Two in One: Endovascular Treatment of Acute Tandem Occlusions in the Anterior Circulation

C. J. Maurer · F. Joachimski · A. Berlis

Abstract
Purpose Acute major stroke with high-grade stenosis or occlusion of the extracranial internal carotid artery (ICA) and additional intracranial large artery occlusion is increasingly treated with a mechanical endovascular approach by extracranial stenting and intracranial thrombectomy due to poor response to systemic thrombolysis with recombinant tissue plasminogen activator (rtPA). This article presents a single centre cohort of this challenging subtype of stroke, describing the technical procedure and analysing the angiographic and clinical outcome.
Methods Clinical and imaging data of all consecutive patients between July 2008 and March 2013 with intracranial artery occlusion in the anterior circulation and additional occlusion or pseudo-occlusion of the cervical ICA were retrospectively analysed with respect to demographical and clinical characteristics. Technical approach, recanalization rate, recanalization time and short-term clinical outcome were determined.
Results A total of 43 patients with tandem occlusion in the anterior circulation met the inclusion criteria. Out of these, 32 (74.4%) occlusions and 11 (25.6%) pseudo-occlusions of the extracranial ICA with additional occlusion of the distal segment of the ICA in 7.0% (3/43), the M1-segment of the middle cerebral artery (MCA) in 81.4% (35/43) or the M2-segment of the MCA in 11.6% (5/43) of cases were treated with combined endovascular approach including extracranial stenting with angioplasty and intracranial mechanical thrombectomy. In 76.7% of cases, an angiographic recanalization result of 2b or 3 using the Thrombolysis in Cerebral Infarction (TICI) score was achieved. Mean time from first angiographic series to recanalization was 103 min. A modified Rankin Scale (mRS) score of ≤ 2 was achieved in 32.6% at the time of discharge.
Conclusion Endovascular therapy of patients with tandem occlusion in the anterior circulation with emergency extracranial stenting and intracranial mechanical thrombectomy appears to be safe and may lead to a satisfactory angiographic result and clinical outcome.

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Introduction

In acute major stroke with proximal artery occlusion, the optimal selection of patients and the technique of endovascular treatment are still being elucidated. The subgroup of patients with both extracranial occlusion of the internal carotid artery (ICA) and downstream intracranial vessel occlusion (tandem occlusion) is particularly challenging. While the clinical outcome with intravenous (i.v.) or intraarterial (i.a.) thrombolysis with recombinant tissue plasmin-

ogen activator (rtPA) alone is poor [1–4], an endovascular approach with emergency ICA stenting and intracranial thrombectomy showed promise in several case series [5–12] despite potential pathophysiological adverse effects such as exposing the infarcted brain to reperfusion effects from recanalization of the ICA and to antiplatelet medication. We retrospectively reviewed all patients with major stroke in the anterior circulation as a result of occlusion or pseudo-occlusion of the extracranial ICA and concomitant intracranial vessel occlusion, who underwent endovascular therapy, analysing technical approach, safety, recanalization rate and time as well as short term clinical outcome.

Materials and Methods

Patients

Between July 2008 and March 2013 all acute stroke patients with tandem occlusion of the anterior circulation with symptomatic intracranial occlusion of the middle cerebral artery (MCA) or the terminal segment of the ICA and occlusion or pseudo-occlusion of the ipsilateral cervical ICA who underwent endovascular treatment in our centre were retrospectively identified. Pseudo-occlusion was defined as high-grade ICA stenosis with residual non-functional flow in the distal ICA. Demographic data of all patients and the aetiology of stroke were extracted from the medical charts.

As per standard operating procedure in our centre, on admission, all stroke patients were assessed by a neurologist, who obtained the National Institute of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS). A baseline non-enhanced cranial computed tomography (CT) scan was performed to exclude an intracranial haemorrhage and major infarction in the territory of the MCA. CT angiography (CTA) of the cervical and intracranial arterial vessels was performed documenting the intracranial arterial occlusion and the extracranial high-grade stenosis or occlusion of the ICA. In patients who were reported after 4.5 h of symptom onset CT perfusion imaging was added to identify the extent of infarct core and tissue at risk.

Treatment

If there were no contraindications, i.v. thrombolysis with rtPA was immediately started. The patient was then transported to the angiography suite where general anaesthesia and endotracheal intubation were initiated, unless good cooperation during the angiographic procedure was expected. All endovascular procedures were performed by or under close supervision of three fully trained experienced interventional neuroradiologists. In all patients an angiography of the contralateral ICA, the ipsilateral common carotid artery and the dominant vertebral artery was obtained to assess the site of the vessel occlusion and the localization and degree of collateral flow.

