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Modified treatment in cerebral ischemia 1 versus modified treatment in cerebral ischemia 0 before endovascular stroke treatment in middle cerebral artery's M1-occlusion: Predictor for revascularization success and outcome?

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Abstract

Background: Little is known about the implications for revascularization success of target vessel occlusions (TVOs) with persisting antegrade perfusion before initiation of endovascular stroke treatment (EST) (modified treatment in cerebral ischemia (mTICI 1)) compared to a complete occlusion (mTICI 0). Here, we compared these two states of TVO.

Methods: Retrospective, single-center analysis of patients treated for M1-segment middle cerebral artery (MCA) occlusion with EST from January 2015 until May 2020 in a tertiary stroke center. Primary study endpoint was successful recanalization (mTICI 2c-3) after one thrombectomy attempt. Secondary endpoints were clinical outcome (modified Rankin Scale (mRS) 90 days after stroke onset), complication rate, and rate of underlying atherosclerotic disease. The two study groups were compared in univariate analysis including patient characteristics and procedural details.

Results: In this study, 422/581 patients (72.6%) presented with complete M1-occlusion compared to 159/581 (27.4%) with incomplete M1-occlusion. Neither did the recanalization success rate differ between the study groups nor the rate of complications (mTICI 0: 2.4%, mTICI 1: 0.6%, $p = 0.304$) or underlying atherosclerotic disease. Patients with incomplete initial occlusion showed a lower mRS at discharge (median interquartile range (IQR) mTICI 0: 4 (3–5) vs. mTICI 1: 3 (2–6), $p = 0.014$), but a comparable mRS 90 days after stroke onset (mTICI 0: 3 (2–6) vs. mTICI 1: 4 (2–6), $p = 0.479$).

Conclusion: Complete M1-occlusions (mTICI 0) and incomplete occlusions (mTICI 1) show the same recanalization success, comparable complication rate, and clinical outcome as well as the same rate of underlying atherosclerotic disease. Thus, incomplete M1-occlusions do not allow for an individualized interventional approach.

Keywords

Middle cerebral artery stroke, cerebral angiography, thrombectomy

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Introduction

Since endovascular stroke treatment (EST) became a standard treatment option in acute ischemic stroke in recent years,[1] many procedural and technical details were uncovered that are associated with a higher chance of clinical recovery after ischemic stroke and EST. Among these, successful revascularization of the target vessel occlusion (TVO) plays a pivotal role for a favorable clinical outcome.[2] This lead to a growing interest in predicting the revascularization success of different thrombectomy techniques and occlusion shapes of the TVO in digital subtraction angiography imaging during EST.

So far, different types of angiographic occlusion shapes were described predicting the ensuing revascularization success. Baek et al. found a difference between truncal-type and branching type occlusion with more stent-retriever failure for truncal-type occlusions.[3] Consoli et al. reported differences of regular and irregular occlusion shape in responding to stent-retriever thrombectomy and contact aspiration.[4] Further occlusion shapes described so far are the so-called meniscus sign and the claw sign, referring to

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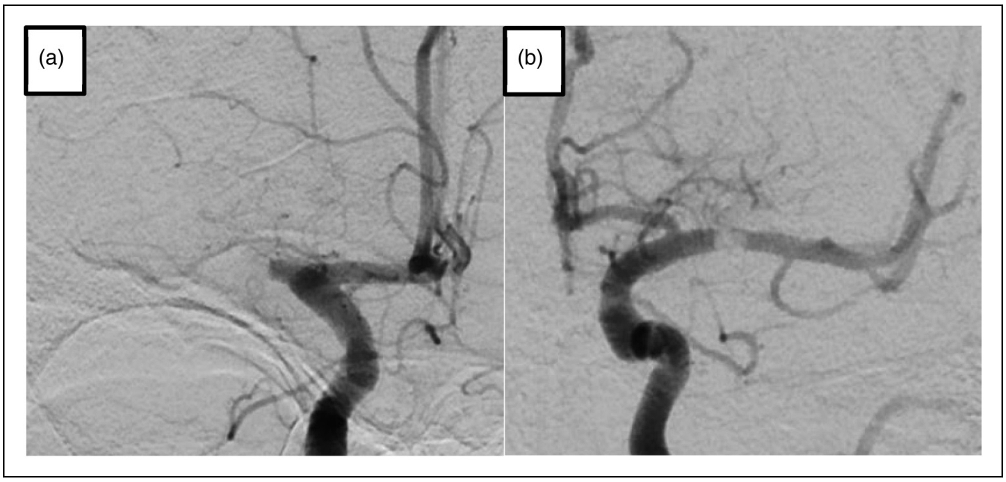

