Contents

Supplemental Results

Results Based on Occlusion Location at Presentation:

41/226 (18%) patients demonstrated an ICA occlusion at presentation, of which 32 (78%) received bridging therapy (BT). Excellent outcomes (BT: 12 (38%) vs dEVT: 3 (33%), p>0.99) and functional independence (BT: 16 (50%) vs dEVT: 4 (44%), aOR: 0.62, 95% CI=0.11-3.50, p=0.59) were numerically higher in patients who received BT. Similarly, an ordinal analysis also failed to demonstrate a significant improvement in functional outcomes with the use of bridging therapy (adj. cOR: 0.68, 95% CI=0.14-3.27, p=0.63).

Of 136 (60%) patients with an M1 occlusion, 99 (73%) received BT and 37 (27%) were treated with dEVT approach. The rate of excellent outcomes (BT: 40 (40%) vs dEVT: 12 (32%), p=0.40) and functional independence (BT: 55 (56%) vs dEVT: 16 (43%), aOR; 2.32, 95% CI= 0.80-5.80, p=0.11) were similar between patients who did and did not receive bridging therapy. No improvement in functional outcome was observed in patients receiving IV alteplase after adjusting for covariates (adj. cOR: 2.18, 95% CI=0.92-4.54, p=0.12).

49/226 (22%) patients exhibited M2 occlusion. And of these, 31 (63%) patients received IV alteplase administration. Numerically higher rates of excellent outcomes (BT: 17 (55%) vs dEVT: 6 (33%), p=0.15) and functional independence (BT: 21 (68%) vs dEVT: 8 (44%), aOR: 2.86, 95% CI: 0.54-15.05, p=0.22). An ordinal analysis of functional outcomes also did not show a significant improvement with IV alteplase administration (adj. cOR: 3.32, 95% CI=0.64-16.34, p=0.18).

Multiplicative interaction terms between clot location and bridging therapy use were not statistically significant (using ICA and dEVT as reference categories and a two-way interaction between clot location and IV tPA use: p-value for multiplicative interaction between M1 and IV tPA: 0.19, p-value for multiplicative interaction between M2 and IV tPA: 0.15).

Supplemental Tables

Table e-1. Reasons for IV tPA ineligibility in patients presenting within 4.5 hours of last known well.

No. of patients	**Reasons for not administering IV tPA**
9	Arrived within 4.5 hours but tPA could not be delivered within eligibility window
24	Due to Anticoagulants
2	Infarct >1/3rd of the MCA territory
3	significant head trauma
12	Major Surgery
8	Coagulation Disorder
2	History of ICH
1	Loaded with Heparin and Plavix
1	Suspected chest malignancy
1	Unknown LKW at the time, ascertained later
2	recent stroke
1	Significant body trauma
1	Unknown outpatient medications
1	Recent IV tPA use for MI

*The reasons are not mutually exclusive.

Table e-2. Outcomes of patients with NIHSS less than 15 presenting within 4.5 hours.

	No IV-tPA (n=30)	**Received IV-tPA (n=60)**	**p-value**
90-day Functional Independence (mRS 0-2), n (%)	15 (50%)	50 (83%)	<0.001[b]
90-day Favorable Functional Outcome (mRS 0-1), n (%)	12 (40%)	42 (70%)	0.006[b]
90-day Mortality, n (%)	4 (13%)	0 (0%)	0.011[c]
Symptomatic ICH – ECASS III, n (%)	1 (3%)	3 (5%)	>0.99[c]
Asymptomatic ICH, n (%)	11 (37%)	20 (33%)	0.75[b]
Neurological Worsening, n (%)	2 (7%)	6 (11%)	0.71[c]
Successful Reperfusion (mTICI ≥ 2b), n (%)	27 (90%)	49 (82%)	0.37[b]
Final Infarct Volume (cc), median (IQR)	7.23 (1.70, 19.57)	13.46 (4.21, 46.25)	0.21[a]
Infarct Growth (cc), median (IQR)	3.82 (-2.52, 11.22)	7.09 (-0.46, 35.27)	0.48[a]

mTICI: modified Thrombolysis in Cerebral Ischemia, IV: intravenous, tPA: tissue plasminogen activator, mRS: modified Rankin Scale, ICH: intracranial hemorrhage, DWI: diffusion weighted imaging, IQR: interquartile range

[a] Assessed using Mann-Whitney U Test

[b] Assessed using Pearson's $\chi 2$ Test

[c] Assessed using Fisher's Exact Test

Table e-3. Outcomes of patients with NIHSS more or equal than 15 presenting within 4.5 hours.

