PTE/50824-5/2022

Doctoral School of Health Sciences
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Diagnostic and therapeutic aspects of neuroradiology in acute ischemic stroke affecting the anterior circulation

Ph.D. Thesis

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Programme Nr. 2 / PR-2:
Cardiovascular Health Science
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Area of study:
K-22 Improving quality of life in patients with neurovascular and peripheral vascular diseases

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Doctoral School
Faculty of Health Sciences
University of Pécs
2022

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ABBREVIATIONS

5-HIAA	5-hydroxyindoleacetic acid
ACA	Anterior cerebral artery
ADEM	Acute demyelinating encephalomyelitis
AIS	Acute ischemic stroke
ASPECTS	Alberta Stroke Program Early CT Score
BA	Basilary artery
BAT	Balloon-assisted tracking (technique)
CBF	Cerebral blood flow
CBV	Cerebral blood volume
CCA	Common carotid artery
CDUS	Color Doppler ultrasound
CE MRA	Contrast-enhanced magnetic resonance angiography
CF	Cerebrospinal fluid
COW	Circle of Willis
CT	Computed tomography
CTA	Computed tomography angiography
CTP	Computed tomography perfusion
DE CTA	Dual-energy computed tomography angiography
DSA	Digital subtraction angiography
DWI	Diffusion-weighted magnetic resonance imaging
ECA	External carotid artery
ELFO	Electrophoresis
EVT	Endovascular treatment
FLAIR	Fluid-attenuated inversion recovery magnetic resonance imaging
GBS	Guillain–Barré syndrome
GSR	German Stroke Registry
HM	Hemiplegic migraine
ICA	Internal carotid artery
ICH	Intracerebral hemorrhage

ICHD	International classification of headache disorders
ISR	In-stent restenosis
IU	International unit
IVT	Intravenous therapy
LVO	Large vessel occlusion
MCA	Middle cerebral artery
MIP	Maximum intensity projection
MPR	Multiplanar reformation
MR	Magnetic resonance imaging
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
mRS	Modified Rankin scale
MTT	Mean transit time
NCCT	Non-contrast computed tomography
NIHSS	National Institute of Health stroke scale
OR	Odds ratio
PACS	Picture archiving and communication system
PC MRA	Phase contrast magnetic resonance angiography
PTCA	Percutaneous transluminal coronary angioplasty
RCT	Randomized control trial
rtPA	Recombinant tissue plasminogen activator
SWI	Susceptibility-weighted magnetic resonance imaging
TIA	Transient ischemic attack
TICI	Thrombolysis in cerebral infarction (scale)
TM	Transverse myelitis
TO	Tandem occlusion
TOF MRA	Time-of-flight magnetic resonance angiography
US	Ultrasound
VR	Volume rendering

PUBLICATIONS

This thesis is based on the following:

I. **Nagy C** , Bajzik G , Skobrák A , Csorba E , Lajtai A , Balogh G , Nagy F , Vajda Z . Gyermekkori sporadikus hemiplegiás migrén arteria cerebri media hipoperfúzióval [Childhood sporadic type of hemiplegic migraine with arteria cerebri media hypoperfusion]. *Ideggyogy Sz*. (2017) 30;70(9-10): 343-348. – case report; **IF: 0,252**

II. **Nagy C**, Héger J, Balogh G, Gubucz I, Nardai S, Lenzsér G, Bajzik G, Fehér M, Moizs M, Repa I, Nagy F, Vajda Z. Endovascular Recanalization of Tandem Internal Carotid Occlusions Using the Balloon-assisted Tracking Technique. *Clin Neuroradiol*. (2021) doi: 10.1007/s00062-021-01078-2. – original publication; **IF: 3,649**

III. **Nagy C**, Bajzik G, Király I, Balogh G, Nagy F, Vajda Z. Diagnostic value of dual-energy CT angiography in the assessment of supra-aortic in-stent restenotic lesions: comparison with Doppler US findings. *Interventional Neuroradiology* (2017) 23: Suppl. 1 Paper: P607, 1 p. – poster; **IF: 0**

Additional publications, not related to the thesis:

I. **Nagy C**, Király I, Bánsághi Z, Doros A. Revascularisatio az aortában, a veseartériákban és az alsó végtagok artériás rendszerében [Revascularisation of the aorta, of the renal and of the lower limb arterial systems]. Orv Hetil. 2015 Apr 26;156(17):665-73. Hungarian. doi: 10.1556/OH.2015.30154. PMID: 26047149.
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INTRODUCTION

Acute ischemic stroke is a cerebrovascular accident resulting from insufficient focal cerebral blood flow. The blockage diminishes essential oxygen and glucose perfusion to the brain, leading to damage or death of brain cells. If circulation isn't restored in time, brain damage can be unavoidable. The importance of this disease is that it causes major social and economic burdens to society because it can be a significant cause of morbidity with long lasting disability and mortality. Globally, stroke is the second leading cause of death and is a leading cause of serious long-term disability. [1][2] Rapid recanalization of arterial occlusion and restoration of blood flow can prevent disability and save lives. The TOAST classification suggests that there are four main subtypes of ischemic stroke. [3] These are large vessel atherosclerosis, small vessel disease (lacunar infarcts), cardioembolic stroke and at last stroke of other determined or undetermined etiology. The cause and pathophysiology are different in each of these groups. Irrespective of stroke subtype, it is critical to know that with each minute of large vessel ischemic stroke untreated, near two million neurons go down. Understanding acute stroke and its treatment is the most important that should be kept in mind, because "time is brain".

ACUTE ISCHEMIC STROKE IN THE ANTERIOR CIRCULATION

Stroke is a syndrome with a broad spectrum and more importantly a medical emergency also known as a cerebrovascular accident. Anterior circulation ischemic strokes are the most common of all ischemic strokes and account for approximately 70% of ischemic stroke cases. The main cause of this disease is the obstruction of one of the large arteries of the anterior circulation or the small perforator arteries. Lacunar strokes are caused by lipohyalinotic intrinsic degeneration of the small penetrating

vessels. As many as 20% of ischemic strokes are penetrating branch occlusions of the middle or anterior cerebral arteries supplying the deep white and gray matter resulting in lacunar infarcts which most of the times are asymptomatic.

The middle cerebral artery (MCA) is the largest of the intracerebral vessels and supplies almost the whole convex surface of the brain. The lenticulostriate branches arise from the MCA supplying the basal ganglia and parts of the internal capsule. Occlusion of the MCA or its branches is the most frequent type of anterior circulation infarct. Causes of arterial occlusion involving the major cerebral arteries mainly are emboli arising from atherosclerotic arterial stenosis at the bifurcation of the common carotid or the origin of the internal carotid artery, from cardiac sources and from atheroma in the aortic arch. Symptoms and severity depend on the level and length of occlusion. Internal carotid artery occlusion can take place at the proximal 2 cm of the artery and intracranially. Extent of infarction depends on the speed of occlusion and systemic blood pressure. Occlusion of the internal carotid artery can be silent when collaterals open up if the occlusion occurs steadily over a period of time. In other cases, tandem occlusion of the internal carotid artery can develop which is characterized by proximal occlusion of ICA, either due to acute thrombosis of an unstable atherosclerotic plaque or dissection, resulting in the embolic blockage of the ICA terminus and/or the main trunk (M1 segment) of the middle cerebral artery. The condition is responsible for up to 20% of acute ischemic stroke cases [4], responds poorly to intravenous thrombolysis [5] and is associated with poor prognosis without timely and successful recanalization [6]

NON-INVASIVE IMAGING TECHNIQUES

Rapid neurovascular imaging is critical in identifying eligible patients for endovascular therapy. Recent innovations in neuroimaging have allowed

for better assessment of risks/benefits of endovascular therapy and appropriate triage of patients. Primary and most cost-effective tool used in case of suspected acute stroke is non-contrast computed tomography. [7] Patients with acute ischemic stroke non-contrast computed tomography (NCCT) might be normal or show slight changes as hyperdense MCA sign, insular ribbon sign or hypodensity due to cytotoxic edema, loss of gray-white differentiation, cortical swelling and effacement of sulci. The ASPECTS (Alberta Stroke Program Early CT Score) is a quantitate, standardized score that measures the extent of early ischemic changes in the anterior circulation on initial non-contrast head computed tomography. Limitations of this method is that it is not valid for lacunar strokes and strokes involving the posterior circulation. More advanced non-invasive imaging techniques are computed tomography angiography either expanded with perfusion study or magnetic resonance imaging with different sequences including angiography.

