

MECHANICAL THROMBECTOMY VERSUS BEST MEDICAL TREATMENT IN THE LATE TIME WINDOW IN NON-DEFUSE-NON-DAWN PATIENTS

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BACKGROUND

We assessed the efficacy and safety of mechanical thrombectomy (MT) in adult stroke patients with anterior circulation large vessel occlusion (LVO) presenting in the late window who did not fulfill the DEFUSE-3 and DAWN inclusion criteria.

METHODS

Cohort study of adults with LVO admitted between 6 and 24 hours after last-seen well at five participating Swiss Stroke Centers between 2014 and 2021. Mismatch was assessed by CT or MRI perfusion with automated software (RAPID or OLEA). We excluded patients meeting DEFUSE-3 and DAWN inclusion criteria and compared those who underwent MT with those receiving best medical treatment alone (BMT) by inverse probability of treatment weighting (IPTW) using the propensity score. The primary efficacy endpoint was a favorable functional outcome at 90 days, defined as a modified Rankin Scale (mRS) score shift toward lower categories. The primary safety endpoint was symptomatic intracranial hemorrhage (sICH), the secondary safety endpoint was all-cause mortality within 90 days.

RESULTS

Among 278 patients with LVO presenting in the late window, 190 (68%) did not meet the DEFUSE-3 and DAWN inclusion criteria and thus were included in the analyses. Of those, 102 (54%) received MT. In the IPTW analysis, patients in the MT group had higher odds of favorable outcomes compared to the BMT group (mRS shift: acOR 0.68 [0.47-0.99], $p=0.04$) and lower odds of all-cause mortality within 90 days (aOR 0.59 [0.37-0.93], $p=0.02$). There were no significant differences in sICH (MT vs BMT: 5% vs 2%, $p=0.63$).

	All patients (N=190)	MT (N=102)	BMT (N=88)	P value
Clinical characteristics				
Age (yr) – median [IQR]	78 [68, 85]	77 [68, 84]	79 [69, 85]	0.59
Age ≥ 80 (yr) – no. (%)	87 (46)	45 (44)	42 (48)	0.73
Male sex – no. (%)	85 (45)	42 (41)	43 (49)	0.36
Atrial fibrillation – no. (%)	78 (41)	43 (42)	35 (40)	0.85
Diabetes mellitus – no. (%)	34 (18)	14 (14)	20 (23)	0.15
Hypertension – no. (%)	135 (71)	72 (71)	63 (72)	1.00
Previous ischemic stroke or transient ischemic attack – no. (%)	40 (21)	21 (21)	19 (22)	0.39
Premorbid mRS 0-2 – no. (%)	142 (79)	74 (76)	68 (81)	0.56
NIHSS score at admission – median [IQR]	12 [5, 18]	12 [5, 19]	10 [5, 18]	0.22
Stroke onset known – no. (%)				
Yes	32 (17)	12 (12)	20 (23)	0.06
No				
On awakening	81 (43)	42 (41)	39 (44)	
Unwitnessed during wakefulness	77 (41)	48 (47)	29 (33)	
Imaging characteristics †				
Onset to imaging time (min) – median [IQR]	702 [538, 897]	665 [533, 804]	745 [547, 1'006]	0.06
Door to imaging time (min) – median [IQR]	28 [20, 38]	25 [16, 33]	32 [24, 47]	0.01
ASPECTS – median [IQR]	8 [7, 10]	8 [7, 10]	8 [6, 10]	0.26
Perfusion imaging type – no. (%)				
CT	166 (87)	89 (87)	77 (87)	1.00
MRI	24 (13)	13 (13)	11 (13)	1.00
Infarct core volume (ml) – median [IQR]	8 [0, 28]	7 [0, 25]	10 [0, 40]	0.50
Perfusion lesion volume (ml) – median [IQR]	67 [36, 124]	81 [52, 127]	52 [25, 118]	0.01
Mismatch volume (ml) – median [IQR]	53 [24, 88]	69 [43, 100]	29 [14, 55]	<0.001
Occlusion site – no. (%)				
Internal carotid artery	45 (24)	22 (22)	23 (26)	0.57
M1	89 (47)	54 (53)	35 (40)	0.10
M2	75 (40)	35 (34)	40 (46)	0.16
A1	5 (3)	2 (2)	3 (3)	0.87

Table 1. Admission characteristics of Non-DEFUSE-Non-DAWN patients presenting 6 to 24 hours after symptom onset

MT: Mechanical thrombectomy
mRS: Modified Rankin Scale (mRS)
CT: Computed tomography
MRI: Magnetic resonance imaging

BMT: best medical treatment alone
NIHSS: National Institutes of Health Stroke Scale
ASPECTS: Alberta Stroke Program Early CT Score

† ASPECTS were available for 145/190 (76%) patients. Occlusion sites were not mutually exclusive. Mismatch was assessment with automated software (RAPID for CT-based, OLEA for MRI-based perfusion imaging)

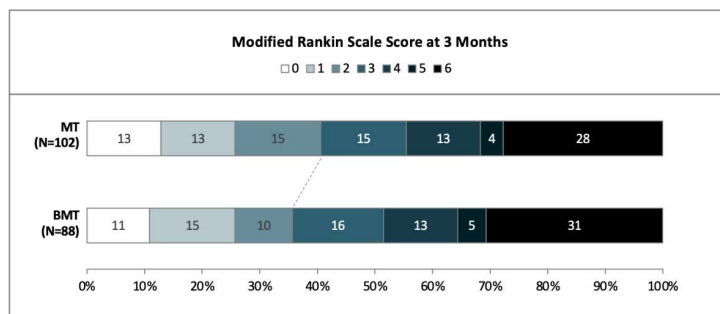


Figure 1. Functional outcome at 90 days in Non-DEFUSE-Non-DAWN patients receiving mechanical thrombectomy versus best medical treatment alone.

MT: Mechanical thrombectomy
BMT: Best medical treatment alone

	IPTW analysis using ordinal logistic regression †		
	acOR	95%CI	P-value
Efficacy outcome measures (MT vs BMT) mRS at 90 days	0.68	0.47-0.99	0.04
	IPTW analysis using binary logistic regression †		
	aOR	95%CI	P-value
Efficacy outcome measures (MT vs BMT) mRS 0-2 at 90 days	1.40	0.91-2.17	0.12
Safety outcome measures (MT vs BMT) Mortality at 90 days	0.59	0.37-0.93	0.02

Table 2. IPTW analysis of efficacy and safety outcomes of Non-DEFUSE-Non-DAWN patients presenting 6 to 24 hours after symptom onset

IPTW: Inverse probability of treatment weighting using the propensity score

MT: Mechanical thrombectomy

BMT: Best medical treatment alone

mRS: Modified Rankin Scale

sICH: Symptomatic intracranial hemorrhage (sICH)

† Adjusted odds ratios (aOR) (binary regression) and adjusted cumulative odds ratios (cOR) (ordinal regression) are reported. We state 95% confidence intervals (CI). Covariates used in the analyses are: hypoperfusion lesion volume, mismatch volume, age, arterial hypertension, diabetes mellitus, atrial fibrillation, occlusion site, NIHSS score at admission, premorbid mRS score, and tPA treatment. Cases with missing data for one or more covariates (N=9) were excluded from the analyses (N_{total}=181)

CONCLUSIONS

Two out of three patients with LVO presenting in the late window did not meet the DEFUSE-3 and DAWN inclusion criteria. In these patients, MT was associated with higher odds of favorable functional outcomes without increased rates of sICH. These findings support the enrolment of patients into ongoing randomized trials on MT in the late window with more permissive inclusion criteria.

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