	No IV-tPA (n=34)	**Received IV-tPA (n=102)**	**p-value**
90-day Functional independence (mRS 0-2), n (%)	13 (38.2%)	42 (41.2%)	0.76[b]
90-day Favorable functional outcome (mRS 0-1), n (%)	9 (26.5%)	27 (26.5%)	1.00[b]
90-day Mortality, n (%)	10 (29.4%)	17 (16.7%)	0.11[b]
Symptomatic ICH – ECASS III, n (%)	3 (8.8%)	7 (6.9%)	0.71[c]
Asymptomatic ICH, n (%)	8 (23.5%)	41 (40.2%)	0.080[b]
Neurological Worsening, n (%)	4 (12.5%)	12 (11.9%)	>0.99[c]
Successful Reperfusion (mTICI ≥ 2b), n (%)	26 (76.5%)	84 (84.0%)	0.32[b]
Final Infarct Volume (cc), median (IQR)	46.00 (4.74, 121.82)	45.62 (7.25, 97.92)	0.84[a]
Infarct Growth (cc), median (IQR)	10.12 (2.14, 68.63)	20.84 (2.13, 69.49)	0.95[a]

mTICI: modified Thrombolysis in Cerebral Ischemia, IV: intravenous, tPA: tissue plasminogen activator, mRS: modified Rankin Scale, ICH: intracranial hemorrhage, DWI: diffusion weighted imaging, IQR: interquartile range

[a] Assessed using Mann-Whitney U Test

[b] Assessed using Pearson's $\chi 2$ Test

[c] Assessed using Fisher's Exact Test

Table e-4. Outcomes of patients with core size less than 50cc presenting within 4.5 hours.

	No IV-tPA (n=56)	**Received IV-tPA (n=139)**	**p-value**
90-day Functional independence (mRS 0-2), n (%)	26 (46.4%)	86 (61.9%)	0.048[b]
90-day Favorable functional outcome (mRS 0-1), n (%)	19 (33.9%)	65 (46.8%)	0.10[b]
90-day Mortality, n (%)	10 (17.9%)	7 (5.0%)	0.004[b]
Symptomatic ICH – ECASS III, n (%)	3 (5.4%)	6 (4.3%)	0.72[c]
Asymptomatic ICH, n (%)	18 (32.1%)	50 (36.0%)	0.61[b]
Neurological Worsening, n (%)	5 (9.3%)	10 (7.4%)	0.66[b]
Successful Reperfusion (mTICI ≥ 2b), n (%)	47 (83.9%)	115 (83.9%)	>0.99[b]
Final Infarct Volume (cc), median (IQR)	10.92 (2.55, 52.78)	19.16 (4.73, 62.36)	0.24[a]
Infarct Growth (cc), median (IQR)	6.10 (1.49, 32.79)	9.48 (0.72, 47.39)	0.48[a]

mTICI: modified Thrombolysis in Cerebral Ischemia, IV: intravenous, tPA: tissue plasminogen activator, mRS: modified Rankin Scale, ICH: intracranial hemorrhage, DWI: diffusion weighted imaging, IQR: interquartile range

[a] Assessed using Mann-Whitney U Test

[b] Assessed using Pearson's $\chi 2$ Test

[c] Assessed using Fisher's Exact Test

Table e-5. Outcomes of patients with core size more or equal than 50cc presenting within 4.5 hours.