Usually, a 6 French guiding sheath was positioned in the distal common carotid artery. A 0.014-inch microwire was then advanced through the cervical occlusion to the base of the skull. Generally, a microcatheter was positioned in an extradural segment of the ICA. By repetitive injection and withdrawal of the microcatheter the correct intraluminal position was documented and the site of the distal occlusion and the length of the proximal stenosis were determined.

Stenting of the carotid occlusion or pseudo-occlusion was performed by using a Carotid WALLSTENT (Boston Scientific, Natick, Massachusetts, USA) in majority of the cases. If the occlusion was located further distally or in tortuous vessels it required a different approach; other stents were used or added such as Neuroform (Stryker Neurovascular, Fremont, California, USA), Wingspan (Stryker Neurovascular, Fremont, California, USA) or OMEGA (Boston Scientific, Natick, Massachusetts, USA). Embolic protection devices were not employed. Percutaneous transluminal angioplasty (PTA) before stenting was only performed, if the primary passage with the stent carrying catheter was not possible. Afterwards, a PTA was performed within the stent to treat the residual stenosis of the vessel, if necessary. Directly before stent placement, the patient received a loading dose of i.v. aspirin (500 mg) and an i.v. bolus of heparin (5000 IU), alternatively tirofiban.

After stent placement a control angiogram was carried out to assess the potential change in haemodynamics. In case of a persisting intracranial occlusion recanalization of the vessel was attempted using different methods depending on anatomy, accessibility and extent of the occlusion. The primary method of intracranial intervention was stentretrieving with different devices (Solitaire FR (Covidien/ev3, Irvine, California, USA), Trevo Pro/Trevo ProVue (Stryker, Kalamazoo, Michigan USA) and pREset (Phenox, Bochum, Germany)). Frequently, an intermediate catheter (Navien (Covidien/ev3, Irvine, California, USA), DAC (Stryker Neurovascular, Fremont, California, USA)) was used to gain distal access, especially in patients with very tortuous vessels, to avoid retrieving through the extracranial stent and to prevent thrombus dislocation into the anterior cerebral artery. The catheter was positioned as far distal as possible in the ICA and aspiration was performed during the retrieving manoeuvre. Further therapy options included direct thrombus aspiration, i.a. thrombolysis or intracranial PTA and stenting (Neuroform or Solitaire) when indicated.

Postprocedural flat-detector CT in the angio suite or, if not available conventional CT was obtained to exclude periprocedural haemorrhage. After nasogastric intubation, a loading dose of clopidogrel (600 mg) or ticragelor (180 mg) was given. Follow-up CT was performed after 24 h or ear-

lier in case of neurological deterioration to show the extent of the infarction and haemorrhage. An illustrative case study is presented in Fig. 1.

Outcome

The angiographic outcome was determined by two independent neuroradiologists with 20 years of experience in stroke treatment and 3 years of experience, respectively, using the modified Thrombolysis in Cerebral Infarction (TICI) score [13]. Cases of disagreement were reconciled by consensus.

The NIHSS and mRS at the time of discharge were assessed by a stroke neurologist. In case of fatal stroke no NIHSS was obtained; the patients were classified as mRS of 6.

Good angiographic outcome was defined as TICI score 2b and 3 and good clinical outcome defined as mRS score of ≤2 at time of discharge.

Results

A total of 43 patients met the inclusion criteria—see Table 1 for the clinical characteristics. Occlusion of the cervical ICA was found in 32 patients (74.4%) and pseudo-occlusion in 11 patients (25.6%). During treatment, 35 patients (81.4%) underwent general anaesthesia for the endovascular procedure. As many as 33 patients received i.v. rtPA as a bridging therapy with an average dose of 59 mg. In 38 cases (88.4%) a carotid WALLSTENT was deployed in the occluded or highly stenosed ICA. In two cases a second WALLSTENT was added further distally in the cervical ICA. In one case two self-expanding Wingspan stents were used, in a further case a balloon expandable coronary stent (OMEGA) was applied in the cervical ICA. In another case no dedicated carotid stent was used. Recanalization was achieved with two Neuroform stents positioned in the distal cervical ICA. In four cases (9.3%) no extracranial stent was used at all. In three cases (7.0%) the passage of the proximal occlusion site with the microwire was unsuccessful while in one case (2.3%) recanalization was obtained with mechanical thrombectomy alone.

