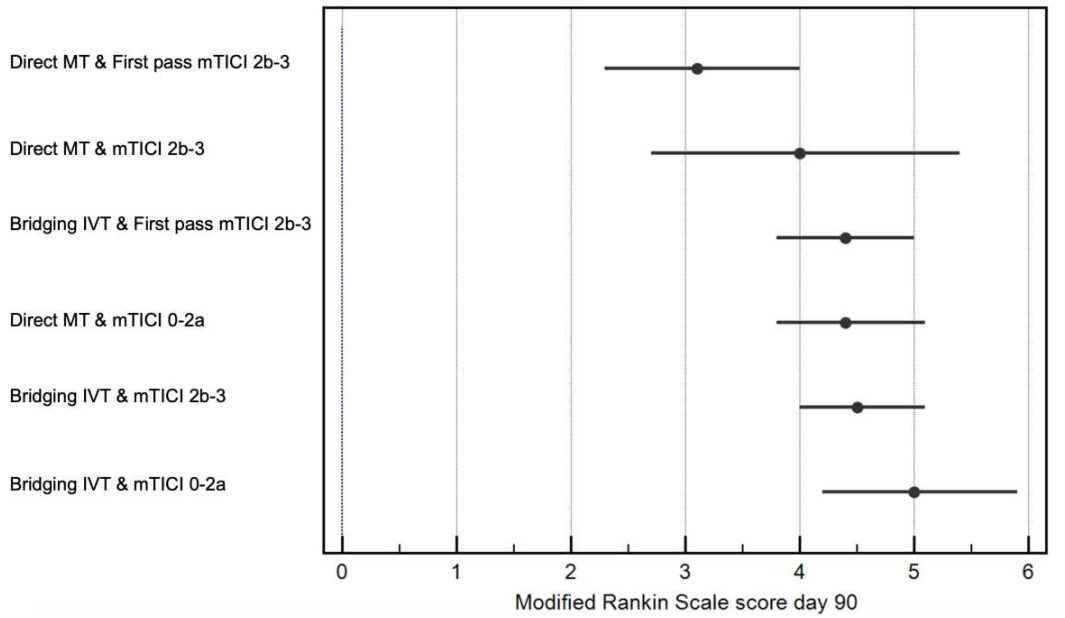
SUPPLEMENTAL MATERIAL

Supplemental Figure 1: Impact of IVT according to thrombectomy success, stratified by functional outcome.



MT, Mechanical Thrombectomy, mTICI, modified Thrombolysis in Cerebral Infarction, IVT, Intravenous Thrombolysis (i.e. with alteplase). Points indicate mean and brackets indicate 95% confidence intervals.

Supplemental Table 1

	Modified Rankin Scale score at day 90	**95% confidence interval**
Direct MT + first pass mTICI 2b-3	3.1	2.3 – 4.0
Direct MT, mTICI ≥2b	4.0	2.7 – 5.4
Bridging IVT + first pass mTICI 2b-3	4.4	3.8 – 5.0
Direct MT + mTICI 0-2a	4.4	3.8 – 5.1
Bridging IVT + mTICI≥2b	4.5	4.0 – 5.1
Bridging IVT + mTICI 0-2a	5.0	4.2 – 5.9

Overview of treatment and functional outcome (mRS at day 90) corresponding to supplemental Figure 1

Supplemental Table 2

	Proportion of patients with mRS 0-2, %	**Proportion of patients with sICH, %**
Direct MT	24.4 (16.5-32.2)	6.4 (-0.001 – 12.9)
IVT only	15.1 (10.1-20.0)	10.4 (6.3 – 14.4)
Bridging IVT	14.4 (7.1-21.8)	17.8 (11.7 – 23.8)
No IVT / no MT	3.2 (0 – 12.0)	0.0 (-0.07 – 0.07)

***means in % and 95% confidence intervals**

Supplemental Methods - Revascularization protocol

IVT was administered to patients applying established laboratory and conventional clinical inclusion and exclusion criteria, as deemed appropriate by the treating physician [7, 21, 22].

MT was performed via a femoral artery approach under general anesthesia or conscious sedation. Endovascular procedures using approved devices (i.e. stent retriever and/or aspiration catheters) were performed according to the standards of the participating centers. The choice of thrombectomy device was left to the discretion of the attending neurointerventionalist.

Supplemental Results – Treatment effect including all patients versus MT patients only

Supplemental Table 3: Inverse-probability weighted regression adjustment (IPWA) analyzing the effect of IVT on all patients versus MT patients only.

Endpoint	***Effect coefficient IVT -MT patients-***	***Effect coefficient IVT -All patients-***
mRS 0-2, %	-16.8 (-27.4 – -6.2, p=0.002)	5.5 (-1.0 – 12.0, p=0.1)
sICH, %	19.4 (9.6 – 16.9, p<0.0001)	12.2 (6.7 – 17.7, p<0.0001)

Proportion of patients in % with 95% confidence intervals

Supplemental Table 4: Multivariable logistic regression analysis (for model details see manuscript) analyzing the effect of IVT on all patients versus MT patients only.