	No IV-tPA (n=8)	**Received IV-tPA (n=23)**	**p-value**
90-day Functional independence (mRS 0-2), n (%)	2 (25%)	6 (26%)	>0.99[c]
90-day Favorable functional outcome (mRS 0-1), n (%)	2 (25%)	4 (17%)	0.63[c]
90-day Mortality, n (%)	4 (50%)	10 (43%)	>0.99[c]
Symptomatic ICH – ECASS III, n (%)	1 (13%)	4 (17%)	>0.99[c]
Asymptomatic ICH, n (%)	1 (13%)	11 (48%)	0.11[c]
Neurological Worsening, n (%)	1 (13%)	8 (36%)	0.37[c]
Successful Reperfusion (mTICI ≥ 2b), n (%)	6 (75%)	18 (78%)	0.85[b]
Final Infarct Volume (cc), median (IQR)	137.23 (59.09, 207.63)	105.70 (53.15, 201.97)	0.96[a]
Infarct Growth (cc), median (IQR)	49.3 (-71.57, 157.77)	36.9 (-28.1, 125.47)	0.91[a]

mTICI: modified Thrombolysis in Cerebral Ischemia, IV: intravenous, tPA: tissue plasminogen activator, mRS: modified Rankin Scale, ICH: intracranial hemorrhage, DWI: diffusion weighted imaging, IQR: interquartile range

[a] Assessed using Mann-Whitney U Test

[b] Assessed using Pearson's $\chi 2$ Test

[c] Assessed using Fisher's Exact Test

Table e-6. Outcomes of patients presenting directly within 4.5 hours to a comprehensive stroke center.

	No IV-tPA (n=43)	**Received IV-tPA (n=107)**	**p-value**
90-day Functional independence (mRS 0-2), n (%)	22 (51.2%)	66 (61.7%)	0.24[b]
90-day Favorable functional outcome (mRS 0-1), n (%)	19 (44.2%)	49 (45.8%)	0.86[b]
90-day Mortality, n (%)	8 (18.6%)	10 (9.3%)	0.11[b]
Symptomatic ICH – ECASS III, n (%)	3 (7.0%)	5 (4.7%)	0.69[c]
Asymptomatic ICH, n (%)	10 (23.3%)	35 (32.7%)	0.25[b]
Neurological Worsening, n (%)	3 (7.1%)	10 (9.5%)	0.76[c]
Successful Reperfusion (mTICI ≥ 2b), n (%)	35 (81.4%)	92 (86.8%)	0.40[b]
Successful reperfusion with single pass (n, %)	20 (47.6%)	61 (59.8%)	0.18[b]
Final Infarct Volume (cc), median (IQR)	14.28 (1.70, 72.63)	25.72 (4.68, 66.90)	0.68[a]
Infarct Growth (cc), median (IQR)	6.22 (-2.41, 68.63)	7.25 (.07, 47.39)	0.92[a]

mTICI: modified Thrombolysis in Cerebral Ischemia, IV: intravenous, tPA: tissue plasminogen activator, mRS: modified Rankin Scale, ICH: intracranial hemorrhage, DWI: diffusion weighted imaging, IQR: interquartile range

[a] Assessed using Mann-Whitney U Test

[b] Assessed using Pearson's $\chi 2$ Test

[c] Assessed using Fisher's Exact Test

Table e-7. Outcomes of patients transferred within 4.5 hours to a comprehensive stroke center.

	No IV-tPA (n=21)	**Received IV-tPA (n=55)**	**p-value**
90-day Functional independence (mRS 0-2), n (%)	6 (29%)	26 (47%)	0.14[b]
90-day Favorable functional outcome (mRS 0-1), n (%)	2 (10%)	20 (36%)	0.024[c]
90-day Mortality, n (%)	6 (29%)	7 (13%)	0.10[b]
Symptomatic ICH, n (%)	1 (5%)	5 (9%)	>0.99[c]
Asymptomatic ICH, n (%)	9 (43%)	26 (47%)	0.73[b]
Neurological Worsening, n (%)	3 (15%)	8 (15%)	>0.99[c]
Successful Reperfusion (mTICI ≥ 2b), n (%)	18 (86%)	41 (76%)	0.53[c]
Successful reperfusion with single pass (n, %)	10 (48%)	16 (30%)	0.14[b]
Final Infarct Volume (cc), median (IQR)	14.62 (3.37, 60.68)	34.94 (8.44, 140.38)	0.12[a]
Infarct Growth (cc), median (IQR)	5.53 (3.59, 14.67)	24.68 (3.56, 69.38)	0.18[a]

mTICI: modified Thrombolysis in Cerebral Ischemia, IV: intravenous, tPA: tissue plasminogen activator, mRS: modified Rankin Scale, ICH: intracranial hemorrhage, DWI: diffusion weighted imaging, IQR: interquartile range