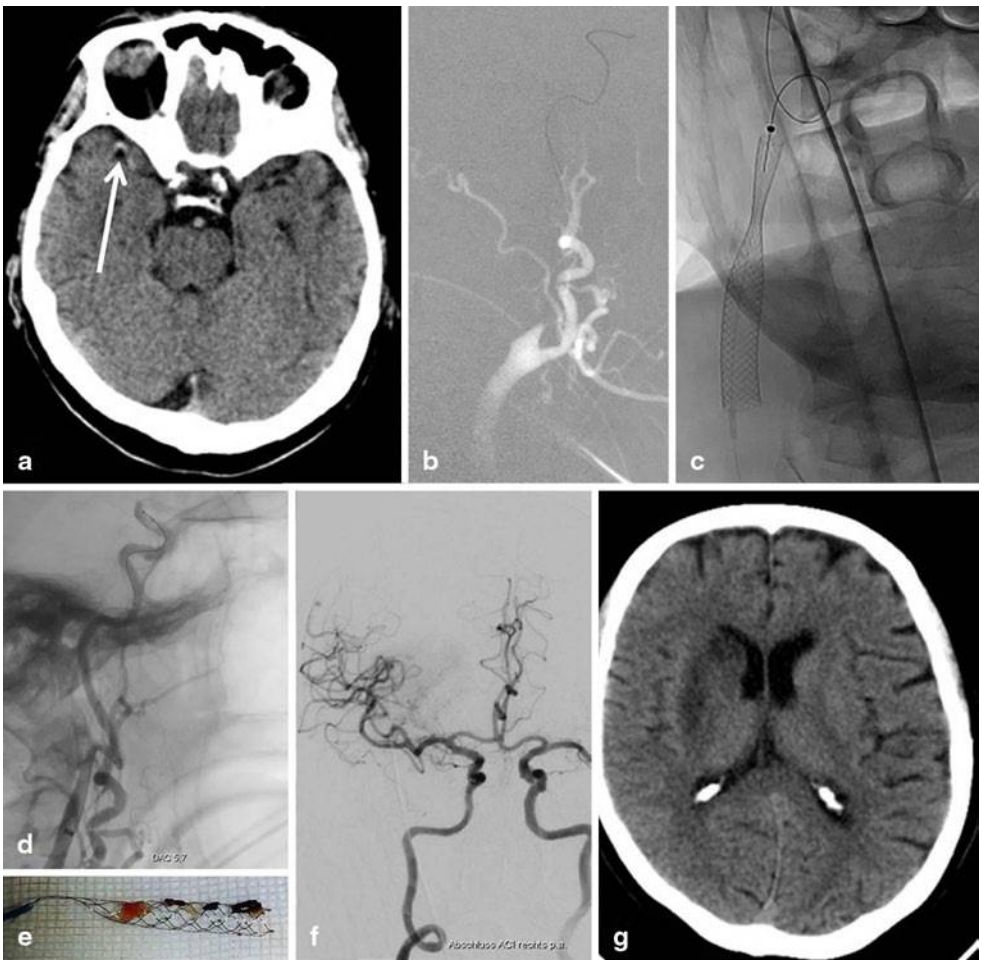

Fig. 1 Patient 20, female, 71-year-old, presented with right hemispheric symptomatic, National Institute of Health Stroke Scale (NIHSS) 13, computed tomography (CT) showed no early ischemic changes except a dense artery sign (*arrow*) of the right middle cerebral artery (MCA) (**a**). Roadmap image depicts proximal occlusion and wire passage (**b**). Carotid WALLSTENT after deployment (**c**). For distal access in elongated anatomy a triaxial approach was made with an intermediate catheter (DAC) in the distal internal carotid artery (ICA) (**d**). Thrombectomy was performed (**e**) with complete recanalization Thrombolysis in Cerebral Infarction (TICI) score of 3 (**f**). CT scan 3 days after onset showed only circumscriptive infarction in the right basal ganglia (**g**). mRS on discharge was 0

Table 1 Clinical characteristics ($n=43$)

Demographic and clinical Data	
Age, Mean ± SD in years	68 ± 13
Female	13 (30.2%)
Male	30 (69.8%)
NIHSS, Mean ± SD	12.9 ± 5.2
Aetiology	
Dissection	7 (16.3%)
Atherosclerosis	33 (76.7%)
Post CEA	1 (2.3%)
Undetermined	2 (4.7%)
Site of intracranial occlusion	
Terminal Segment ICA	3 (7.0%)
MCA M1	35 (81.4%)
MCA M2	5 (11.6%)