IMAGING OF THE NEURO-VASCULATURE

The first and most crucial step in the treatment of neurovascular emergencies is proper preprocedural imaging. For treating ischemic stroke, the most important is a rapid and accurate diagnosis and the exact cause and location of the blot clot is essential. Computed tomography is a tool that can be used to differentiate between ischemic and hemorrhagic stroke and can show the exact location of the blood clot in a timely manner with a low cost. [8] Since CT scanners have been installed throughout the country CT became widely available all the year round. In an acute setting there are relatively few contraindications, and the scanning time is extremely rapid. Novel methods like artificial intelligence can also help and speed up the decision-making process. Eventhough intravenous thrombolysis can be administered after plain head CT ruled out hemorrhage, many centers even in hospitals with lower level for stroke

treatment routinely perform supra-aortic computed tomography angiography (CTA). Findings on the CTA have triage consequences and preventive implications for the stroke patient. Diagnosing supra-aortic large vessel stenosis or occlusion referable to the neurological symptoms is essential for acute stroke patients to warrant the adequate treatment option. Specialized computed tomography especially perfusion studies and magnetic resonance imaging (MRI or MR) are helpful for expanding the time window or aid further therapeutic guidance. Computed tomography perfusion (CTP) allows us to acquire real-time physiology parameters from the brain parenchyma as well as cerebral blood flow (CBF), cerebral blood volume (CBV) or mean transit time (MTT). By measuring the quantity of irreversibly damaged brain tissue and salvageable brain this method is eventually one of the most helpful tools in stroke diagnostics. MR is an advanced tool and has also the advantages as CT perfusion, but it is time consuming and the availability all year round is far from optimal. [9]

COMPUTED TOMOGRAPHY ANGIOGRAPHY (CTA)

Computed tomography is well established initial tool for neurological emergencies which rapidly gives comprehensive information regarding the therapeutic decision-making process. Nevertheless, since endovascular treatment options could be applicable and efficient up to 24 hours after last seen well, none-enhanced CT and CT angiography has become the standard of care for the primary imaging of stroke patients. Treatment should never be delayed by removing the patient from the scanner for further evaluation of the images, so CT angiography should always follow plane CT in an acute stroke patient. [10] In general, CT angiography has been favored for the vascular assessment and treatment planning of stroke patients despite the radiation exposure. The main reason is the rapid technical progression in hardware and software,

allowing every hospital to perform state-of-the-art vessel imaging. Since the introduction of multi-detector CT scanners high-resolution angiographic images can be acquired of the supra-aortic vascular tree in just blink of an eye with small amount of single bolus contrast injection. At least 64-section scanner can visualize from the aortic arch through the intracranial vessels in less than 3 seconds at submillimeter isotropic resolution. [11] Basic CT and CTA may be complemented by multiphase CTA or CT perfusion, which can offer further information on collateral circulation and tissue viability. Artefacts or poor evaluation of vascular pathologies even in heavily calcified vessels or in the presence of metallic implants can be avoided with artefact reduction software and dual-energy scanning. [12] Dual-energy CT angiography (DE CTA) of the head has a high sensitivity and specificity compared to 3D DSA as the standard of reference. [13] Postprocessing can be performed by the technologist from raw data on the scanner in conventional planes and sent to the picture archiving and communication system (PACS) server. The available thinnest axial slices also should be sent to the PACS serves for additional reconstruction by the neuroradiologist or interventionalist even later. Depending on the vascular pathology maximum intensity projection (MIP), volume rendering (VR) and multiplanar reformation (MPR) should help in the assessment. Relative contraindications of CT angiography in an acute stroke patient can be allergic reaction to contrast agents, pregnancy, hyperthyroidism, metformin use, and chronic or acutely worsening renal function, but usually the potential benefit of rescuing the patient from life-long disability or even death outweighs the risk. [14]

MAGNETIC RESONANCE ANGIOGRAPHY (MRA)

Magnetic resonance imaging requires no radiation exposure. MR is widely available, noninvasive, great and advanced tool for neuroimaging and identifying the subgroup of stroke patients who may benefit from

revascularization therapies. [15] MR like CT has the capability to visualize intracranial and extracranial vasculature either artery or vein. In stroke our major goal is to delineate steno-occlusive vascular pathology that can be associated with the neurological deficit. There are two main techniques for MR angiography. Contrast-enhanced MRA (CE MRA) uses gadolinium as contrast, while time-of-flight (TOF) or phase contrast (PC) MRA depends on physiologic circulation. Routine MR imaging commonly includes time-of-flight MRA. Despite no contrast medium is required for this sequence it has some major drawbacks. It has a limited spatial coverage which excludes the extracranial vasculature and very sensitive to motion artifacts since the MR signal is generated by the motion of the blood. [16] [17] Contrast-enhanced MR angiography is less affected by flow disturbances. Compared to time-of-flight MRA it can cover the whole supra-aortic region with a quicker acquisition time, but on the other hand it does not reach the spatial resolution of time-of-flight angiography. [18] Contrast medium has a relatively high cost, and the administration requires an extra sequence for bolus-tracking. Nephrogenic systemic fibrosis is another concern in patients with impaired renal function. [19] Nevertheless contrast enhanced MR angiography can be a diagnostic option next to CT angiography and DSA in the comprehensive evaluation of neck and head arteries, since it precisely detects clinically significant diseases in the carotid and vertebrobasilar system as well. As the magnetic field strength increases future holds new directions in MR imaging such as higher spatial resolution and reduced acquisition time. Along with the technological advancements in MR hardware and software the promising unenhanced MR methods will most likely open new horizons and take over vascular imaging avoiding the need for additional contrast administration.

NEUROVASCULAR ANGIOGRAPHY AND NEUROINTERVENTION IN ACUTE ISCHEMIC STROKE

DIGITAL SUBTRACTION ANGIOGRAPHY – DSA

Since Sven Ivar Seldinger introduced his technique in 1953 to obtain safe access to blood vessels a rapid evolution took place in the last decades in the field of interventional radiology and interventional neuroradiology. With the use of catheters an x-ray-based imaging guidance the cervical and cerebral blood vessels can be precisely envisioned. Digital subtraction angiography has been considered the gold standard for imaging evaluation of blood vessels and hemodynamics despite the advances in noninvasive diagnostic neuroimaging, mostly because of the spatial and temporal resolution the DSA can offer. Amongst its limitations is the invasive nature of the procedure, which is associated with even a 0,7% of stroke risk due to the necessity of intraarterial catheterization of precerebral cervical vessels. In a high-voulme neurointerventional practice the major complication rate associated with diagnostic angiography should approach zero. [20] The experience and procedural volume of the operator in charge is crucial to guarantee the safety of this procedure. As the number of advanced noninvasive imaging tools and examinations increase the catheter-based diagnostic procedures will probably decrease. On the other hand, the field of neurointervention is continuously expanding requiring well-trained and experienced neurointerventional operators. Advances in endovascular technologies offer thin wall hollow structures for accessing the neurovasculature with ease and safety. A routine DSA protocol either diagnostic or therapeutic involves an arterial access usually on an extremity. Nowadays in the daily routine a femoral or radial/brachial access is used. After selecting a cervical vessel, a DSA run is obtained at 3–4 frames per second to assess cerebral blood flow until the venous phase. By using a biplane angiosuite two projections can be acquired at once. Biplane system can enhance the

operator's confidence, but the reduction in radiation dose, complication rate or procedure time could not be significantly enhanced. [21] Still recent developments in angiography systems using flat panel detector improved image quality and reduced radiation exposure. [22] Angiosuites equipped with flat panel detectors are capable of 3 D image acquisitions and recent developments offer even flat panel CT on the table. Eventhough it is just "CT-like" cross sectional imaging and has not been approved as real CT, the advances in flat panel technology resulted in high resolution image quality and improved soft-tissue contrast resolution. A future perspective of cone-beam CT is 4D-DSA which enables time-resolved 3D imaging in angiography. [23]

ROLE OF INTERVENTIONAL NEURORADIOLOGY IN ACUTE ISCHEMIC STROKE

Historically, the earliest approved treatment for acute ischemic stroke in 1996 was thrombolysis by intravenous recombinant tissue plasminogen activator (rtPA), but almost two decades passed by when the results of five published trials revolutionized the treatment of large vessel occlusions (LVO) eligible to endovascular treatment. [24][25] Interventional neuroradiology performs minimally invasive procedures using catheters through the vasculature to treat vascular diseases. Advanced imaging capabilities are needed to perform these procedures. Recent developments in acute ischemic stroke therapy with endovascular thrombectomy have shown significant reduction in stroke morbidity and mortality. Eventhough great efforts have been done to avoid delays in stroke treatment, still many patients are excluded from the first-line thrombolytic therapy due to contraindications of drug administration especially time window overruns. Randomized controlled trials (RCT) verified that patients who had acute ischemic stroke with anterior-circulation large vessel occlusion have a benefit from endovascular treatment when intraarterial treatment is carried out within 6 hours after

stroke onset. [26] Later on two clinical trials have demonstrated evidence that a subgroup of patients can benefit from reperfusion therapy after 16 or even 24 hours from stroke onset. [27][28] Regardless of intravenous therapy, consideration for endovascular therapy not only could but should be performed. During mechanical thrombectomy the embolus is physically removed from the artery avoiding further damage within the penumbra. It is estimated that around 15% of patients with acute ischemic stroke are eligible for mechanical thrombectomy presenting within 6 h of symptom onset. [29] However, in high-volume centers distal to ICA and MCA occlusions the possibility of catching emboli from MCA (M2 and M3) or ACA (A1 and A2) branches or even from posterior circulation (BA and P1) is not beyond our reach. In view of this it is easily noticeable the advances in endovascular therapy have revolutionized the way we diagnose and treat acute stroke patients. From 15%, the number of stroke patients eligible for thrombectomy is increasing as the growing evidence and expanding guidelines permit more patients to be treated effectively without harm.