Endpoint	***Odds ratio for IVT -MT patients-***	***Odds ratio for IVT -All patients-***
mRS 0-2	0.38 (0.14 – 1.02, p=0.05)	5.5 (-1.0 – 12.0, p=0.1)
mRS 5-6	2.22 (1.05 – 4.72, p=0.04)	1.77 (0.97 – 3.27, p=0.06)
sICH	4.89 (1.84 – 13.03, p=0.001)	3.06 (1.05 – 8.85, p=0.04)

Odds ratio with 95% confidence intervals

Supplemental Results - Sub-group analysis of patients with ASPECTS 3-5

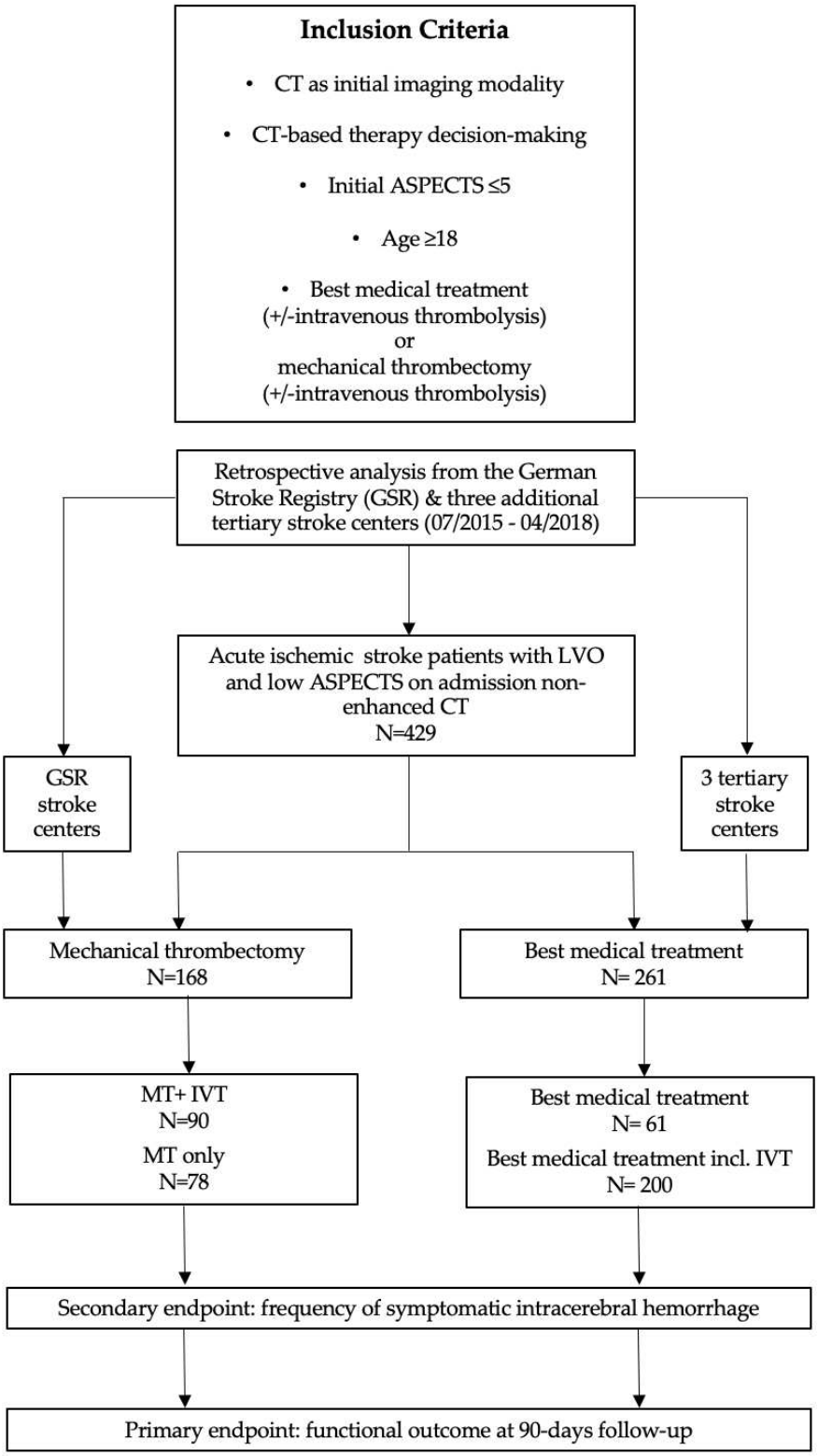
336 patients presented with an ASPECTS of 3-5 (78%), while 93 had an ASPECTS of 0-2 (22%). There were no significant differences in age (median 73 versus 74 years, p=0.34) or time from onset to imaging (median 120 minutes to 118 minutes, p=0.32) between these patient groups. The median NIHSS, however, was higher in patients with an ASPECTS 0-2 (20 versus 18, p<0.001).

The rate of sICH was 6.7% (95%CI: 0-13.7%) in patients with direct MT, compared to 19.5% (95%CI: 12.9-26.1%) in patients with bridging IVT (p=0.03).

In a multivariable logistic regression analysis with good functional outcome as the dependent variable, age, sex, NIHSS, ASPECTS, IVT, mTICI, and number of passages were tested as independent variables for all patients with ASPECTS 3-5. IVT was by trend associated with a reduced likelihood for good outcome (OR: 0.38, 95%CI: 0.13-1.07, p=0.06). Higher degree of reperfusion (OR: 1.89, p=0.03), fewer retrieval attempts (OR: 0.63, p=0.03), and younger age (OR: 0.92, p<0.001) were significant predictors of good functional outcome.

A further multivariable logistic regression analysis with very poor outcome as the dependent variable was also performed, using with the same independent variables as above. Here, IVT was significantly and independently associated with an increased likelihood for very poor outcome (OR: 2.23, 95%CI: 1.04-4.84, p=0.04). In a final step, a multivariable logistic regression model with sICH as the dependent variable was performed. IVT was observed to be a significant predictor of sICH (OR: 3.67, 95%CI: 1.22-10.99, p=0.02), as were ASPECTS (OR: 0.54, p=0.04) and, by trend, higher degree of reperfusion (OR: 0.71, p=0.06).

Supplemental Figure 2: Flow chart patient selection



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