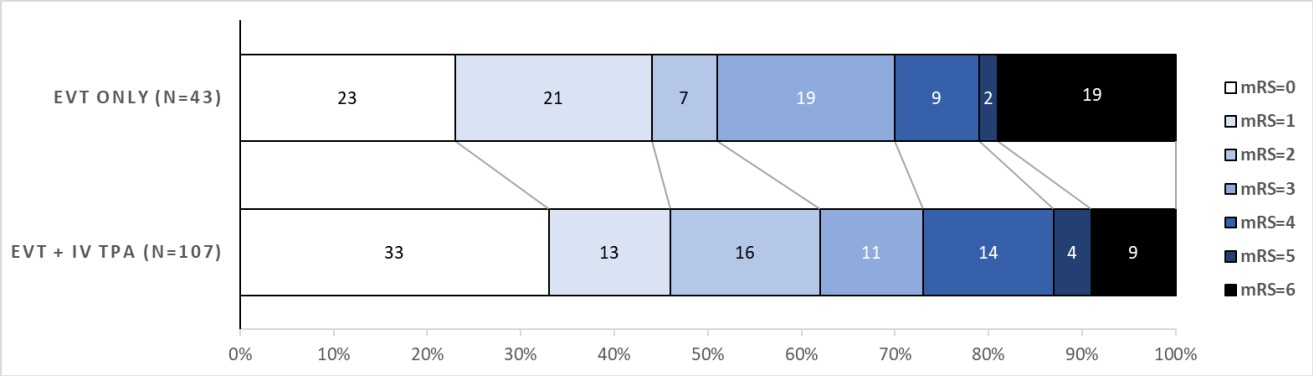
[a] Assessed using Mann-Whitney U Test

[b] Assessed using Pearson's $\chi 2$ Test

[c] Assessed using Fisher's Exact Test

Supplemental Figures

Figure e-1a and b. Distribution of the modified Rankin Scale scores at 90 days according to the history of intravenous tissue plasminogen activator pretreatment in patients presenting within 4.5 hours of stroke onset a) directly to a comprehensive stroke center and b) transferred to a comprehensive stroke center.



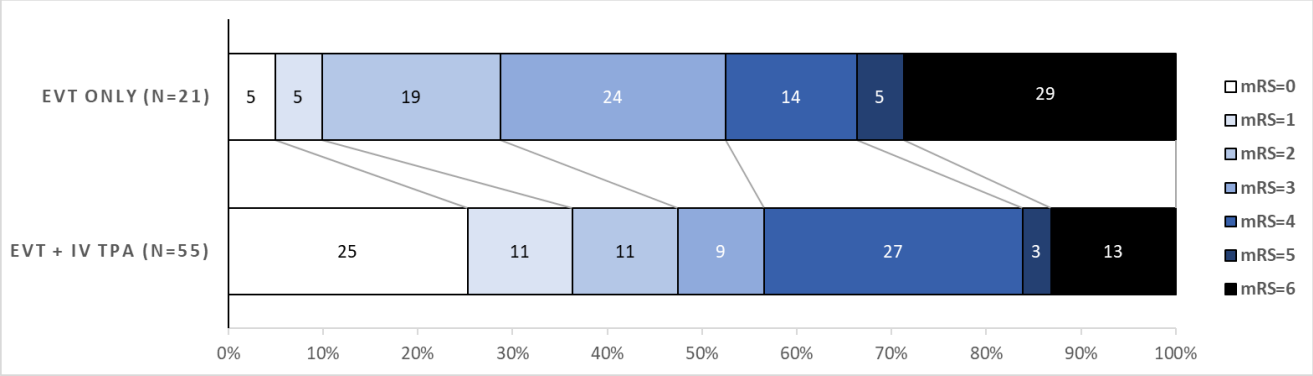


Figure e-2. Subgroup analyses on the probability of functional independence (mRS 0-2) at 90 days according to the history of intravenous tissue plasminogen activator pretreatment in patients presenting within 4.5 hours directly to a comprehensive stroke center.