ENDOVASCULAR RECANALIZATION IN ACUTE ISCHEMIC STROKE

The main goal in acute ischemic stroke is the rapid and technically straightforward recanalization as soon as possible. For the recanalization of large vessel occlusion in acute ischemic stroke besides intravenous thrombolytic therapy is endovascular mechanical clot removal. The originally used local intra-arterial fibrinolysis did not revolutionize stroke therapy and it was not further developed and studied. [30] In the early 2000s the first dedicated tools were engineered and approved for endovascular intracranial thrombectomy. These first-generation devices reached a certain acceptance, but their efficacy was limited, and some safety concerns came up. [31] Penumbra came out with an aspiration catheter as well as an aspiration pump in 2006 and has been emphasizing

the role of aspiration ever since. In 2008 after an unsuccessful intracranial thrombectomy attempt with conventional devices a Solitaire stent was successfully used for mechanical thrombectomy the first time in human for this purpose. [32] This was an incidental success, but after a few years stent-retriever based randomized controlled trials proved the safety and efficacy of mechanical thrombectomy in acute ischemic stroke. [24] [25] Since then many manufacturers developed their own stent-retriever device, mainly using the same principle as the Solitaire stent. Some newer generation devices have more complex construction to grab and hold the embolus without any distal embolization. But the main stent-retriever concept has not changed since the first successful case. Along with stent-retriever development newer and newer large bore aspiration catheters also have been designed, approved, and thrown to the market. At first, case series showed success with the aspiration catheter alone, but at that time the standard of care was the stent-retriever thrombectomy. The evidence for recanalization had already been established so only the efficacy and safety had to be proven. A multicenter randomized control trial showed that a direct aspiration as first-pass technique (ADAPT) to remove clot from the anterior circulation in patients with acute ischemic stroke was not superior (or inferior) to firs-line stent-retriever thrombectomy in achieving successful recanalization. [33] Even 20% of acute ischemic strokes are caused by tandem occlusion of intracranial anterior large vessel and concomitant extracranial internal carotid artery. Although the literature on the endovascular treatment of TO in AIS is rapidly expanding, data on the safe and efficient maneuvers for the recanalization of the occluded ICA plaque is still sparse. Stenting of the occluded or severely stenosed ICA for safe and easy passage to the intracranial circulation is an option. But due to the mandatory initiation of at least one, but occasionally two antiplatelet therapies in an acute stroke patient makes it even more complicated for the staff to figure out the optimal postoperative medication. There is no significant increase, only a trend toward higher bleeding risk in the stented population. [34] Another

revascularization method is the balloon-assisted tracking technique (BAT), where a partially deflated balloon is exposed out of the catheter tip to facilitate its passage through stenosed or spastic arterial segments which was initially introduced by interventional cardiologists [35], and recent case studies proposed the applicability of the technique in the field of neurointervention as well [36] [37].

Diagnostic difficulties in AIS and hemiplegic migraine as a stroke mimic

Stroke mimics can be a significant percentage of acute stroke hospital admissions, but in these cases a non-vascular condition causes neurological deficit alike in acute stroke patients. [38] Despite state-of-the-art imaging modalities available in daily routine excluding conditions which only imitate stroke still takes time. But treating stroke patients time is the most important circumstance that we must consider, so to be aware and understand these conditions is mandatory to those diagnosing and treating stroke patients. Migraine can be overlooked or underdiagnosed in the daily routine. Migraine affects 10-15% of the population, making it the most common primary headache in children and adolescents. [39] Hemiplegic migraine (HM) is a rare form of headaches, and it often starts in childhood. [40] The frequency of the attacks is varying; its significance is due to the difficulty of the differential diagnosis of the first attack. In accordance with the current international classification of headaches, HM is diagnosed if the patient has at least two completely reversible aura with motor and sensory symptoms and speech disorder, at least one of the symptoms is unilateral and the motor symptoms do not last for more than 72 hours. Differential diagnosis of the first HM attack in childhood is very challenging, detailed laboratory along with imaging studies are required and symptoms have to be closely monitored.

VALUE OF CT ANGIOGRAPHY IN THE FOLLOW-UP OF NEUROVASCULAR STENTS

Supra-aortic stenting has been shown to increase the therapeutic value of balloon angioplasty for the treatment of these arterial lesions in preventing acute ischemic stroke. The main drawback of stent placement is the mandatory initiation of dual antiplatelet therapy besides the occurrence of in-stent restenosis (ISR). The major cause of in-stent restenosis is neointimal hyperplasia. The occurrence of in-stent restenosis can be as high as 10,6% in the extracranial internal carotid artery, 31% in the intracranial arteries and 15.9% in the orifice of the vertebral arteries. [41] [42] [43] The extracranial internal carotid artery is the vessel where color-coded duplex sonography can visualize the vessel lumen for adequate screening and follow up after interventions, nevertheless ultrasound may have limitations due to anatomical anomalies or technical difficulties. Besides the extracranial internal carotid artery is the less prone to restenosis. For intracranial and vertebral orifice stents conventional DSA is the current criterion standard follow up examination. In a high-volume neurointerventional department the risk of neurologic complications during conventional DSA is close to zero, still the complication rate can range as high as 0,3% due to its invasive nature. [44] Promising new noninvasive alternative tool could be the cone beam CT after intravenous contrast medium administration performed in an angiographic suite equipped with flat-detector. The downside of this method is the lack of bolus tracking and the accessibility, which can be a limitation for the method to unfold. [45] Using MR imaging exact depiction of the stent lumen and exact measurement of the in-stent restenosis is not possible. A non-invasive alternative method for assessment of the stented supra-aortic vessels would be highly desired.

AIMS

1. STROKE MIMICS

Through a case report one of our aims is to show how challenging can be to assess patients with stroke mimics especially with hemiplegic migraine starting in childhood. Our objectives were to describe a diagnostic work up and differential diagnostic algorithm which could be helpful in understanding and discovering stroke mimics.

2. BALLOON-ASSISTED TRACKING TECHNIQUE IN TANDEM LESIONS

We introduced a novel method the balloon-assisted tracking technique (BAT) in the treatment of tandem large vessel occlusive lesions in acute ischemic stroke cases causing neurological symptoms, which account for up to 20% of acute ischemic stroke patient and associated with poor prognosis if complete recanalization is not achieved. Our aim was to describe the technique in detail and demonstrate our experience using the BAT technique in the endovascular recanalization of tandem occlusive lesions showing its applicability, feasibility, safety and efficacy, because endovascular recanalization might be challenging due to difficulties in the safe passage of the occluded plaque at the origin of the internal carotid artery (ICA).

3. MODALITY OF CHOICE FOR THE FOLLOW UP AFTER SUPRA-AORTIC STENTING

In a retrospective study we aimed to determine whether the 64-slice dual energy CT angiography after intravenous contrast medium administration is suitable for the evaluation of luminal patency and in-stent restenosis

after supra-aortic percutan transluminal angioplasty and stenting involving intracranial and extracranial atherosclerotic lesions, which stenoses are an established risk factor for stroke. Nevertheless, our aim was to estimate the feasibility of this non-invasive tool instead of catheter-based examinations.

METHODS

1. MIDDLE CEREBRAL ARTERY HYPOPERFUSION IN A PATIENT WITH MIGRAINE

In a case report the diagnostic difficulties were shown and demonstrated stroke mimics which have to be taken into account when treating these patients. In our case a 13-year-old girl without any comorbidities was admitted to the emergency department due to left temporal headache associated with vomiting, speech disorder and confusion. The headache was throbbing in nature, stronger than moderate (VAS 5) and lasted for several hours longer than the aura symptoms. The pain was accompanied by sensitivity to light and sound and was aggravated by physical activity. The patient answered the questions regarding the headaches only days after the disorder when her aphasia resolved. After the head CT was performed on admission, progression was seen, facial asymmetry and slight right sided hemiparesis were detected. The patient's symptoms, confusion and speech disorder showed a fluctuating course. After admission, neurological symptoms progressed further, sensorimotor aphasia, disorientation, and somnolence developed. 5-6 hours after her admission, her level of consciousness varied from somnolence to sopor. Routine laboratory and microscopic examination of the cerebrospinal fluid was carried out as well as electrophoresis (ELFO) of the cerebrospinal fluid (CF). Initial head CT followed by head MRI with time-of-flight (TOF) MRA was performed.

2. IMPROVING THE SAFETY AND EFFICIENCY OF ENDOVASCULAR RECANALIZATION OF TANDEM OCCLUSIVE LESIONS IN ACUTE ISCHEMIC STROKE

Tandem occlusion (TO) of the internal carotid artery is characterized by proximal occlusion of ICA, either due to acute thrombosis of an unstable atherosclerotic plaque or dissection, resulting in the embolic blockage of the ICA terminus (ICA-T) and/or the main trunk (M1 segment) of the middle cerebral artery. The condition is responsible for up to 20% of acute ischemic stroke cases [46], responds poorly to intravenous thrombolysis [5] and is associated with poor prognosis without timely and successful recanalization. [47] Despite the high incidence and large clinical impact, the initial large, randomized trials showing the efficiency of endovascular treatment (EVT) of large vessel occlusion in acute ischemic stroke either did not report key technical and clinical results from this subgroup or entirely excluded these patients from the analysis. [25] This is likely explained at least in part by the fact that tandem occlusions challenge the surgeon with a thrombotic-atherosclerotic (occluded plaque at the origin of the ICA) and a thromboembolic (distal ICA and/or MCA occlusion) pathology at the same time, each requiring different endovascular techniques and paradigms. Although the literature on the endovascular treatment of TO in AIS is rapidly expanding, data on the safe and efficient maneuvers for the recanalization of the occluded ICA plaque are still sparse. The balloon-assisted tracking technique, where a partially deflated balloon is exposed out of the catheter tip to facilitate its passage through stenosed or spastic arterial segments was introduced by interventional cardiologists [48], and recent case studies proposed the applicability of the technique in the field of neurointerventions as well. [36] In our study we report our detailed experience with the BAT technique in the endovascular recanalization of 107 AIS patients with tandem occlusion.

