ONLINE SUPPLEMENTAL

for manuscript entitled

Efficacy and safety of bridging thrombolysis initiated before transfer in a drip-and-ship stroke service

Purrucker JC, *et al. Stroke Vasc Neurol* 2021;0:1–7. doi: 10.1136/svn-2021-001024

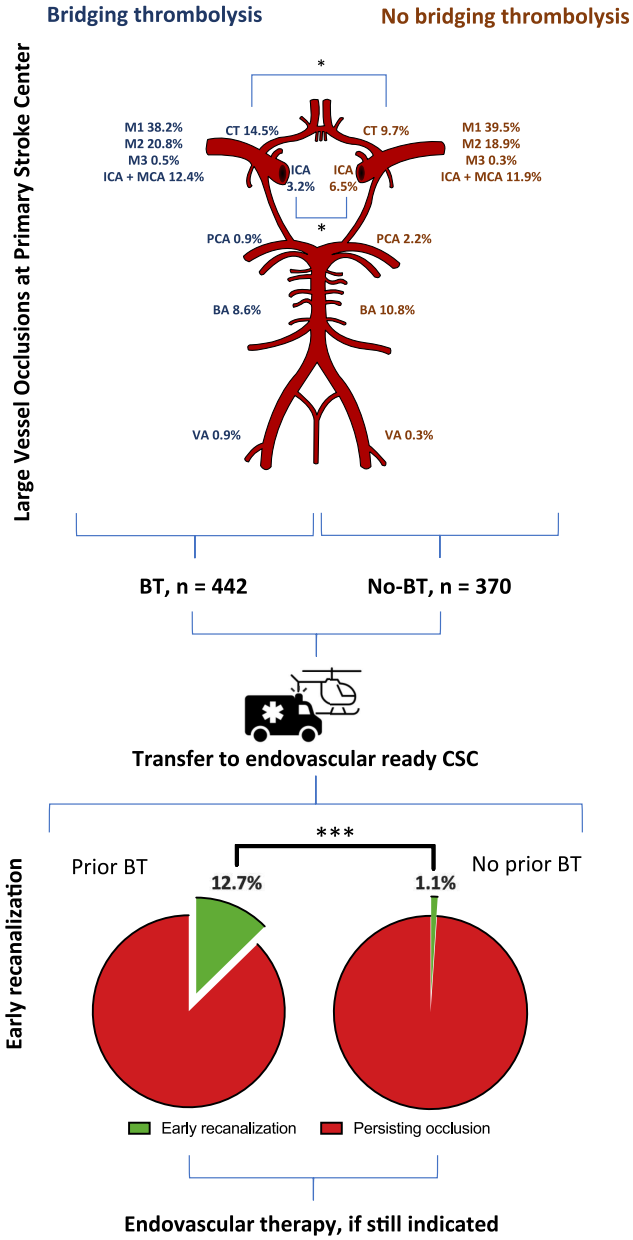

Figure SF1. Visualization of occlusion sites and rates of early recanalization according to treatment with bridging thrombolysis (BT) or no-BT. Abbreviations: BA, basilar artery; CSC, comprehensive stroke center; ICA, internal carotid artery; MCA, middle cerebral artery; M1–M3, segments of the MCA; PCA, posterior cerebral artery; VA, vertebral artery.

Full patient cohort analysis including posterior circulation stroke

Definition: Acute ischemic stroke and LVO (internal carotid artery [ICA], carotid T, middle cerebral artery [MCA, segments M1–M3], posterior cerebral artery (PCA), vertebral artery [VA], basilar artery [BA]).

Baseline characteristics

In a total of 442 patients (54.4%) BT was initiated at the referring hospital (table S1). Reasons for not performing BT are listed in table S2. In patients for whom the exact time of stroke onset was known (BT, 87.8% vs. no-BT, 49.7%), time to first recanalization therapy, i.e., intravenous thrombolysis in the BT group, was shorter in the BT group (table S1). High-grade stenosis or occlusion was present in all patients before transfer, with isolated M1 or M2 occlusions being the most frequent occlusion sites (38.8%, and 20%, respectively). Distribution of LVO was similar between patients treated with BT or not (table S1). Thrombus migration was observed more often with BT than without (BT, M1 to M2, n=6, M2 to M3, n=7; no-BT, M1 to M2, n=1, M1 to M3, n=1).

