for difference in 3-month mRS score and chi-square tests for difference in proportions of other outcomes

EVT: endovascular treatment; SD: standard deviation; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; IQR: interquartile range; ASPECTS: Alberta Stroke Programme Early CT Score; ICA: internal carotid artery; MCA: middle cerebral artery; ACA: anterior cerebral artery; IVT: intravenous thrombolysis; LSW: last seen well; DSA: digital subtraction angiography; eTICI: extended Treatment In Cerebral Infarction

**Supplemental table 2. Baseline characteristics and outcomes of late window patients with EVT  $\geq$ 6.5hrs who received CT perfusion imaging vs. late window patients with EVT  $\geq$ 6.5hrs who did not receive CT perfusion imaging**

	Late window patients with EVT $\geq$ 6.5hrs with CT perfusion imaging (n=21)	Late window patients with EVT $\geq$ 6.5hrs without CT perfusion imaging (n=85)	<i>p</i> value*
<b>Baseline characteristics</b>			
Age (years); mean (SD)	65.8 (14.4)	67.4 (14.7)	0.65
Sex (male)	10/21 (47.6%)	37/85 (43.5%)	0.74
Pre-stroke mRS 0-1	18/21 (85.7%)	68/85 (80.0%)	0.55
Pre-stroke mRS 0-2	20/21 (95.2%)	76/85 (89.4%)	0.41
NIHSS at presentation; median [IQR]	13 [8-17] (n=19)	16 [12-20] (n=84)	<b>0.01</b>
ASPECTS at presentation; median [IQR]	7 [5-9] (n=20)	9 [7-10] (n=82)	0.09
Location of occlusion			0.12
ICA	5/21 (23.8%)	24/81 (29.6%)	
MCA M1-segment	10/21 (47.6%)	47/81 (58.0%)	
MCA M2-segment	5/21 (23.8%)	10/81 (12.3%)	
Other (M3, ACA)	1/21 (4.8%)	0	
Collateral status			0.80
Absent collaterals	0	2/82 (2.4%)	
Filling $\leq$ 50% of occluded area	6/19 (31.6%)	24/82 (29.3%)	
Filling 51-100% of occluded area	6/19 (31.6%)	32/82 (39.0%)	
Filling 100% of occluded area	7/19 (36.8%)	24/82 (29.3%)	
Treated with IVT	4/21 (19.0%)	20/84 (23.8%)	0.64
Unknown time of onset	19/21 (90.5%)	74/85 (87.1%)	0.67
Time between onset/LSW and groin puncture in minutes; mean (SD); median [IQR]	540 (146) (n=21) 518 [420-609]	563 (181) (n=85) 505 [415-664]	0.58
Time between onset/LSW and sheath from groin in minutes; mean (SD); median [IQR]	577 (159) (n=18) 523 [478-649]	625 (190) (n=77) 571 [463-719]	0.33
Performed procedure			0.85
	19/21 (90.5%)	78/85 (91.8%)	

Attempt for thrombectomy	2/21 (9.5%)	7/85 (8.2%)	
Catheterization/DSA only			
<b>Outcomes</b>			<i>p</i> value†
<u>Primary outcome</u>			
Median 3-month mRS score [IQR]	2 [2-4] (n=21)	3 [2-6] (n=83)	0.83
<u>Secondary outcomes</u>			
Functional independence (3-month mRS 0-2)	42.9% (9/21)	43.4% (36/83)	0.97
Successful reperfusion (eTICI ≥2B)	68.4% (13/19)	54.2% (45/83)	0.26
Significant early clinical improvement (≥4 points decrease on NIHSS or NIHSS 0)	27.8% (5/18)	50.6% (41/81)	0.08
<u>Safety outcomes</u>			
Peri-interventional complications	9.5% (2/21)	9.4% (8/85)	0.99
Symptomatic intracranial hemorrhage	14.3% (3/21)	2.4% (2/85)	<b>0.02</b>
Mortality at 3 months	14.3% (3/21)	26.5% (22/83)	0.24

\*Chi-square tests for categorical variables and independent t-tests or Mann-Whitney U tests for continuous variables with complete data.