Figure 1. (a) Right middle cerebral artery (MCA) M1-occlusion (modified treatment in cerebral ischemia (mTICI) 0) and (b) left MCA M1-occlusion (mTICI 1).

angiographically different shapes of TVO before EST. Miranda et al. found the meniscus sign not to be associated with good clinical outcome or revascularization success,[5] while Yamamoto et al. report that the claw sign might predict revascularization success.[6]

All of the described occlusion types share that the target vessel is completely occluded. According to the modified treatment in cerebral ischemia (mTICI) score, the antegrade contrast flow is completely arrested without further perfusion (mTICI 0)—see Figure 1a. In contrast, little is known about TVOs with persisting minimal antegrade perfusion past the initial occlusion but limited distal branch filling with little or slow distal perfusion (mTICI 1)—see Figure 1b. These incomplete occlusions might represent side wall attached or semi-perfused thrombi, which are potentially easier or harder to extract than thrombi with consecutive complete vessel occlusion and might therefore influence the thrombectomy technique. Also, incomplete occlusions might be associated with underlying atherosclerotic stenosis of the TVO, which influence the recanalization success and interventional procedure or they might lead to a lower complication rate during EST because the branching distal to the TVO is contrasted to some extent and therefore visible during probing.

The aim of this study was to identify differences in the revascularization success, periprocedural complication rate, rate of underlying atherosclerotic disease, and clinical outcome comparing complete and incomplete occlusions in the middle cerebral artery (MCA)'s M1-segment.

Methods

This is a retrospective single-center analysis with prospectively collected data from a tertiary stroke care center. Patients were included with a MCA M1-occlusion, who were eligible for EST between January 2015 and May 2020. The local ethics committee approved this work. Patient consent was waived due to the retrospective nature of this study. Patients with complete occlusion of the extracranial internal carotid artery (tandem occlusion) were excluded because of the missing imaging of the intracranial TVO before intervention. Also, patients with poor quality of initial angiographic imaging of the TVO, for example, due to motion artifacts and patients with no thrombectomy pass performed, were excluded—see Figure 2.

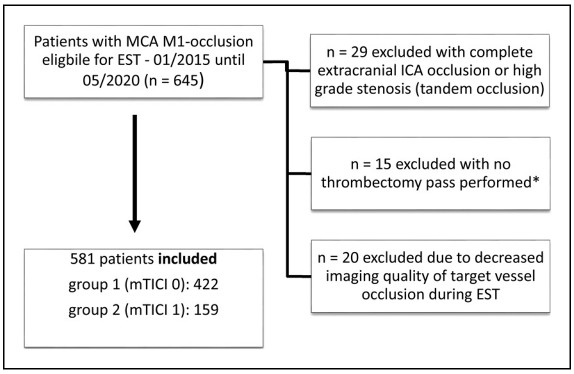

Figure 2. Flowchart of patient selection and study groups. *n = 14 patients with failed probing of aortic arch and internal carotid artery, n = 1 patient deteriorated at the start of EST. EST: endovascular stroke treatment, MCA: middle cerebral artery, mTICI: modified treatment in cerebral ischemia.

Study groups and study endpoints

The two study groups were defined as group 1 with complete occlusion of the MCA M1-segment TVO (mTICI 0) and group 2 with persisting antegrade perfusion of the TVO (mTICI 1)—see Figure 1. The EST's angiographic imaging was reviewed by two experienced interventional neuroradiologists blinded to the clinical outcome (with 6 and 12 years of clinical practice) to assess the mTICI score in initial imaging of the TVO before intracranial probing. Consensus reading was performed in case of differing assessments. The primary study endpoint was *first pass* *effect* (FPE) with complete reperfusion after one thrombectomy maneuver (stent-retriever thrombectomy or contact aspiration), defined as mTICI 2c or 3.[7,8] Secondary endpoints were the occurrence of procedural complications (vessel perforation, dissection, vasospasm, and thromboembolism during EST), the rate of relevant underlying atherosclerotic stenosis (>70% of vessel diameter), and the clinical outcome at discharge and 90 days after stroke onset according to the modified Rankin Scale (mRS).