THE BALLOON-ASSISTED TRACKING TECHNIQUE

We only found only a few case series describing novel techniques about how tandem occlusions are treated in different centers by different operators. [49] [50] [51] [52] All of them had a small number of patients at a single center. We also describe our experience and the technical aspects of our method in detail which was carried out on more than 100 patients and has been a well-established method to treat tandem occlusions. In our practice interventions were carried out on a monoplane angiosuite (Axiom Artis, Siemens, Erlangen, Germany) under anesthesiology standby including conscious sedation or general anesthesia if necessary. The right or left common femoral artery was accessed by an 8 F introducer sheath and 5000 international units (IU) of unfractionated heparin was administered intravenously. No antiplatelet therapy was administered beforehand in these cases. An 8F guiding catheter (Guider Softip, Boston Scientific) was advanced into the common carotid artery (CCA) on the affected side. The ICA occlusion was then confirmed with a prolonged run after contrast injection through the guide catheter. The runs were repeated in various projections until the tiny stump of the occluded ICA could be clearly visualized, when possible. The recanalization of the occluded ICA was performed through the guide-catheter using a slightly shaped hydrophilic 0.014” micro guidewire supported by a low profile 4 mm PTCA balloon catheter (Ryujin, Terumo). For crossing the ICA occlusion, a neuro microguidewire [(Traxcess (Microvention), Portal (Phenox) or Chikai Black (Asahi)] was used in 81 out of the 107 cases (76%) or a PTCA guidewire [CHOICE Extra Support or PT GRAPHIX (Boston Scientific)] was used in 26 out of the 107 (24%) cases, depending on the lesion and on the operator’s preference. In 39 cases (36%) additional wires were used for crossing the ICA occlusion, maintaining stability or replacing the crooked wire. The wire was carefully

advanced through the occluded plaque with special attention to keep the wire in a true intraluminal position by navigating it through the tiny stump of the ICA identified on initial angiographic series. This was followed by angioplasty of the plaque using the undersized, 4 mm balloon catheter, following intravenous administration of atropine if necessary. The balloon was partially deflated thereafter and the guide catheter was advanced to partially cover it, with the half-deflated balloon protruding out from the catheter tip, forming a streamlined outline of the balloon-catheter tip complex, so that the rim of the catheter tip cannot get in contact with the irregular plaque surface, then the guide catheter was gently advanced with the half-inflated balloon acting as a „stylet" through the ruptured plaque and occluded cervical segment of ICA to prevent the razor effect of the rim of the guide catheter. [37] The balloon was then slowly deflated and removed together with the microguidewire. The 8F guiding catheter was detached from the hemostatic valve and carefully moved and torqued forth and back under gentle manual aspiration using a 50 ml perfusor syringe, removing thereby the thrombotic material in the cervical ICA segment. Extra care was taken during this step to prevent the vessel wall to be sucked in by the tip of the catheter to prevent dissection. The hemostatic valve was then reattached and stent-retriever or direct aspiration thrombectomy of the carotid-T or MCA was performed in the usual technique. During distal thrombectomy the guide catheter was kept in the newly opened proximal ICA causing flow arrest and acting as dilator on the ICA plaque as described by Dotter et al. earlier. [53] Following the successful recanalization of the dependent intracranial arteries, the 8F guide catheter was retrieved into the CCA under continuous manual aspiration with the micro guidewire left in the distal segment of the ICA to maintain access and an angiogram was done to evaluate the reopened ICA plaque. In case of high-grade recoiling, an additional angioplasty was performed using a 6 mm balloon. Stent implantation was performed only in case of flow limiting residual stenosis, immediate reocclusion after repeated angioplasty, visible floating thrombus on the plaque or flow

limiting dissection. A schematic drawing of the BAT maneuver is shown in Figure 1 and an illustrative case using the technique is presented in Figure 2.

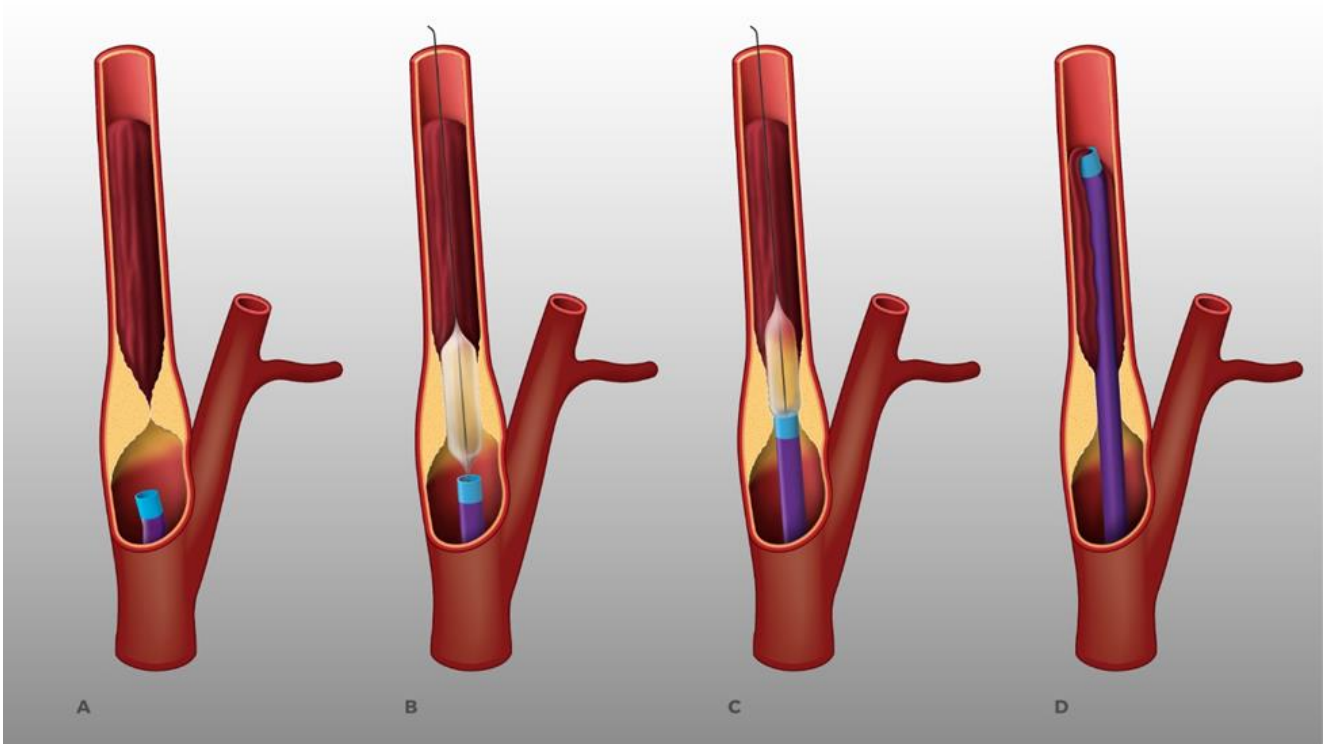

Figure 1. Schematic drawing illustrating key steps of the application of the balloon-assisted tracking technique in the recanalization of an occlusive plaque at the origin of the ICA. (A) A guide catheter is positioned in front of the ICA stump. (B) A 0.014” micro-guidewire is carefully passed through the ICA stump and angioplasty is performed with an undersized, low-profile balloon. (C) The guide catheter is then tracked by the partially deflated balloon over the plaque into the occluded lumen of the ICA. The protruding balloon acts as a stylet preventing contact between the irregular plaque surface and the catheter rim. (D) Finally, the balloon and microwire are removed and the thrombus is extracted by aspiration.

