

Mechanical Thrombectomy in Patients with Acute Ischemic Stroke and Lower NIHSS Scores: Recanalization Rates, Periprocedural Complications, and Clinical Outcome

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ABSTRACT

BACKGROUND AND PURPOSE: Mechanical thrombectomy, in addition to intravenous thrombolysis, has become standard in acute ischemic stroke treatment in patients with large-vessel occlusion in the anterior circulation. However, previous randomized controlled stroke trials were not focused on patients with mild-to-moderate symptoms. Thus, there are limited data for patient selection, prediction of clinical outcome, and occurrence of complications in this patient population. The purpose of this analysis was to assess clinical and interventional data in patients treated with mechanical thrombectomy in case of ischemic stroke with mild-to-moderate symptoms.

MATERIALS AND METHODS: We performed a retrospective analysis of a prospectively collected stroke data base. Inclusion criteria were anterior circulation ischemic stroke treated with mechanical thrombectomy at our institution between September 2010 and October 2015 with an NIHSS score of ≤ 8 .

RESULTS: Of 484 patients, we identified 33 (6.8%) with the following characteristics: median NIHSS = 5 (interquartile range, 4–7), median onset-to-groin puncture time = 320 minutes (interquartile range, 237–528 minutes). Recanalization (TICI = 2b–3) was achieved in 26 (78.7%) patients. Two cases of symptomatic intracranial hemorrhage were observed. Favorable (mRS 0–2) and moderate (mRS 0–3) clinical outcome at 90 days was achieved in 21 (63.6%) and 30 (90.9%) patients, respectively.

CONCLUSIONS: The clinical outcome of patients undergoing mechanical thrombectomy for acute ischemic stroke with mild stroke due to large-vessel occlusion appears to be predominately favorable, even in a prolonged time window. However, although infrequent, angiographic complications could impair clinical outcome. Future randomized controlled trials should assess the benefit compared with the best medical treatment.

ABBREVIATION: IQR = interquartile range

In several randomized multicenter stroke trials, mechanical thrombectomy has proved to be an effective treatment for large intracranial vessel occlusion in patients with acute ischemic stroke in the anterior circulation.^{1–5} With the exception of the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) trial⁴ and Extending the Time for Thrombolysis in Emergency

Neurological Deficits–Intra-Arterial (EXTEND-IA),¹ all of those stroke trials did not include patients with minor-to-moderate stroke symptoms but focused on patients with a moderate or severe stroke with a score of at least 6–8 or higher on the National Institutes of Health Stroke Scale. Consequently, the median NIHSS score for patients who underwent mechanical thrombectomy was about 15–17 in all trials; including the MR CLEAN and EXTEND-IA trials.

Large intracranial vessel occlusions are not necessarily associated with a high baseline NIHSS score and could be missed in patients with low NIHSS scores.⁶ In a large single-center cohort, 72% of the patients presenting with mild stroke symptoms did not undergo advanced stroke imaging (eg, CT angiography or CT perfusion) before intravenous thrombolysis. However, visualization of a possible proximal occlusion is essential for further treatment decisions. If thrombus length exceeds 8 mm, intravenous thrombolysis has almost no potential to recanalize the occluded vessel.^{7,8} The chance for a good clinical outcome

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(mRS 0–2) is only 7.7% in such cases.⁷ Furthermore, despite intravenous thrombolysis, mortality is 1.3%, and 30.3% of the patients who presented with mild initial stroke symptoms could not ambulate independently at discharge.⁹

Even though the complication rate in mechanical thrombectomy is low, the clinical benefit for the patient has to outperform the cost and potential risks. Here, we assessed the outcome of patients with acute ischemic minor-to-moderate stroke who underwent mechanical thrombectomy at our institution. We present data on the location of occlusions, thrombus length, collateral status, recanalization rates, periprocedural complications, and clinical outcome.

MATERIALS AND METHODS

Patient Selection

This analysis was approved by our local ethics committee. Due to its retrospective character, the requirement for subsequent written informed consent was waived.