†Mann-Whitney U test for difference in 3-month mRS score and chi-square tests for difference in proportions of other outcomes

EVT: endovascular treatment; SD: standard deviation; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; IQR: interquartile range; ASPECTS: Alberta Stroke Program Early CT Score; ICA: internal carotid artery; MCA: middle cerebral artery; ACA: anterior cerebral artery; IVT: intravenous thrombolysis; LSW: last seen well; DSA: digital subtraction angiography; eTICI: extended Treatment In Cerebral Ischemia

**Supplemental table 3. Baseline characteristics and outcomes of patients with known time of stroke onset treated with EVT beyond versus within 6.5 hours.**

	Late window patients with EVT $\geq$ 6.5 hours after known time of stroke onset (n=13)	Early window patients with EVT <6.5 hours after known time of stroke onset (n=2316)	<i>p</i> value*
<b>Baseline characteristics</b>			
Age (years); mean (SD)	67.7 (17.4)	69.3 (14.1)	0.69
Sex (male)	3/13 (23.1%)	1246/2316 (53.8%)	<b>0.03</b>
Pre-stroke mRS 0-1	11/13 (84.6%)	1879/2269 (82.8%)	0.86
Pre-stroke mRS 0-2	0	2038/2269 (89.8%)	0.23
NIHSS at presentation; median [IQR]	15 [9-19] (n=12)	15 [11-19] (n=2278)	0.72
ASPECTS at presentation; median [IQR]	9 [7-10] (n=13)	9 [8-10] (n=2245)	0.90
Location of occlusion			0.80
ICA	2/13 (15.4%)	589/2203 (26.7%)	
MCA M1-segment	9/13 (69.2%)	1276/2203 (57.9%)	
MCA M2-segment	2/13 (15.4%)	322/2203 (14.6%)	
Other (M3, ACA)	0	16/2203 (0.7%)	
Collateral status			0.55
Absent collaterals	0	127/2169 (5.9%)	
Filling $\leq$ 50% of occluded area	3/13 (23.1%)	768/2169 (35.4%)	
Filling 51-100% of occluded area	7/13 (53.8%)	853/2169 (39.3%)	
Filling 100% of occluded area	3/13 (23.1%)	421/2169 (19.4%)	
CT perfusion performed	2/13 (15.4%)	218/1201 (18.2%)	0.80
Transfer from another hospital to intervention center	9/13 (69.2%)	1306/2316 (56.4%)	0.35
Treated with IVT	6/13 (46.2%)	1825/2309 (79.0%)	<b>&lt;0.01</b>
Time between onset/LSW and groin puncture in minutes; mean (SD); median [IQR]	516 (172) (n=13) 449 [405-553]	187 (64) (n=2316) 180 [140-225]	<b>&lt;0.01</b>

Time between onset/LSW and sheath from groin in minutes; mean (SD); median [IQR]	501 (63) (n=9) 481 [455-548]	243 (72) (n=2147) 235 [190-290]	<b>&lt;0.01</b>
Performed procedure			0.48
Attempt for thrombectomy	12/13 (92.3%)	1972/2308 (85.4%)	
Catheterization/DSA only	1/13 (7.7%)	336/2308 (14.6%)	
<b>Outcomes</b>			<b>p value†</b>
Primary outcome			
Median 3-month mRS score [IQR]	2 [1.5-5.5] (n=13)	3 [2-6] (n=2155)	0.65
Secondary outcomes			
Functional independence (3-month mRS 0-2)	61.5% (8/13)	43.3% (933/2155)	0.19
Successful reperfusion (eTICI ≥2B)	46.2% (6/13)	61.2% (1377/2251)	0.27
Significant early clinical improvement (≥4 points decrease on NIHSS or NIHSS 0)	45.5% (5/11)	54.9% (1136/2068)	0.53
Safety outcomes			
Peri-interventional complications	7.7% (1/13)	9.0% (208/2316)	0.87
Symptomatic intracranial hemorrhage	7.7% (1/13)	6.0% (139/2316)	0.80
Mortality at 3 months	23.1% (3/13)	27.0% (581/2155)	0.75

\*Chi-square tests for categorical variables and independent t-tests or Mann-Whitney U tests for continuous variables with complete data

†Mann-Whitney U test for difference in 3-month mRS score and chi-square tests for difference in proportions of other outcomes

EVT: endovascular treatment; SD: standard deviation; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; IQR: interquartile range; ASPECTS: Alberta Stroke Programme Early CT Score; ICA: internal carotid artery; MCA: middle cerebral artery; ACA: anterior cerebral artery; IVT: intravenous thrombolysis; LSW: last seen well; DSA: digital subtraction angiography; eTICI: extended Treatment In Cerebral Infarction