NIHSS National Institutes of Health Stroke Scale, *CEA* carotid endarterectomy, *MCA* middle cerebral artery, *ICA* internal carotid artery, *SD* standard deviation

First line treatment of the intracranial occlusion consisted of mechanical thrombectomy by use of various stentretrieving devices in 27 patients (62.8%). In 14 of these cases an additional intermediate catheter was used to gain access to the distal occlusion and to avoid retrieving through the proximal stent. As many as 20 patients (46.5%) received additionally or exclusively i.a. thrombolysis, especially in cases of emboli distal of the M1-segment, that were deemed not safely manageable with mechanical methods. In seven cases (16.3%) an intracranial stent (1 Neuroform and 6 Solitaire) was deployed due to failed thrombectomy (three cases) or pre-existing atherosclerotic intracranial stenosis. In one case stent deployment was performed via the contralateral ICA and the anterior communicating artery because of unsuccessful recanalization of the ipsilateral proximal occlusion.

Average time to recanalization as documented by the time stamp of the initial and the final series of the angiogram was 102 min (ranging from 33 to 273 min). There was no significant difference between patients treated in general anaesthesia or conscious sedation (102 min vs 102 min). Complete or partial recanalization of the intracranial occlusion graded as TICI-score of 2b or 3 was achieved in 33 patients (76.7%) whereas four cases were graded as TICI 2a.

At the time of discharge 14 patients (32.6%) had modified Rankin score of 2 or less. The average NIHSS was 6.8. A total of nine patients (20.9%) died during their hospital stay. Of these, five had parenchymal haemorrhage in the post-procedural CT within 24 h after onset; four of those patients had received i.v. thrombolysis as a bridging therapy. One patient had a subarachnoid haemorrhage due to intraprocedural dissection of the anterior choroid artery, which had to be occluded using N-butyl cyanoacrylate glue. In this and two other cases intracranial hypertension due to swelling of a large accompanying MCA infarction led to the death of the patient. One patient died because of secondary infections.

Discussion

In our institution stentretrievers were first introduced in May 2009. The swiftness of mechanical thrombectomy and its clinical success led to a steep increase in endovascular stroke therapy and reflected in a change of our institutional standard operating procedures, which now routinely requires a joint neurological and neuroradiological discussion of endovascular treatment options in each case of large vessel occlusion. Age, premorbid status, time to treatment, collateral flow, thrombus length [14] and density [15] are considered in order to weigh the limited efficacy of i.v. thrombolysis [3, 4, 16] against the periprocedural risk (vessel perforation, anaesthesia). While recanalization sharply improves outcome [17], it also increases the risk of haemorrhage and hyperperfusion.

Tandem occlusions have an exceedingly poor prognosis, when treated with i.v. thrombolysis alone [18]. The recanalization rate in these patients is low and an outcome of severe disability or death ensues in a large majority of the cases [1, 3]. In our series recanalization with an angiographic outcome of TICI 2b or 3 was achieved in 76.7%. The clinical outcome at the time of discharge is consistent with the literature on tandem occlusions [7–9] and seems to improve on reported numbers for i.v. thrombolysis, although the usually stated outcome after 90 days is not available in our series.

There is only limited data about complications in mechanical thrombectomy. The rate of symptomatic intracranial haemorrhage (sICH) in two recent studies with single intracranial occlusions is 5% in a retrospective single-centre analysis [20] and 4.9% in the SOLITAIRE™ with the intention for thrombectomy (SWIFT) trial [21]. In our series five patients (11.6%) died of sICH. Malik et al. [12] report a mortality rate of 23% and 10.4% of postprocedural haemorrhage; Soize et al. [19] report a significantly different rate of sICH in tandem occlusions (9.7%) vs in single occlusions (0%). These findings suggest a higher risk of intracranial haemorrhage in patients with tandem occlusions compared with those with single thromboembolic occlusions. Possible causes include the need for antiplatelet therapy as well as the elevated risk of a hyperperfusion syndrome due to the pre-existing ICA stenosis (Table 2).