From a prospectively collected acute ischemic stroke data base, we selected patients who presented with a minor or moderate stroke (NIHSS ≤ 8) and underwent mechanical thrombectomy at our institution between September 2010 and October 2015. The NIHSS cutoff of ≤ 8 was used because of the lack of a consistent definition for minor or mild stroke symptoms in the literature.¹⁰ Furthermore, this specific NIHSS inclusion criterion was used to fill the gap between (almost) nonexistent symptoms and the NIHSS inclusion criteria covered by most of the large randomized stroke trials. Each patient was examined by a neurologist, including a detailed assessment of the NIHSS score, in the emergency department on admission. Patients with suspected acute ischemic stroke underwent a standardized stroke imaging protocol: either CT (including a non-contrast-enhanced CT, CT perfusion, and CT angiography) or MR imaging (including axial DWI, TOF-MRA, axial SWI, axial FLAIR, contrast-enhanced MRA of the aortic arch and cervical arteries, and axial PWI) for assessment of eligibility for intravenous thrombolysis and mechanical thrombectomy. The decision between MR imaging and CT was made individually, depending on MR imaging eligibility and the availability of MR imaging and CT scanners, the patient's condition, and known or unknown time of symptom onset.

Stroke Therapy

Administration and dosing of intravenous thrombolysis followed national and international guidelines and was limited to patients treated within 4.5 hours after symptom onset.

Patients were considered eligible for mechanical thrombectomy by the treating neurologist and neurointerventionalist if an occlusion of a major artery was detected by CTA or MRA and initial imaging excluded hemorrhage. In case of unknown symptom onset, patients were considered eligible for mechanical thrombectomy according to imaging criteria. There was no lower limit to stroke severity, and identical stroke severity thresholds were used for mechanical thrombectomy and intravenous thrombolysis. No age limit was defined, but eligibility for mechanical thrombectomy was made individually on the basis of the patient's

comorbidities, prestroke condition, and the assumed will of the patient.

Intraprocedural use of mechanical and/or pharmacologic treatment remained at the discretion of the treating physicians. General anesthesia was routinely administered during mechanical thrombectomy between September 2010 and July 2013. Since August 2013, procedures were also performed with the patient under conscious sedation.¹¹ Peri-interventional management and monitoring of physiologic target values, according to our in-house standard operating procedure adapted to the patient and situation, were performed by the neurointensivist.

Postinterventional Management

All patients were admitted to either our neurologic intensive care unit or stroke unit after mechanical thrombectomy and treated according to in-house standard operating procedures. Follow-up imaging (either CT or MR imaging) was routinely performed at 20–36 hours after treatment or earlier if neurologic deterioration occurred. Postinterventional NIHSS and modified Rankin Scale scores were assessed by detailed physical examinations performed by the treating physicians in our wards. Follow-up assessment (including the modified Rankin Scale score) after 3 months was obtained by an inpatient visit or a structured telephone interview by a neurologist not blinded to the type of treatment.

Data Collection

Data collection included baseline demographics (age and sex) and medical history (eg, atrial fibrillation, hypertension, congestive heart failure, coronary artery disease, hypercholesterolemia, diabetes mellitus, history of smoking, and previous stroke) and symptom-onset time and stroke severity as measured by the NIHSS. The time of stroke imaging and the start of angiography were captured automatically by the CT scanners and angiography system. The location of the occlusion and thrombus length were assessed on angiographic images, and the degree of collateral supply was scored according to Tan et al¹²: 0 = absence of collateral vessels in the MCA territory; 1 = collateral supply filling of $>0\%$ but $\leq 50\%$ of the occluded MCA territory; 2 = collateral supply filling $>50\%$ but $<100\%$ of the occluded MCA territory; 3 = 100% collateral supply filling the occluded MCA territory. Devices and medication used during the intervention procedures, number of thrombectomy maneuvers, and intraprocedural complications were evaluated according to the treatment protocols. Angiographic outcome by the modified Thrombolysis in Cerebral Infarction scale¹³ and complications (eg, vessel perforation, dissection) were assessed by a senior neurointerventionalist (M.M.). Cerebral infarction and posttreatment intracranial hemorrhage (by the criteria from the Heidelberg Bleeding Classification¹⁴) were assessed by using routine follow-up imaging performed 20–36 hours after intervention or earlier in case of clinical deterioration.

Statistical Analysis

All statistical analyses were performed by using SPSS Statistics 21.0.0.0 (IBM, Armonk, New York).