EST treatment protocol and neurological assessment

In all patients, the choice of material and the primary thrombectomy approach (contact aspiration or stent-retriever thrombectomy under continuous aspiration) was decided by the interventionalist. In our center, the standard set up for EST in the anterior circulation is a triaxial system. This comprises a balloon-guided catheter (Merci 9F 95cm or Flowgate 8F 95 cm, Stryker, Kalamazoo, USA), an intermediate catheter (e.g. Sofia 5F/6F, Microvention, Aliso Viejo, California, USA) and a microcatheter/microwire system (mostly Rebar18 and Traxcess14). The two stent-retrievers being used the most in this study are Solitaire X (Medtronic, Irvin, CA) and Trevo (Stryker, Kalamazoo, USA). Stent-retriever thrombectomy attempts were performed during continuous aspiration using a VacLok Syringe® at the aspiration catheter and a VacLok Syringe at the guiding catheter. Conscious sedation or general anesthesia was used according to the patient's clinical presentation. Anesthesia surveillance was performed by intensive care experienced neurologists. Clinical and neurological baseline characteristics (NIHSS and pre-stroke mRS) were assessed by neurologists. Clinical outcome after discharge (90 days after stroke onset) was performed in person or on telephone by neurologists or clinical scientific assistants.

Data acquisition and statistical analysis

Source data were generated from a prospectively collected stroke database. Additionally, all data included in the present analysis were validated retrospectively. Groups were compared for differences in thrombectomy technique, clinical outcome, imaging, and procedural aspects with a Kruskal–Wallis test with Dunn's correction for multiple comparisons or the Mann–Whitney U test when combining groups and comparing two groups only. Frequencies were compared with a chi squared test for multiple groups or Fisher's exact test for two groups in case groups were combined. Statistical analysis was conducted using SPSS 25.0. For all statistical tests, the significance level was set to $p = 0.05$. Medians are given with interquartile range (IQR). All confidence intervals (CIs) are quoted as 95% CI.

Results

The patients included in the study analysis showed a complete TVO in the majority of cases (mTICI 0: 72.6%; n = 422/581 patients) and a persisting antegrade perfusion in a large minority (mTICI 1: 27.4%; n = 159/581 patients). The patients presenting with complete occlusion (mTICI 0) showed a higher NIHSS compared to incomplete occlusions (NIHSS for mTICI 0, median (IQR): 16 (11–21) vs. mTICI 1 14 (8–19.5), $p = 0.015$). For patients with complete occlusion, the mRS at discharge was higher (mRS median (IQR) in patients with mTICI 0: 4 (3–5) vs.mRS: 3 (2–6) in patients with mTICI 1, p = 0.014) despite a comparable pre-stroke mRS (in patients with mTICI 0, pre-stroke mRS was 1 (0–3) vs. pre-stroke mRS was 1 (0–2) in patients with mTICI 1, $p = 0.6$) while the patient age was higher in the mTICI 1 study group (mTICI 0: median age of 78 (67–82) vs. mTICI 1: median age of 79 (69–85), $p = 0.043$)—see also Table 1. Pre-stroke anticoagulation or antiplatelet therapy was found more often in patients with incomplete initial TVO (mTICI 0 33.9% vs. mTICI 1 43.3%, $p = 0.042$). While comorbidities, procedure times (time from symptom onset to groin puncture and time from groin puncture to recanalization), and Alberta Stroke Program Early CT Score (ASPECTS) of baseline imaging were equally distributed between the study groups, patients with an incomplete occlusion showed a higher ASPECTS in follow-up imaging (mTICI 0: median ASPECTS of 7 (5–8) vs. mTICI 1: median ASPECTS of 8 (5.5–9), $p = 0.045$).

Both study groups did not show any difference in the recanalization success during EST with an FPE of 45.7% for mTICI 0 occlusions and 44.7% for mTICI 1 occlusions ($p = 0.709$). This did not change when comparing ESTs, where stent-retriever maneuvers under continuous aspiration were performed as first thrombectomy approach (FPE for mTICI 0: 100 (23.8%) vs. mTICI 1: 40 (25.2%), $p = 0.745$) or for thrombectomies, in which contact aspiration was performed as first thrombectomy approach—see Table 2. Furthermore, the two study groups did not show a differing rate of underyling relevant vessel stenosis with a comparable rate of intracranial stenting during EST during the hospital stay of the incidence stroke and detection of underlying stenosis without stenting during EST was alike—see also Table 2.