Treatment modalities

Of 442 patients treated with BT, 360 (81.4%) underwent DSA. Of these, 25 (8.2%) did not need any extra- or intracranial endovascular therapy. In those 370 patients in whom BT was not initiated at the referring hospital, 8 patients received intravenous thrombolysis at our comprehensive stroke center (n=3 intravenous thrombolysis only, 0.8%) and in 367 DSA was performed (99.2%), there ultimately being no need for endovascular therapy in 4/367 patients (1.1%).

Efficacy

More patients in the BT group with documented LVO before transfer were recanalized without endovascular therapy (56/442, 12.7%) than patients who did not receive BT before transfer (4/370, 1.1%; p<0.0001) (figure SF1). BT remained the strongest independent predictor of early recanalization in a multivariate analysis (adj. OR 14.55, 95% CI 5.15–41.1, p<0.001; table S3). Time window was excluded from the main model because it constituted a major reason for withholding BT while it otherwise showed a strong correlation with initiation of BT. However, BT remained the strongest independent predictor of early recanalization (adj. OR 10.56, 95% CI 1.4–79.99, p=0.022) in a sensitivity analysis including only patients for whom the exact time window for stroke onset was known < 4.5 h (n=424).

In patients in whom diagnostic or therapeutic DSA was performed, reperfusion grades were similar between patients pretreated with BT and those who were not (excellent reperfusion [mTICI 2c–3], 224/360, 62.2% vs. 219/367, 59.7%; good reperfusion [mTICI 2b] 88/360, 24.4%

vs. 84/367, 22.9%), but no reperfusion was observed more often in non-BT patients ([mTICI 0], BT 25/360, 6.9% vs. non-BT 42/367, 11.4%, p=0.04).

In univariate analysis, patients treated with BT had a better functional outcome at 3 months (BT, median mRS 3 [IQR 2–5] vs. no-BT, 4 [2–6], p=0.023), and more patients had an excellent favorable outcome (mRS 0–1, 22.7% vs. 14.6%, p=0.004). In binary logistic regression analysis adjusting for confounders, BT remained an independent predictor for an excellent favorable outcome (mRS 0–1) or return to prestroke mRS at 3 months (adj. OR 1.42, 95% CI 1.02–1.98, p=0.04; table S3). By excluding patients with posterior circulation stroke or distal MCA occlusion, a trend remained (adj. OR 1.38, 95 % CI 0.97–1.96, p=0.077).

Safety

Bleeding complications did not differ between patients who received BT and those who did not (table S4 for Heidelberg Bleeding Classification). Fatal intracranial hemorrhage developed in 7/434 (1.6%) patients in the BT group and 4/386 (1.0%) in the non-BT group (p=0.509). There was no difference in overall mortality (25.7% vs. 27.5%, p=0.619).

Table S1 Baseline demographics and clinical characteristics (full cohort)

	Bridging Thrombolysis (BT)	No Bridging Thrombolysis (no-BT)	p-value
N (%)	442 (54.4%)	370 (45.6%)	-
Age, mean yr (SD)	74.3 (11.7)	75.8 (11.9)	0.073
Women, n (%)	238 (53.8%)	204 (55.1)	0.724
Comorbidities, n (%)			
Arterial hypertension	352 (79.6%)	298 (80.5 %)	0.792
Diabetes mellitus	99/441 (22.4%)	103 (27.8%)	0.087
Hyperlipidemia	152/440 (34.5)	140/367 (38.1%)	0.304
Ischemic heart disease	119/441 (27%)	102/369 (27.4%)	0.874
Peripheral artery disease	31/440 (7%)	33/380 (8.7%)	0.434
Stroke/TIA	82/440 (18.6%)	96/369 (26%)	0.013
Current Smoker	62/428 (14.5%)	52/364 (14.3%)	>0.99
Atrial fibrillation*	178/440 (40.5%)	200/368 (54.3%)	<0.001
Prestroke mRS			
median (IQR)	0 (0–2)	1 (0–3)	<0.001
0–1	308/440 (70.0%)	210/367 (57.2%)	<0.001
2–5	132/440 (30.0%)	157/367 (42.8%)	<0.001
NIHSS, median (IQR)	15 (9–21)	15 (8–20)	0.168
ASPECTS, median (IQR)	9 (7–10)	9 (8–10)	0.354
Occlusion site, n (%)			
ICA	14 (3.2%)	24 (6.5%)	0.03
ICA plus MCA	55 (12.4%)	44 (11.9%)	0.830
Carotid T	64 (14.5%)	36 (9.7%)	0.042
MCA, M1	169 (38.2%)	146 (39.5%)	0.772
MCA, M2	92 (20.8%)	70 (18.9%)	0.538
MCA, M3	2 (0.5%)	1 (0.3%)	>0.99
PCA	4 (0.9%)	8 (2.2%)	0.156
BA	38 (8.6%)	42 (10.8%)	0.339
VA	4 (0.9%)	1 (0.3%)	0.383
Time window†, median (IQR)	1:50 (1:20–2:55)	6:38 (4:18–10:25)	<0.001