Table 1: Baseline characteristics of patients with minor to mild stroke who received mechanical thrombectomy

	Patients (n = 33)
Age (yr) (mean) (SD)	68 (16)
Male (%)	14 (42.4)
Hypertension (%)	21 (63.6)
Diabetes mellitus (%)	4 (12.1)
Atrial fibrillation (%)	13 (39.4)
Coronary artery disease (%)	7 (21.2)
Congestive heart failure (%)	3 (9.1)
Hypercholesterolemia (%)	8 (24.2)
Previous stroke (%)	0
History of smoking (%)	8 (24.2)
Prestroke mRS	
0 (%)	28 (84.8)
1 (%)	2 (6.1)
2 (%)	1 (3)
3 (%)	2 (6.1)
Initial NIHSS score (median) (IQR)	5 (4–7)
CT	n = 18
MR imaging	n = 15
ASPECTS ^a (median) (IQR)	
CT	10 (9–10)
MR imaging	8 (7–9) ^b
Time from stroke onset to imaging (min) (median) (IQR)	175 (72–279)
Intravenous tPA (%)	22 (66.7)
Time from stroke onset to intravenous tPA ^c (min) (median) (IQR)	156 (94–238)
Time from stroke onset to groin puncture (min) (median) (IQR)	320 (237–528)
Occlusion site	
ICA (excluding carotid T) (%)	4 (12.1)
Tandem occlusion (cervical ICA and carotid T/M1)	3 (9.1)
Carotid T (%)	2 (6.1)
M1 (%)	17 (51.5)
M2 (%)	7 (21.2)
Collateral status	
0 (%)	0
1 (%)	2 (6.1)
2 (%)	7 (21.2)
3 (%)	24 (72.7)
Thrombus length (mm)	12 (10–16)

^a According to modality.^b MR-ASPECTS assessed on axial diffusion-weighted images.^c For patients eligible for intravenous thrombolysis.

RESULTS

Between September 2010 and October 2015, 484 patients underwent mechanical thrombectomy due to acute ischemic stroke in the anterior circulation at our institution. Thirty-three of these (6.8%) patients were identified with a pretherapeutic NIHSS score of ≤ 8 (for patient baseline characteristics, see Table 1). Most often, mechanical thrombectomy was performed with a stent retriever with distal aspiration with an intermediate catheter ($n = 29$; 87.9%). Four patients (12.1%) were treated with primary aspiration thrombectomy. Ten of 33 (30.3%) patients underwent additional carotid artery stent placement due to cervical carotid artery occlusion ($n = 4$), stenosis ($n = 3$), or dissection ($n = 3$). For the type and manufacturer of the devices used and number of recanalization maneuvers performed, see Table 2.

Angiographic Outcome

With a median of 2 recanalization maneuvers (interquartile range [IQR], 1–3), TICI 2b–3 was achieved in 26/33 (78.8%) patients (TICI 2b: $n = 11$, 33.3%; TICI 2c: $n = 2$, 6.1%; TICI 3: $n = 13$, 39.4%). In 7/33 (21.2%) patients, TICI 2a was achieved.

Periprocedural Complications and Frequency of Infarction and Hemorrhage in the MCA Territory

We observed 1 case of vessel perforation causing a fatal subarachnoid hemorrhage. Additionally, 5/33 (15.1%) patients had angiographically occult, minor ipsilateral SAH detected in the routine follow-up CT 20–36 hours after mechanical thrombectomy without the need of further treatment (Heidelberg Bleeding Classification: class 3c). There were no patients with an embolism in a new vascular territory. Furthermore, no cases of air emboli, vasospasm, or device detachment were observed.

On the basis of previously unknown peripheral artery disease, 1 patient had a subtotal occlusion of the femoral artery with subcritical limb ischemia after deployment of a vascular closure device (Angio-Seal VIP; St. Jude Medical, Minnetonka, Minnesota), requiring surgical removal and endarterectomy.

Follow-up CT imaging revealed partial infarction in the MCA territory in 23/30 (69.7%) patients with a median posttreatment ASPECTS of 8 (IQR, 7–10). In 2/30 (6.7%) patients, hemorrhagic transformation/confluent petechiae without space-occupying effect within the infarcted area in the MCA territory occurred (Heidelberg Bleeding Classification: class 1b/HI2). In addition to the above-mentioned fatal SAH, a second patient sustained a fatal symptomatic intracranial hemorrhage within the infarcted area (Heidelberg Bleeding Classification: class 2/PH2).

Clinical Outcome

At 90 days, clinical outcome according to the modified Rankin Scale was the following—0: $n = 4$ (12.1%); 1: $n = 10$ (30.3%); 2: $n = 7$ (21.2%); 3: $n = 9$ (27.3%); 4: $n = 0$; 5: $n = 0$; 6: $n = 3$ (9.1%).