Concerning periprocedural complications, there were no differences between study groups regarding vessel perforation, vessel dissection, thromboembolism to new territory during EST, or postprocedural vasospasm. This did not change, when evaluating ESTs separately, in which only stent-retriever thrombectomy maneuvers were performed. The rate of intracranial hemorrhage in control imaging after EST was equally comparable—see Table 2. While the mRS at discharge was lower for patients with incomplete occlusions ($p = 0.014$)), this difference did not persist and long-term clinical outcome measured as mRS 90 days after stroke onset did not differ between study groups—see Table 1.

Discussion

In this study, we found that an incomplete occlusion (mTICI 1) of an MCA M1-segment TVO eligible for EST is not

Table 1. Patient characteristics and clinical outcome of study groups.

	mTICI 0 (n = 422)	mTICI 1 (n = 159)	*P*-value
Male, n (%)	164 (38.9)	70 (44.0)	0.297
Wake up, n (%)	142 (33.6)	68 (42.8)	0.078
Age, median (IQR)	78 (67–82)	79 (69–85)	**0.043**
Diabetes, n (%)	85 (20.1)	32 (20.1)	1.0
Hypertension, n (%)	287 (68)	111 (69.8)	0.907
Coronary artery disease, n (%)	82 (19.4)	34 (21.4)	0.725
Atrial fibrillation, n (%)	168 (39.8)	70 (44.0)	0.432
Antiplatelet therapy or Anticoagulation, n (%)	143 (33.9)	69 (43.3)	**0.042**
IV thrombolysis, n (%)	189 (44.8)	51 (32.1)	**0.004**
Baseline ASPECTS, median (IQR)	8 (7–10)	9 (7–10)	0.532
ASPECTS, follow-up, median (IQR)	7 (5–8)	8 (5.5–9)	0.045
Extracranial ICA stenosis, n (%)	31 (7.3)	6 (3.8)	0.130
Time onset to groin puncture, median (IQR)	255 (166–430)	275 (182–591)	0.179
Time groin puncture to recanalization, median (IQR)	25 (17–36)	24 (17–37)	0.800
Baseline neurological presentation and clinical outcome in study groups			
Baseline NIHSS, n (%)	16 (11–21)	14 (8–19.5)	**0.015**
NIHSS 24 h, median (IQR)	10.5 (4–19)	8.5 (3–18)	0.175
Pre-stroke mRS, median (IQR)	1 (0–3)	1 (0–2)	0.561
mRS discharge, median (IQR)	4 (3–5)	3 (2–6)	**0.014**
mRS 90, median (IQR)	3 (2–6)	4 (2–6)	0.479

ASPECTS: Alberta Stroke Program Early CT Score; IQR: inter-quartile range; IV: intravenous; mTICI: modified treatment in cerebral ischemia; mRS: modified Rankin scale.
Bold *P*-values indicate significant group difference in statistical testing ($P < 0.05$).

Table 2. Recanalization result and procedural complications of endovascular stroke treatment (EST) for complete (mTICI 0) and incomplete (mTICI 1) target vessel occlusions (TVOs).

Revascularization result (mTICI post-EST)	mTICI 0 (n = 422)	mTICI 1 (n = 159)	
0–1	33 (7.8)	8 (5)	0.682
2a	26 (6.2)	6 (3.8)	
2b	105 (24.9)	44 (27.7)	
2c	72 (17.1)	34 (21.4)	
3	186 (44.1)	67 (42.1)	
First pass effect (FPE)			
FPE total, n (%)	192 (45.7)	71 (44.7)	0.709
FPE with stent-retriever thrombectomy as first attempt	100 (23.8)	40 (25.2)	0.745
FPE with contact aspiration as first attempt	92 (21.8)	31 (19.5)	0.571
Procedural aspects			
Proximal balloon occlusion (guiding catheter)	119 (28.2)	55 (34.6)	0.465
Contact aspiration as first approach, n (%)	153 (36.6)	61 (38.4)	0.629
Stent-retriever as first approach, n (%)	269 (63.7)	98 (61.6)	0.629
Intracranial stenting during EST or during hospital stay of acute stroke, n (%)	13 (3.1)	7 (4.4)	0.448
Underlying high-grade stenosis without ensuing intracranial stenting, n (%)	6 (1.4)	4 (2.5)	0.532
Procedural complications			
Vessel perforation - Vessel perforation in EST with only SR attempts	10 (2.4) - 5	1 (0.6) - 0	0.304 - 0.330
Vessel dissection	6 (1.4)	0	0.196
Embolus to new territory	4 (0.9)	4 (2.5)	0.224
Vasospasms	8 (1.9)	4 (2.5)	0.744
Intracranial hemorrhage in control CT after EST	144 (34.1)	47 (29.6)	0.317