* known or newly diagnosed; † in patients in whom exact time of onset is known.

Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomography Score; BA, basilar artery; ICA, internal carotid artery; MCA, middle cerebral artery; M1–M3, segments of the MCA; mRS. Modified Rankin scale score; NIHSS, National Institutes of Health Stroke Scale; PCA, posterior cerebral artery; VA, vertebral artery.

Table S2 Reasons for not performing thrombolysis at the referring hospital (full cohort)

Reason	N (%)
Unknown time window	110 (29.7%)
Anticoagulation	102 (27.6%)
Time window ≥ 4.5 h	76 (20.5%)
Contraindication to intravenous thrombolysis	50 (13.5%)
Multiple reasons	21 (5.7%)
Unknown reason	6 (1.6%)
Other	5 (1.4%)

Table S3 Multivariate analyses (full cohort)

Predictors of excellent functional outcome			
	OR	95% CI	p-value
Bridging thrombolysis	1.42	1.02–1.98	0.040
Age	0.98	0.96–0.99	0.001
Atrial fibrillation	1.0	0.69–1.43	0.980
Diabetes mellitus	0.63	0.42–0.95	0.027
Previous stroke	1.08	0.72–1.6	0.719
Occlusion site			
Posterior circulation (BA, PCA, VA)	ref.		
ICA	1.13	0.44–2.9	0.808
ICA plus MCA	1.02	0.51–2.05	0.948
Carotid T	0.75	0.36–0.59	0.456
MCA, M1	1.47	0.83–2.58	0.183
MCA, M2	2.07	1.13–3.8	0.019
MCA, M3	8.27	0.7–98.29	0.094
Predictors of early recanalization			
Bridging thrombolysis	14.55	5.15–41.1	<0.001
Age	1.03	1.01–1.06	0.021
Sex (female)	0.82	0.46–1.49	0.524
Arterial hypertension	0.45	0.23–0.91	0.025
Atrial fibrillation	0.85	0.47–1.56	0.603

Diabetes mellitus	0.73	0.35–1.51	0.395
Hypercholesterinemia	1.61	0.89–2.89	0.115
Occlusion site			
Posterior circulation (BA, PCA, VA)	ref.		
ICA	Did not converge		
ICA plus MCA	0.15	0.03–0.76	0.021
Carotid T	0.17	0.04–0.7	0.014
MCA, M1	0.78	0.33–1.84	0.574
MCA, M2	0.84	0.34–2.09	0.706

Abbreviations: BA, basilar artery; ICA, internal carotid artery; MCA, middle cerebral artery; M1–M2, segments of the MCA; OR, odds ratio.

Table S4 Intracranial hemorrhages according to the Heidelberg Bleeding Classification (full cohort)

Class	Type	Bridging Thrombolysis (BT)	No Bridging Thrombolysis (no-BT)
0	None	328 (74.7%)	269 (73.3%)
1a	HI1	38 (8.7%)	44 (12%)
1b	HI2	10 (2.3%)	16 (4.4%)
1c	PH1	16 (3.6%)	9 (2.5%)
2	PH2	18 (4.1%)	10 (2.7%)
3a	Remote PH	6 (1.4)	1 (0.3%)
3b	IVH	1 (0.2%)	0 (0%)
3c	SAH	22 (5.0%)	17 (4.6%)
3d	SDH	0 (0%)	0 (0%)
Other	nonclassified	0 (0%)	1 (0.3%)

Missing data in n=3 patients in each group. Abbreviations: HI, hemorrhagic infarction; IVH, intraventricular hemorrhage; PH, parenchymal hemorrhage; SAH, subarachnoid hemorrhage; SDH, subdural hematoma.