DISCUSSION

Treatment Rationale

In general, proximal occlusions in acute ischemic stroke are associated with a poor clinical outcome.¹⁵ However, as mentioned earlier, proximal occlusions are not necessarily associated with an initial high NIHSS and could be missed in patients with low NIHSS scores.⁶ In a large single-center cohort, 488/1398 (35%) patients treated with intravenous thrombolysis for acute ischemic stroke presented with mild symptoms.¹⁶ Most of these patients had a favorable outcome after 3 months (mRS 0–2, 82%). However, only 136/488 (28%) patients underwent advanced stroke imaging (CT angiography or CT perfusion) before treatment. For most patients, there was no information on the site of vascular occlusion.¹⁶ Visualization of the proximal occlusion is a key factor for further treatment decisions because intravenous thrombolysis has a very limited potential to recanalize occluded vessels if thrombus length exceeds 8 mm.^{7,8} In our analysis, the median thrombus length was 12 mm.

Previously published data from the Get With The Guidelines—Stroke program by the American Heart Association/American Stroke Association show that 29,200/93,517 (31.2%) patients with

Table 2: List of types, manufacturers, and number of maneuvers for mechanical thrombectomy

Device	Manufacturer	Size	No. of Patients Treated ^a	Total No. of Maneuvers
Capture	MindFrame ^b	4.0 × 20 mm	2	2
Catch Mini	Balt ^c	3 × 15 mm	1	2
ERIC	MicroVention ^d	4 × 24 mm	3	4
Revive	Codman Neurovascular ^e	4.5 × 22 mm	6	17
Solitaire 2	Covidien ^b	4 × 20 mm	15	31
Solitaire 2	Covidien	6 × 30 mm	4	4
Trevo ProVue	Stryker ^f	4 × 20 mm	1	2
Trevo ProVue	Stryker	3 × 20 mm	1	1
SofiaPlus	MicroVention	6F	4 ^g	4
Adapt Stent ^h	Boston Scientific ⁱ	9 × 32 mm	1	
Carotid Wallstent ^h	Boston Scientific	9 × 40 mm	5	
Carotid Wallstent ^h	Boston Scientific	7 × 30 mm	3	
Enterprise Stent ^h	Codman & Shurtleff ^e	4 × 37 mm	1	
Solitaire 2 ^h	Covidien	6 × 30 mm	1	

^a Some patients were treated with different stent retrievers.

^b Irvine, California.

^c Montmorency, France.

^d Tustin, California.

^e Raynham, Massachusetts.

^f Kalamazoo, Michigan.

^g Primary aspiration thrombectomy.

^h Implanted devices.

ⁱ Natick, Massachusetts.

acute ischemic stroke did not receive intravenous thrombolysis because of mild or improving symptoms.¹⁷ Most important, patients with mild strokes who did not receive acute recanalization therapy experienced a poor clinical outcome at 90 days (mRS 3–5 in about 27%–32%; mRS 6, 2%–5%).^{17,18} Hence, according to other authors,^{18,19} it is of major importance to also screen patients with acute ischemic stroke with mild-to-moderate symptoms for large-vessel occlusion. Considering the occlusion site, thrombus length, collateral status, and extent of early signs of ischemia on pretreatment imaging, mechanical thrombectomy should not be withheld.

Major Findings

The main finding of our retrospective analysis is that clinical outcome in patients with acute ischemic stroke due to large-vessel occlusion and a lower NIHSS score is predominately favorable after mechanical thrombectomy. We report favorable clinical outcome (mRS 0–2 at 90 days) in 21/33 (63.6%) and moderate clinical outcome (mRS 0–3 at 90 days) in 30/33 (90.9%) patients. In comparison with data from Strbian et al,¹⁶ clinical outcome of our patients does not seem to differ considerably from that in patients treated with intravenous thrombolysis alone. However, there are some relevant differences in the patient populations of both studies: First, 72% of the patients in the cohort of Strbian et al did not have advanced stroke imaging. Therefore, the presence of a proximal occlusion, occlusion site, thrombus length, collateral status, and perfusion deficit remain uncertain. Second, in our patient cohort, median onset-to-intravenous thrombolysis time was 156 minutes, which means that intravenous thrombolysis was, on average, administered later than in the previously mentioned study. Third, in our patients, mechanical thrombectomy was often initiated after a prolonged time window exceeding the eligibility period for intravenous thrombolysis. Nonetheless, 90 days after mechanical thrombectomy, 30/33 (90.9%) patients had

mRS 0–3, which is comparable with the scores of patients who received only intravenous thrombolysis for mild acute ischemic stroke (460/488; 94%) but were treated within a shorter time window. Our findings might indicate a possible treatment effect in patients with a prolonged window who would otherwise be ineligible for acute stroke treatment.