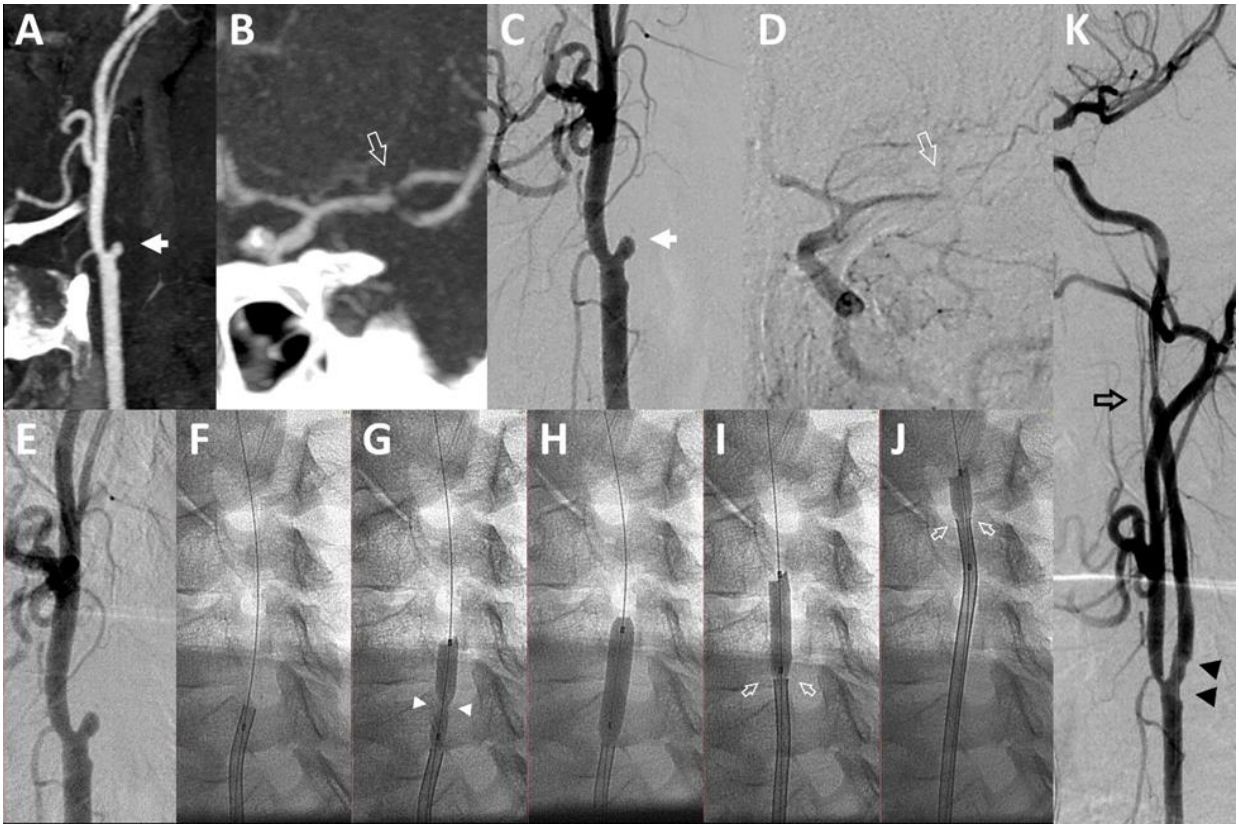

Figure 2. Demonstrative case of the balloon-assisted tracking technique showing the recanalization of a left sided tandem ICA-MCA occlusion in a middle-aged patient with acute onset severe left hemispheric symptoms. (A) Preoperative CTA reveals proximal occlusion of the left ICA with a small, rounded stump (white arrow) and a filling defect in the left M1 bifurcation (B, open white arrow) with apparently good filling of the distal MCA branches. (C) Subtraction angiography confirms the ICA occlusion, but shows a complete flow arrest at the M1 bifurcation (D, open white arrow). The field-of-view position on panels F-G demonstrating the BAT technique corresponds to that of panel E. (F) The procedure begins with the careful penetration of the ICA stump with a 0.014” neuro microguidewire. The large lumen 8F soft tip guide catheter is then moved to the very end of the stump for sufficient backup. (G) A low-profile coronary PTCA balloon with a diameter of 4 mm is positioned across the plaque followed by angioplasty by careful manual inflation of the balloon. The occlusion point (white arrowheads) is easily recognized. After

complete inflation (H) the balloon is deflated passively (i.e., the syringe is detached from the conus) and the guide catheter is advanced over the balloon and then they are moved carefully together into the ICA (I and J). The partially deflated balloon forms a streamlined stylet (white open arrows on I and J), preventing the rim of the catheter to get in contact with the irregular surface of the plaque, precluding thereby shaving off plaque debris or plaque dissection. The balloon is deflated completely thereafter and is removed together with the microwire. The ICA lumen is then recanalized by careful manual aspiration through the guide catheter and the recanalization of the MCA is performed by ADAPT technique. (K) Selective injection of the left CCA at the end of the procedure shows the complete recanalization of the ICA and MCA. The black open arrow indicates the highest level to which the balloon-guide catheter complex was advanced. The recanalized plaque shows a smooth surface (black arrowheads), without signs of dissection, floating thrombus, or high-grade residual stenosis, therefore stent implantation was not pursued at the acute stage. The total time from the selective diagnostic run of the CCA to the complete recanalization (from panel C to panel K) was eight minutes.

STATISTICAL ANALYSIS OF THE PATIENTS TREATED WITH ENDOVASCULAR RECANALIZATION OF TANDEM OCCLUSIVE LESIONS IN ACUTE ISCHEMIC STROKE

We evaluated 107 AIS patients with tandem occlusion lesions. The data was retrospectively collected and analyzed. It was driven to detect the safety and efficacy of the method we used to treat this subgroup of stroke patients. Recorded baseline data included age, sex, history of hypertension, atrial fibrillation, diabetes and dyslipidemia. Admission clinical parameters such as CT ASPECTS score, NIHSS score, ictus to needle time, occlusion site, use of recombinant tissue plasminogen activator (rtPA) was also retrieved. The CT imaging data was reviewed by the radiologist on call and the interventionalist performing the treatment in all cases and ASPECTS values were determined by consensus. Continuous variables were reported as median with range and categorical variables as number and percentage. Categorical variables were compared using the x^2-test or Fisher's exact test for small cell values, p values less than 0,05 were interpreted as statistically significant. Analyses were performed using SPSS, Version 26.0 (IBM, Armonk, NY, USA).

3. FEASIBILITY AND DIAGNOSTIC VALUE OF CT ANGIOGRAPHY AFTER SUPRA-AORTIC STENTING INCLUDING INTRACRANIAL INTERVENTIONS

In this study we evaluated 54 consecutive patients with 72 supra-aortic stents (47 cervical carotid, one brachiocephalic trunk, 5 subclavian, 11 ostial vertebral and 8 intracranial). Recorded baseline data included sex, history of hypertension, diabetes, dyslipidemia and the treated vessel. We compared the diagnostic accuracy of a 64-slice dual energy CT angiography with other modalities and whether it is suitable for the evaluation of luminal patency and in-stent restenosis after supra-aortic percutan transluminal angioplasty and stenting involving intracranial and extracranial atherosclerotic lesions. 72 stents had a supra-aortic dual

energy CT angiography. All CT examinations were done without adverse events following contrast media application and without other complications. Multi-slice CT angiographs were performed in the caudocranial direction with a Siemens Flash Dual Source 64-slice scanner (Siemens, Erlangen, Germany) ranging from the aortic valve to the skullcap. Data acquisition consisted of 64 × 0,6 mm collimation, 100/140 kV (dual energy), 270/270 mAs, a helical pitch of 0,7 and a 0,28 s gantry rotation time. Axial images were reconstructed with a slice width of 1 mm and a reconstruction increment of 1 mm using a sharp kernel. Using care bolus-tracking, 70-80 ml of contrast medium (Iomeron 350, Bracco, Milan) followed by a 30-40 ml saline bolus were administered via power injector with an injection rate of 4-5 ml/s. Centered on the stents, parallel and perpendicular to the stents' centerline reconstructions were performed under a smaller field of view with advanced imaging software (SyngoVia Workstation, Siemens, Erlangen, Germany). Mean multiplanar reconstructions (MPR), maximum intensity projections (MIP) were reconstructed with a 1 mm slice thickness and an increment of 1 mm. Curved planar reformations (CPR) were performed with a 1 mm slice thickness. Images were transferred to a picture archiving and communication system (PACS). The CT angiography after angioplasty mean follow-up time was also noted. To determine the percent of residual or restenosis the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method was used. All stents were classified as patent or re-stenotic. A stenosis of at least 70% according to the NASCET criteria was considered restenotic. All measurements were obtained perpendicular to the center line of the stented segment. Stent patency was evaluated by two experienced neuroradiologists using curved multiplanar reformations and different planes of maximal intensity projection images.