EST: endovascular stroke treatment; mTICI: modified treatment in cerebral ischemia.

associated with different recanalization results nor complication rate compared to complete target vessel M1-occlusion (mTICI 0). Also, when comparing the two major thrombectomy techniques—contact aspiration and stent-retriever thrombectomy—the FPE and revascularization success did not differ between study groups. Hence, we cannot conclude on the superiority of one technique over the other based on the initial mTICI Score. Furthermore, incomplete occlusions were not associated with more cases of underlying atherosclerotic stenosis of the TVOs and did not lead to intracranial stenting in more cases. Although tandem occlusions were excluded from the study beforehand, which could lead to a bias toward less atherosclerotic disease in the whole study cohort, this finding shows that the occlusion state does not allow for an estimated differing stroke etiology. This study is not easily comparable to other studies, which investigated occlusion shapes of the TVO, because they all refer to complete occlusion of the target vessel (mTICI 0). Nevertheless, Miranda et al. also did not find a differing recanalization rate for patients with meniscus sign in M1-occlusions.[5] In contrast, Garcia-Bermejo et al. reported a difference in the recanalization rate when comparing tapered and non-tapered occlusions with atherosclerotic disease underlying more often the tapered occlusions.[9] The complication rate did also not differ between the study groups, although the overall low incidence might have no statistical power since vessel perforation occurred fourfold more often in patients with a complete TVO, where probing beyond the TVO cannot rely on visible, contrasted distal branching of the MCA (10 (2.4%) vs. 1 (0.6%), $p = 0.304$). However, there was also no difference between the study groups concerning the complication rates in stent-retriever thrombectomies, which contradicts this supposition.

Comparable to the influence of the hemispheric collateralization in intracranial large vessel occlusion (Tan-Score) on infarct growth of acute ischemic stroke and clinical outcome,[10,11] the study's mTICI 1 subgroup showed a lower NIHSS at hospital admission before EST and a lower mRS at discharge despite a comparable pre-stroke mRS and despite a higher patient age in patients with incomplete occlusions. However, the effect on clinical outcome did not persist over time and could not be found 90 days after stroke onset with a comparable mRS between study groups at this time point. The higher ASPECTS after EST in the study group with incomplete occlusions may reflect a slower infarct growth. The difference in short-term outcome and follow-up ASPECTS can be explained by the remaining blood flow through the TVO, which is the physiological correlate of mTICI Score 1 and persisting antegrade contrast perfusion. Patients with incomplete occlusions were older in this study cohort, which possibly explains that despite better short term outcome, these patients do not show a better long term outcome compared to younger and therefore more resilient patients with complete occlusions.

Interestingly, patients with complete occlusions had been treated more often with intravenous (IV) thrombolysis before EST. One might expect the contrary, that is, IV thrombolysis as bridging lysis leading to incomplete occlusions in initial angiographic imaging of the TVO. On the other hand, we found more patients treated with antiplatelet medication and/or anticoagulants in the incomplete occlusion group, which means that many of these patients were not eligible for IV thrombolysis and, moreover, the previous antiplatelet or anticoagulant medication might also have an influence on thrombus composition and vessel occlusion properties.

Limitations of this study concern especially the single-center retrospective design. National or local specificities concerning EST's procedural details might affect our study results. However, the large cohort reflecting many years of state-of-the-art EST grant for a certain variety in individual approaches and technical details.

Conclusion

Our study shows no difference concerning the recanalization success during EST, the rate of complications or underlying atherosclerotic disease between complete occlusions (mTICI 0) and incomplete occlusions (mTICI 1) of MCA's M1-segment TVOs. Therefore, incomplete occlusions do not allow for an individualized technical approach during EST. Incomplete occlusions were found more often in older patients. An initial effect on the clinical outcome at discharge (lower mRS for mTICI 1 occlusions) did not persist at 90 days after stroke onset.

Author's contribution

JJ had access to all data, performed data collection, writing and editing of this manuscript. CSW, AP, MOB, MC, and UN performed data collection, writing and editing of this manuscript. SS and MB contributed in writing and editing of this manuscript. MM supervised all steps of the project and helped editing the manuscript.

Declaration of conflicting interests

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Ethical approval

Ethical approval for the stroke database was provided by the ethics committee, University of Heidelberg (Germany).

Informed consent

Written informed consent was waived by the local ethics committee.

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