There is a discussion about the proximal to distal approach when treating tandem lesions. In the majority of published series the proximal to distal approach is used. Mpotsaris et al. [7] report 17 patients with tandem occlusion in their prospective single-centre study treated with extracranial stenting and secondary intracranial thrombectomy; Spiotta et

Table 2 Procedure details for patients who died of symptomatic intracranial haemorrhage (sICH) ($n=5$)

	Patient 10	Patient 17	Patient 20	Patient 25	Patient 41
Sex	M	F	M	F	M
Age (years)	70	72	79	79	79
Stent	ICA	ICA	ICA	ICA	ICA
Intracranial occlusion	M1	M1	M1	M1	Carotid T
NIHSS score at admission	17	19	17	14	18
Length of endovascular procedure (minutes)	119	147	69	122	72
i.v. rTPA	No	Yes	Yes	Yes	Yes
i.a. Lyse (mg)	0	10	10	0	20
Mechanical recanalization	Solitaire 4×20	Solitaire 4×20	Solitaire 4×20	Solitaire 4×20	Trevo ProVue 4×20
Number of retrieving manoeuvre	1	1	1	2	1
TICI score final series	2b	2b	2b	2b	2b

i.v. intravenous, *i.a.* intraarterial, *ICA* internal carotid artery, *rTPA* recombinant tissue plasminogen activator, *NIHSS* National Institute of Health Stroke Scale, *TICI* thrombolysis in cerebral infarction

al. [9] included 16 cases in their retrospective review with stenting of the ICA and intracranial thrombectomy; Malik et al. [12] treated 77 patients in their retrospective analysis with primary stenting and intracranial intervention including i.a. thrombolysis, thrombectomy with the Merci clot retriever or direct aspiration and Kwak et al. [22] describe 35 patients that underwent stent implantation for the proximal ICA and i.a. thrombolysis for the tandem occlusion. On the other hand, Soize et al. [19] used the retrograde approach with primary distal thrombectomy in tandem occlusions in 11 patients whenever possible; Cohen et al. [10] suggest in their case series of seven patients proximal PTA, distal thrombectomy with a stentretriever and stenting at the end of the procedure as the most effective and rapid approach for tandem occlusions. Further case reports present different distal to proximal approaches for primary intracranial aspiration [23] or i.a. thrombolysis [24]. Both approaches seem to be feasible with similar results in terms of recanalization rate and clinical outcome. We see the advantage in reopening the proximal occlusion first in the immediate change of blood flow. In our series, the re-established haemodynamics resolved the distal occlusion partially or completely in six cases (14.0%), thus obviating the need for intracranial treatment, a finding reported by Malik et al. as well in 26.0% of their patients. In the alternative distal to proximal approach, re-occlusion of recanalized intracranial vessels might occur through re-embolism or in-situ-thrombosis, in particular in the distal ICA, due to lack of sufficient blood flow.

Published literature suggests that patients treated under general anaesthesia have a longer time to recanalization [25] and poorer outcome [26] as compared with patients treated under conscious sedation. In our series, eight patients (18.6%) were treated without general anaesthesia. The time to revascularization did not differ between those two groups (102 min vs 102 min). As many as four of eight patients (50.0%) with only sedation had an mRS of 2 or less at the time of discharge, whereas, 11 of 35 patients treated under general anaesthesia had an outcome of 2 or less in terms of mRS. These results seem to confirm the findings of the literature, but there might be a bias in patient selection. For conscious sedation patients were only chosen, if good cooperation during the angiographic procedure was expected.

Before the first use of the Solitaire stent for mechanical thrombectomy, five patients (11.6%) in our series with tandem occlusions were treated by endovascular means. All of them received extracranial stenting and balloon angioplasty for the ICA occlusion or pseudoocclusion. As means of intracranial recanalization i.a. thrombolysis was used in three cases and intracranial stenting in three cases as well. Of these, one patient died, three had an mRS of five and one an mRS of 4. These results suggest an improvement in clinical outcome with the more effective mechanical thrombectomy with stentretrievers. However, the inhomogeneous choice of recanalization devices and endovascular treatment strategies reflect the complexity of the procedure itself as well as the historic development of endovascular treatment in our centre, including increasing operator experience and versatility of devices.

Conclusion

With careful patient selection, endovascular therapy of tandem occlusion in the anterior circulation using a combined approach with i.v. bridging thrombolysis, emergency extracranial stenting and intracranial mechanical thrombectomy can be safe and leads to a satisfactory angiographic and clinical result.

Conflict of Interest C. Maurer received an educational grant from Boston Scientific and Stryker.

A. Berlis has consultancy agreements with Boston Scientific, Stryker and ev3/Covidien

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