**Supplemental table 4. Logistic regression analysis for late vs. early window patients.**

	<u>Late window patients with EVT <math>\geq</math>6.5 hours (n=106) versus early window patients with EVT &lt;6.5 hours (n=3158) after onset or LSW</u>			
	unadjusted OR (95% CI)	<i>p</i> value	adjusted OR (95% CI)*	<i>p</i> value
<b>Primary outcome</b>				
3-month mRS score reduction (shift analysis) †	1.02 (0.72-1.44)	0.92	0.86 (0.58-1.28)	0.46
<b>Secondary outcomes</b>				
Functional independence (3-month mRS 0-2)	1.12 (0.76-1.67)	0.57	0.89 (0.53-1.49)	0.65
Successful reperfusion (eTICI $\geq$ 2B)	0.83 (0.56-1.24)	0.36	0.85 (0.54-1.32)	0.46
Significant early clinical improvement ( $\geq$ 4 points decrease on NIHSS or NIHSS 0)	0.72 (0.48-1.07)	0.11	0.72 (0.46-1.14)	0.17
<b>Safety outcomes</b>				
Peri-interventional complications	1.10 (0.57-2.13)	0.79	1.06 (0.49-2.27)	0.89
Symptomatic intracranial hemorrhage	0.80 (0.32-1.98)	0.62	0.84 (0.30-2.39)	0.75
Mortality at 3 months	0.78 (0.49-1.23)	0.28	0.88 (0.50-1.57)	0.67

\*Adjusted for: age, pre-stroke mRS, NIHSS at presentation, ASPECTS at presentation, location of occlusion, collateral status and treatment with IVT

†Common odds ratio indicating the odds of improvement of 1 point on the mRS

EVT: endovascular treatment; LSW: last seen well; OR: odds ratio; CI: confidence interval; mRS: modified Rankin Scale; eTICI: extended Treatment In Cerebral Infarction; NIHSS: National Institutes of Health Stroke Scale

**Supplemental table 5. Baseline characteristics of matched early window vs. late window patients of the 5 imputed datasets.**

	Matched early window patients with EVT <6.5 hours after onset or LSW (n=1022)*	Matched late window patients with EVT ≥6.5 hours after onset or LSW (n=511)*
Age (years); mean (SD)	67.4 (14.5)	67.7 (14.4)
Sex (male)	546 (53.4%)	224 (43.8%)
Pre-stroke mRS 0-1	836 (81.8%)	411 (80.4%)
Pre-stroke mRS 0-2	932 (91.2%)	461 (90.2%)
NIHSS at presentation; median [IQR]	16 [11-20]	15 [11-20]
ASPECTS at presentation; median [IQR]	8 [7-10]	8 [6-9]
Location of occlusion		
ICA	282 (27.6%)	138 (27.0%)
MCA M1-segment	582 (56.9%)	291 (56.9%)
MCA M2-segment	143 (14.0%)	76 (14.9%)
Other (M3, ACA)	15 (1.5%)	6 (1.2%)
Collateral status		
Absent collaterals	23 (2.3%)	11 (2.2%)
Filling ≤50% of occluded area	284 (27.8%)	153 (29.9%)
Filling 51-100% of occluded area	384 (37.6%)	193 (37.8%)
Filling 100% of occluded area	331 (32.4%)	154 (30.1%)
Treated with IVT	266 (26.0%)	124 (24.3%)

Time between onset/LSW and groin puncture	210 (81)	557 (175)
in minutes; mean (SD); median [IQR]	195 [150-270]	505 [415-634]
Time between onset/LSW and sheath from	267 (89)	592 (195)
groin in minutes; mean (SD); median [IQR]	255 [196-331]	548 [459-672]

\*With a caliper of 0.2, 511 (96.4%) of the 530 late window patients with EVT  $\geq$ 6.5 hours (5 datasets with 106 late window patients per dataset) could be matched in a 1:2 ratio to 1022 early window patients with EVT <6.5 hours after onset or LSW.

EVT: endovascular treatment; LSW: last seen well; SD: standard deviation; mRS: modified Rankin Scale;

NIHSS: National Institutes of Health Stroke Scale; IQR: interquartile range; ASPECTS: Alberta Stroke

Programme Early CT Score; IQR: interquartile range; ICA: internal carotid artery; MCA: middle cerebral artery;

ACA: anterior cerebral artery; IVT: intravenous thrombolysis