RESULTS

1. A SPECIAL CASE OF MIGRAINE MIMICKING ACUTE ISCHEMIC STROKE IN AN ADOLESCENT PATIENT

In our case routine laboratory and microscopic examination of the cerebrospinal fluid, head CT and head MRI of the brain parenchyma did not show any abnormalities. TOF MRA showed diminished flow signal in the end branches of the left MCA. Normal protein pattern was found with electrophoresis (ELFO) of the cerebrospinal fluid. No activity suggestive of epileptic dysfunction was observed with EEG. On the other hand, 5-HIAA measurement was performed from the cerebrospinal fluid during the attack and it showed a level which was 10 times above the normal value. Limited published data is available regarding the 5-HIAA level of the cerebrospinal fluid measured during migraine attacks. Almost all available studies found a decrease in 5-HIAA between attacks. [54] However, during migraine attacks, 5-HIAA levels were elevated in the serum, urine, and cerebrospinal fluid. [55] [56] The role of serotonin metabolic dysregulation in migraine with aura and spreading depression is unquestionable. [57] [58] [59] There is no evidence about serotonin playing a key role in stroke or inflammation as in migraine. Nevertheless, in our publication, the early diagnosis of HM was not based on the elevated level of 5-HIAA but on the clinical status. The 5-HIAA measurement was performed because we had no knowledge of any previous similar attacks at the time of sampling, and we were looking for additional markers due to the differential diagnostic difficulties. Detailed and targeted past medical history collected after the symptoms showed that the patient had one previous episode of headache accompanied by neurological symptoms (numbness of the hand, weakness, speech disorder, confusion). As a result, the clinical status met the diagnostic criteria of sporadic HM in accordance with ICHD-32. There are contradictory data in the literature regarding the diameter and blood flow

of large cerebral vessels during aura and spreading depression. Both decreased [60] and increased [61] perfusions were reported in the cerebral circulation during and after an attack. However, there is no comprehensive study in the literature due to the rarity of the disease. The contradictory results may also be explained by the fact that both possibilities are likely to occur during the course of the attack. [62] It is hypothesized that one of the triggers of the attack may be serotonin release, resulting in a consequent reduction in intracranial flow. This is followed by reflex compensation, which causes an increase in flow. The results in the manuscripts are determined by the phase of the migraine in which the tests were performed. In our case, the MRI was performed at an early stage, while the symptoms were still present. This may explain the hypoperfusion seen within the MCA territory shown on Figure 3. The presented case is considered to be a sporadic HM until the genetic results are received, as the detailed family history did not show a familial accumulation, and the patient's mother had only intermittent tension-type headaches. In the presented case, stroke was suggested to be present due to the sudden onset and progression of unilateral symptoms, aphasia and fluctuating confusion after encephalitis, metabolic disorder and epilepsy was ruled out. The most common conditions to consider in children in case of confusion, hemiparesis, headache, and numbness/paresthesia are summarized in Table 2. Intracranial hemorrhage was ruled out by cranial CT at the beginning of the evaluation, and ischemic stroke could be clearly ruled out by MRI and MRA. T2-weighted and FLAIR MRI sequences did not confirm structural parenchymal lesion, and diffusion-weighted measurements (DWI) did not show a decrease in diffusion suggestive of new ischemia, but TOF MRA confirmed significant spasm of the large arteries supplying the affected hemisphere. Bosemani et al. in a previously reported a case similar to the one presented here, where MRI-based contrast perfusion measurements (PWI) and susceptibility-weighted imaging (SWI) in the acute phase of migraine found tissue hypoperfusion in the affected vascular area, with

slow circulation and elevated deoxyhemoglobin levels in the veins, but early ischemic abnormalities were not present in the DWI sequence. [63] Unfortunately, in our case, the acute MRI did not include perfusion and SWI sequences, and we could not confirm early ischemic abnormalities in the diffusion-weighted images. Based on the above, the development of severe vasospasm in the affected ICA and MCA branches in the initial stage of the migraine aura, resulting in a reduction of perfusion of the affected hemisphere below a critical level and consequently the appearance of neurological focal signs is considered the cause in the background. [64] [65] As the cerebral hypoperfusion did not decrease below a critical limit for ischemic parenchymal damage (12–20 ml/100 g brain tissue/min), therefore neither the acute, nor the check-up MRI performed days later showed any structural lesion in the parenchyma.

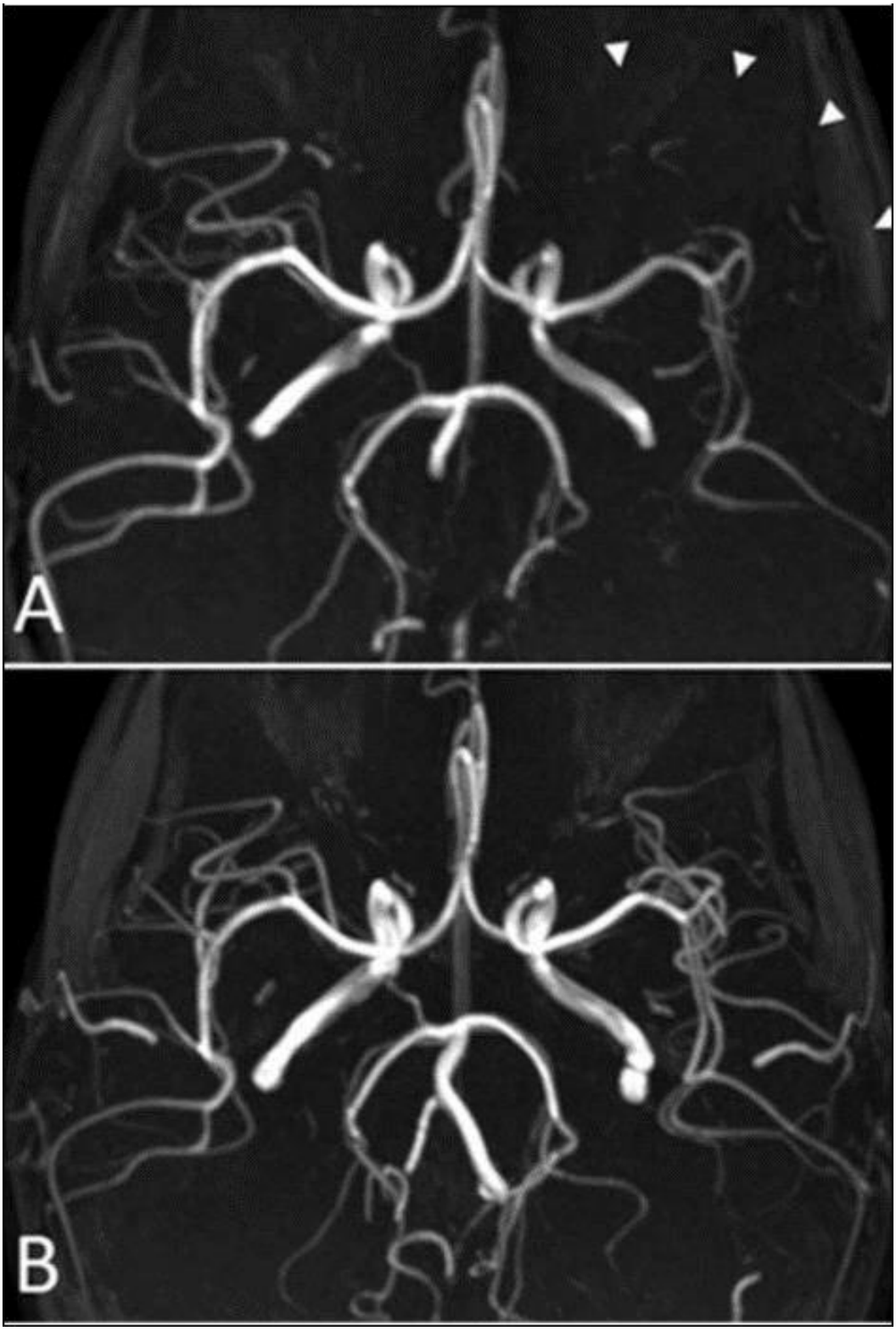

Figure 3. (A) Maximal intensity projection (MIP) reconstruction images of TOF MRA sequences prepared during the attack, spasm of the left ICA

and main branches of the MCA is seen with diminished flow signal in the end branches of the left MCA (arrow heads), suggesting severe hypoperfusion. (B) Check-up TOF MRA prepared four days later showing normal lumen and good flow in all visible arteries.

Table 1. Most common conditions in the differential diagnosis of migraine causing confusion, hemiparesis, headache and numbness/paresthesia in children. Based on the recommendation of the British Medical Journal (BMJ) Best Medical Practice, in order of frequency (source: http://bestpractice.bmj.com/best-practice)

Confusion	Hemiparesis	Headache	Numbness/paresthesia
stroke/TIA			
status post head injury	TIA	concussion	spinal compression
delirium	hemorrhagic stroke	subdural hemorrhage	stroke/TIA
	traumatic brain injury	ventriculoperitoneal shunt dysfunction	brachial or lumbar plexopathy
status post epileptic attack	hypoglycemia	intracranial hypotension	acute demyelinating encephalomyelitis (ADEM)
cardiac (congestive heart failure, ventricular arrhythmias	Todd-paresis (postictal paresis)	epidural bleeding	Guillain–Barré syndrome (GBS)
hyperglycemia	subdural hemorrhage	meningitis	heavy metal poisoning
hypoglycemia	subarachnoid hemorrhage	encephalitis	other (food) poisoning
hypernatremia	hematomyelia	cerebral tumor	rheumatoid arthritis
hyponatremia	dorsal / lumbar spinal injury	intermittent hydrocephalus	SLE
dehydration (volume depletion)	cervical spinal injury	pseudotumor cerebri	granulomatosis (Wegener syndrome)
		subarachnoid hemorrhage	microscopic polyangiitis
hypothermia	encephalitis	ischemic stroke	partial epileptic attack
hypoxia	cerebral abscess	cerebral hemorrhage	intravascular lymphoma
hypercapnia	poliovirus	vascular dissection	neuro-Behcet 's disease
hepatoencephalopathy	Guillain–Barré syndrome (GBS)		
uremia	transverse myelitis (TM)	venous sinus thrombosis	
acute systemic infection	acute hypokalemia	pituitary hemorrhage	
acute psychosis	drug-induced neuropathy		
	toxin-induced dysfunction		hypertensive encephalopathy
alcohol consumption	compartment syndrome		
drug effect	spinal compression		
drug withdrawal			
pulmonary embolism			