Twelve of 33 (36.4%) of our patients had an mRS of 3–6 at 90 days after stroke and therefore would be categorized as having poor clinical outcome in most interventional stroke trials. However, none of our patients were assessed as mRS 4 or 5 after 3 months. Most patients with poor outcome (27.3%) had a moderate disability and were able to walk unassisted. These data are in accordance with previous studies showing that patients with lower NIHSS scores/minor or mild stroke symptoms could have moderate-to-poor clinical outcomes.^{17–19}

Unfortunately, the mortality rate was 9.1% (3/33). Because intravenous thrombolysis did not improve the clinical condition, mechanical thrombectomy was initiated in a prolonged time window in 1 patient with a very poor outcome (mRS 6). Two patients sustained fatal symptomatic intracranial hemorrhage after intravenous thrombolysis and mechanical thrombectomy. From other studies, it is known that patients have a certain risk of symptomatic intracranial hemorrhage after intravenous and/or endovascular stroke therapy of up to 8.1%.^{1–5,16,20} In summary, with the exception of 3 cases, most patients who underwent mechanical thrombectomy for acute ischemic stroke with low NIHSS scores had a favorable or at least moderate clinical outcome after 3 months.

Angiographic outcome based on the recanalization rate (TICI = 2b–3; 78.8%) was similar or even higher than that in previous large interventional stroke trials.^{1–5} There were no unexpected interventional complications such as air emboli, device detachment, or emboli into a new vascular territory. Angiographically occult, minor ipsilateral subarachnoid hemorrhages were detected in 5/33 (15.1%) patients but had no impact on clinical outcome, which is consistent with previously published data.²¹

There were 2 procedure-related complications: a subtotal occlusion of the femoral artery requiring an operation and an intracranial vessel perforation causing a fatal subarachnoid hemorrhage. Groin complications following catheterization are not uncommon (0.4%–9%).^{22–24} The risk of groin complications is higher in an emergency setting, increases with a medical history of peripheral artery disease and the use of larger catheters (≥7F), and varies depending on the vascular closure device deployed.^{23–25} Asymptomatic subarachnoid hemorrhage and angiographically occult vessel perforations can be detected quite frequently in follow-up imaging after mechanical thrombectomy in

up to 16.1% of patients.^{21,26} Angiographically apparent vessel perforations and symptomatic subarachnoid hemorrhage occur in 0.6%–2.9% of patients after mechanical thrombectomy,^{1,4,5,27,28} and reports addressing the immediate treatment of vessel perforation after mechanical thrombectomy have been published.²⁹ In our case, despite stent deployment without any problems and after a previous retrieval maneuver that had already recanalized the middle cerebral artery main branch, symptomatic subarachnoid hemorrhage occurred following a second retrieval maneuver, causing an MCA perforation (distal M2 segment).

Limitations

This study has several limitations. There is a potential selection bias in this analysis because all patients underwent advanced stroke imaging (including CT or MR angiography and CT or MR perfusion) before treatment. Patients who did not undergo advanced stroke imaging during the observation period might have been missed for treatment evaluation. Furthermore, we did not have a control group of patients with low NIHSS scores and confirmed proximal occlusion who did not receive mechanical thrombectomy. Due to its focus on acute ischemic stroke in the anterior circulation, this analysis has only a limited value for acute ischemic stroke in the posterior circulation.

There are several uncertainties in patient selection for stroke treatment, and the small sample size of this analysis does not allow a clear NIHSS value as a cutoff for the recommendation for interventional stroke treatment. However, very low NIHSS scores were identified as a potential equipoise point with the least consensus on treatment decision.³⁰ Therefore, our results with an overall favorable clinical outcome after acute ischemic stroke with low NIHSS scores due to large-vessel occlusion underscore the need for a randomized controlled trial in these patients.

CONCLUSIONS

The clinical outcome of patients undergoing mechanical thrombectomy for acute ischemic mild stroke due to large-vessel occlusion appears to be predominately favorable, even in a prolonged time window. However, although infrequent, angiographic complications could impair clinical outcome. Future randomized controlled trials should assess the benefit compared with the best medical treatment.

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