2. APPLICATION OF THE BALLOON-TRACKING TECHNIQUE IN THE RECANALIZATION OF TANDEM ICA-MCA OCCLUSIONS IN PATIENTS WITH ACUTE ISCHEMIC STROKE

Between June 2013 and December 2020, 592 patients with acute ischemic stroke were treated by endovascular recanalization at our Institution (Neurovascular and Interventional Unit, Somogy County Moritz Kaposi Teaching Hospital) in Kaposvár. Tandem occlusion of the ICA and MCA was the primary pathomechanism in 113 (19%) cases. Of these patients 6 (5%) were excluded from the analysis because of having proximal ICA dissection as pathomechanism. The remaining 107 (77, 72% male, median age 66 years, range 45–87 years) cases with atherosclerotic origin were included in the study. The median (IQR, range) for ASPECTS and NIHSS on admission were 8 (2, 3-10) and 14 (6, 3-22), respectively. Median onset-to-groin time was 346 minutes (158–1405 minutes), median total procedural time was 51 minutes (10-178 minutes) and the median time from groin puncture to the passage of the 8F guide catheter into the cervical segment of the ICA through the thrombosed plaque was 16 minutes (5-108 minutes). Successful recanalization of the cervical ICA could be achieved in 100 (93%) cases. Details of the unsuccessful 7 (7%) cases were: in two patients (2%) the occluded ICA plaque could not be passed even after multiple attempts; in one patient (1%) the mid segment of the cervical ICA and in one patient (1%) the terminal segment of the ICA was perforated with guidewire and active extravasation could not be sealed with a balloon, so the ICA had to be reoccluded with coils; in three cases (3%) the microguidewire penetrated into the subintimal space during the ICA recanalization attempt and no reentry could be achieved at any level even after multiple attempts. Successful intracranial recanalization, defined asTICI2b-3 was achieved in 88 (82%) patients, thereof TICI2b in 50 (46.7%) and TICI3 in 38 (35.5%) cases. Bail-out stenting of the intracranial ICA and/or the MCA using a

bare-metal coronary stent was required in 3 (3%) cases. Attempts of intracranial revascularization following the successful recanalization of the cervical ICA failed in 12 (11%) patients, resulting in TICI0 in 1 (1%) and TICI2a in 11 (10%) cases. Intraprocedural stent implantation in the proximal ICA followed by balloon angioplasty was performed in 40 (37%) patients due to high-grade (>70%) residual stenotic lesion resistant to angioplasty, flow limiting dissection and/or visible floating thrombus on the recanalized ICA plaque. Wallstent (Boston Scientific) was used in 80% (32/40) and Roadsaver (Terumo) stent in the remaining 20% (8/40) of these emergent stenting cases. Regular ultrasound (US) follow-up of patients with emergent stenting was available in 20 (50%) cases and revealed complete stent patency, without high-grade in-stent restenosis in 19 (98%) of the patients. Delayed occlusion of the stent implanted in the acute setting occluded in 1 (2%) of the case, and the single ICA stent reocclusion case was asymptomatic. Out of the 60 cases without emergent stent implantation, 7 (12%) patients died during the acute postoperative period and 11 (18%) patients were lost to follow-up after discharge. Out of the 42 (70%) patients with regular US follow-up of the recanalized ICA, 6 (10%) reoccluded without any newly developed neurological deficit and 21 (35%) received delayed stent placement due to asymptomatic, but progressive high-grade restenosis (>70%) in a second session, giving a combined rate of reocclusion and revascularization of 45% (27/60). The combined rate of emergent and delayed stenting was 61% (61/100). Intraprocedural complications occurred in 9 (8%) patients: subarachnoid hemorrhage Fisher grade 1 in 7 (6%) cases, intracranial vessel perforation resulting in Fisher grade 4 subarachnoid hemorrhage in 1 (1%) case and termination of the procedure due to extracranial vessel perforation in 1 (1%) case. None of the complications were related to the BAT technique. In two cases (2%), embolization into new vascular territories occurred. In both procedures, the proximal ICA occlusion was passed as described, then selective ICA injection revealed a proximal MCA occlusion, which was recanalized with

a stent-retriever using the SOLUMBRA technique, resulting in TICI2a and TICI2b recanalization of the affected vascular territories; however, peripheral emboli in the ipsilateral anterior cerebral artery were seen in both cases. Clinical follow-up 3 months later revealed mRS 1 and mRS 0 in the patients with TICI2a and TICI2b recanalization, respectively. The rate of postprocedural adverse events was 6 (5%). Intracerebral hemorrhage (ICH) developed in 4 (4%) cases (type 1 and 2 in 2 and 2 cases, respectively). A non-significant trend could be observed towards developing an ICH following emergent stent implantation (p= 0,407, OR= 3,15, 95% CI= 0,35–27,94). Space-occupying infarction of the affected brain area developed in 2 (2%) patients, requiring craniectomy in 1(1%) case. The development of ICH and space-occupying infarction was not significantly associated with differences in adequate reperfusion: 67% (4/6) versus 33% (2/6) in patients with successful versus unsuccessful recanalization, but the odds of developing a postprocedural adverse event were higher in patients with successful revascularization (p= 0,148, OR= 3,12, 95%CI= 0,68-14,29). Good functional outcome (mRS 0–2) at 3 months was observed in 54 (50%) patients, 27 (25%) patients were still severely disabled (mRS 3-5) at 3 months and 26 (24%) patients died (mRS 6) before the follow up at 3 months. Successful intracranial recanalization was significantly associated with good clinical outcome (mRS 0–2): 59% (52/88) in the TICI2b-3 group versus 11% (2/19) in the TICI0-2a group, (p< 0.001, OR= 12,28, 95% CI= 2.67-56.45). Emergent stenting versus angioplasty did not significantly influence the rate of favorable clinical results, although there was a trend towards good clinical outcome in stented group (mRS 0-2 in the emergent stenting group: 58%, 23/40; mRS 0-2 in angioplasty group 52%, 31/60; p=0,261, OR= 1,57, 95% CI= 0,71–3,46). Mortality was not affected by emergent stenting (p=0.737, OR= 1.17,95% CI= 0.46–2.95). A summary of demographic, baseline medical, neurological, imaging, procedural and follow-up data are given in Table 1.

Table 2. Summary of demographic, baseline medical, neurological, imaging, procedural and follow-up data.

Number of patients (n)	107
Baseline characteristics	
Age [years] (median, range)	66 (45-87)
Male n (%)	77 (72%)
Left-hemispheric stroke n (%)	62 (58%)
Arterial hypertension n (%)	79 (74%)
Atrial fibrillation n (%)	5 (5%)
Diabetes mellitus n (%)	31 (29%)
Dyslipidemia/Obesity n (%)	7 (7%)
NIHSS baseline [median, IQR (range)]	14, 6 (3-22)
IVT n (%)	47 (44%)
ASPECTS baseline [median, IQR (range)]	8, 2 (3-10)
Occlusion site	
CCA-ICA-MCA n (%)	2 (2%)
ICA-MCA n (%)	104 (97%)
ICA-ACA n (%)	1 (1%)
Time intervals, procedural data	
Onset to groin [min] (median, range)	346 (158-1405)
Groin to ICA passage [min] (median, range)	16 (5-108)
Groin to complete revascularization [min] (median, range)	51 (10-178)
Successful reperfusion ICA/intracranial (TICI 2b-3) n (%)	100 (93%) / 88 (82%)
TICI 2B recanalization n (%)	50 (47%)
TICI 3 recanalization n (%)	38 (36%)
Intraprocedural ICA stent implantation n (%)	40 (37%)
Intraprocedural complications n (%)	9 (8%)
Postprocedural adverse events n (%)	6 (5%)
Clinical outcome	
mRS <=2 at 90 days n (%)	54 (50%)
Mortality at 90 days n (%)	26 (24%)
Delayed proximal ICA revascularization with stent implantation n (%)	21 (31%)
Delayed reocclusion / stent thrombosis n (%)	6 (10%) / 1(2%)

3. DIAGNOSTIC VALUE OF CT ANGIOGRAPHY IN THE FOLLOW-UP OF ICA STENTS AND DETECTION OF IN-STENT RESTENOTIC LESIONS

54 consecutive patients with 72 stents (47 cervical carotid, one brachiocephalic trunk, 5 subclavian, 11 ostial vertebral and 8 intracranial) were evaluated. 21 (29%) stents were suspected restenotic. In 11 instances, these patients with suspected restenosis underwent catheter based digital subtraction angiography. 5 patients had significant restenosis, 6 did not. In another group of patients twenty conventional digital subtraction angiographies were performed after the CT angiography. The sensitivity of CT angiography was 67% and the specificity was 91%. The negative predictive value was much stronger than the positive predictive value (95%, 50% respectively). Thirty-four patients underwent extracranial carotid artery stenting in our study group. In this group results obtained from CT angiography were compared with duplex ultrasonography which has gained wide acceptance to estimate restenosis rate. More than 70% of these cases with suspected restenosis found on ultrasonography was confirmed with CT angiography and in only four cases additional invasive procedures had to be done to confirm the diagnosis. Color Doppler ultrasound (CDUS) had a sensitivity of 92% and a specificity of 62% in our cohort, and this method also has a strong negative predictive value.

DISCUSSION

1. SPECIAL CASE OF MIGRAINE AS A STROKE MIMIC

Differential diagnosis of stroke and migraine with aura of hemiplegic migraine, especially in cases of first attack in childhood is very challenging, detailed laboratory and imaging studies are required, symptoms must be closely monitored. To the best of our knowledge, the presented case is the first case of HM in Hungary in which the spasm of the branches of the large arteries supplying the cerebral area responsible for the symptoms was confirmed by imaging during an attack. The presented case confirms the role of acute MRI in the differential diagnosis of acute diseases with severe neurological symptoms in childhood and may help us understand the pathomechanism of HM as well.

2. APPLICATION OF THE BALLOON-TRACKING TECHNIQUE IN THE ENDOVASCULAR TREATMENT OF ICA OCCLUSIONS

Although there is a rapid expansion in the literature on the treatment of tandem occlusions in acute ischemic stroke recently, key aspects including distal-to-proximal versus proximal-to-distal recanalization approach, placement versus non-placement of a stent in the acute setting, perioperative and postoperative antithrombotic medication and the role of embolic protection devices are still debated. The pathophysiology of the disease is a combination of several distinct vascular and hemostatic pathologies: atherothrombosis, artery-to-artery thromboembolism and less frequently dissection. [66] In severe atherosclerotic carotid disease, a progressive high-grade stenotic lesion at the origin of the ICA will gradually slow down the flow in the cervical segment; however, apart from a truly isolated ICA combined with a high-grade stenotic lesion at the ECA

origin, flow in the intracranial ICA segment is maintained through the circle of Willis (COW) and the ECA-to-ICA collaterals, most importantly the ethmoidal-ophthalmic and meningo-ophthalmic collateral pathways. In the moment of occlusion of the ICA plaque, as a consequence of the rupture of the unstable thinned fibrotic cap and subsequent thrombosis of the already filiform lumen, the cervical segment of the ICA begins to fill up with large amount of fresh thrombotic material, followed by one of three possible sequences: (i) the ICA fills up with thrombus up to the inflow of the most proximal ECA or COW collateral, through which the arterial supply of the dependent intracranial arteries is maintained uninterrupted, resulting in an asymptomatic ICA occlusion, with a prevalence of 16% according to a meta-analysis of data from 4406 patients [67]; (ii) until the cervical ICA segment is not completely thrombosed, the growing occlusive thrombus at the origin of the ICA can be flushed distally, leading to an intracranial large-vessel occlusion. In this case, an M1 or ICA-T lesion is seen on angiography, together with a preocclusive filiform stenosis at the origin of the ICA. This scenario might result in the so-called pseudo-occlusion phenomenon on CTA [68]; (iii) thrombotic occlusion of the atherosclerotic lesion at the ICA origin, with the angiographic image of a tiny stump at the ICA origin and absence of flow in the cervical segment and the dependent intracranial branches. This third pathology can be de facto named tandem occlusion and only patients having this type of lesion were included in our study. The key steps of the recanalization are the safe passage of the ICA plaque with the microwire avoiding perforation and dissection, and the access of the cervical ICA segment with a large lumen catheter for aspiration and further intracranial recanalization. In our opinion, emergent implantation of a stent in the ICA origin to facilitate access to the cervical and intracranial segments before removing the bulk of the thrombotic material from the cervical ICA might be counterproductive and in cases of heavily calcified plaques and/or extensive supra-aortic elongation, the struts of a partially wall-adapted stent can indeed hamper the access to the ICA and can result in serious

difficulties at the withdrawal of a stent-retriever during the intracranial recanalization. There is no consensus in the literature regarding the extracranial versus intracranial first approach. A recent meta-analysis of data from the German Stroke Registry (GSR) with endovascular treatment of 607 AIS patients with tandem lesions found significantly shorter procedural times (53,5 versus 72,0 min) and a higher nonsignificant probability of successful reperfusion defined as mTICI2b/3 (92,1% versus 86,1%) and good clinical outcome (45,8% versus 33,0%) using the intracranial first approach. [69] In the present work, the BAT technique allowed the exquisite use of the extracranial first approach in all the cases, with a median total procedural time of 51 min combined with a good clinical outcome rate of 50%. Interestingly, the better clinical outcome in our cohort was achieved with poorer reperfusion success rate (86,1% in GSR versus 82% in our cohort). A possible explanation would be the higher rates of periprocedural complications in the GSR extracranial-first cohort (24% versus 8%), although it should be noted that only severe complications are reported in our cohort, whereas minor complications, such as vasospasm and high proportion of not detailed (other) complications are included in the GSR data, limiting the possibilities of comparison. In the present series, the large lumen guiding catheter could safely be inserted into the occluded cervical ICA segment over the thrombosed plaque using the BAT technique in all cases, without the need for a stent implantation. The primary angioplasty of the ICA plaque is done with a 4 mm balloon, which is only slightly larger than the catheter, resulting in recoiling of the plaque and the proximal ICA around the perimeter of the catheter, providing flow arrest and thereby an inherent proximal protection against embolization during intracranial thrombectomy/aspiration, eliminating the need of an embolic protection device. For the same reason, balloon guide catheters were not used, as in our experience the additional benefit of embolic protection is offset by poorer navigability due to the stiffness of these catheters in elongated vessels. Tortuosity of the cervical ICA is commonly encountered,

especially in older patients, usually involving the proximal segment with angles ranging from 90° up to 140–150°. The use of an atraumatic technique during the recanalization of these vessels of paramount importance. In these cases, we tracked the half-deflated balloon on a longer distance with the guiding catheter, using it practically as a streamlined stylet together with the micro guidewire, slightly straightening the tortuous, kinked ICA segment. Additionally, careful torquation of the guiding catheter with an angulated tip allowed the operator to adapt the outline the microwire-balloon guiding catheter structure to follow as much as possible the course of the ICA. Accordingly, none of the unsuccessful ICA recanalization attempts were attributed to the elongation of the ICA. Using the BAT technique, tiny emboli in new territories were detected only in 2 patients, both of them recovering to mRS 0–1 at the 3 months clinical follow-up. In selecting the appropriate catheter for the recanalization of the occluded ICA, the operator must balance between stability that is especially important in cases of extensive supra-aortic elongation, found mostly in older patients and requires a certain degree of rigidity of the proximal segment of the catheter for good maneuverability through the thrombosed and often stiff and calcified ICA plaque and an atraumatic distal tip, as the wall of the collapsed cervical ICA becomes more prone to injury in response to mechanical manipulation, easily resulting in iatrogenic dissection, which may completely block further recanalization efforts. In the presented patient cohort, the 8F guide catheter Guider Softip (Boston Scientific) provided a good combination of proximal stability and atraumatic distal tip. The emergence of large-bore aspiration catheters, e.g. ACE68 (Penumbra Inc., Alameda, CA, USA) or SOFIA Plus 6F (Microvention) and the evidence supporting the safety and efficacy of first-line thrombectomy with contact aspiration (ASTER trial) has changed the standard practice for intracranial revascularization. [70] The design of large-bore aspiration catheters with numerous transition zones in the shaft facilitates stability and pushability in the proximal portion and trackability through tortuous vessels in the distal segment and

the main purpose of these catheters is to deliver aspiration vacuum to the distal tip of the catheter; however, in order to remain atraumatic, the distal tip of these catheters is prone to external compression, which at least in our hands, substantially limits their ability to penetrate the rigid atherosclerotic plaque at the ICA origin. During the advancement of the catheter over the plaque, the half-deflated balloon hangs out of the catheter tip like a streamlined stylet, facilitating the passage over the irregular surfaced plaque and preventing the razor-like effect of the rim of the catheter on the vessel wall, minimizing the risk of iatrogenic dissection. [37] Accordingly, there were no procedural complications attributable to the BAT technique in the present series. Potential disadvantages of the BAT technique should however be noted. In cases of plaque dissection, unnoticed by the operator prior to the angioplasty, the inflation of the balloon can lead to progression of the intimal tear, rendering further recanalization attempts impossible and extreme cases can result in vessel perforation and serious extravasation. On the other hand, the undersized balloon, and the narrow diameter of the guiding catheter relative to the terminal CCA and proximal ICA might prove insufficient to efficiently prevent distal embolization following the recanalization of the occluded proximal plaque. In our experience, a steep learning curve can be achieved with the technique, bypassing the abovementioned potential disadvantages. Following the successful recanalization of the ICA and the intracranial arteries, the large lumen catheter is withdrawn into the CCA while access is maintained by a microwire left behind in the ICA and the status of the recanalized ICA origin is assessed. Stent implantation is deemed mandatory only in the case of acute or imminent reocclusion, flow-limiting dissection or large apposed thrombus on the plaque surface and was performed in 37% of the patients in the present series, which is lower compared to the 54% reported in the STRATIS EVT registry. [71] There was no significant difference in good clinical outcome and mortality between patients treated with emergent stenting versus angioplasty alone, supporting the findings

of a recent meta-analysis. [72] Another recent meta-analysis found a non-significant trend in good clinical outcome favoring emergent stenting over angioplasty with a cumulative OR of 1,43, albeit combined with a trend towards increased rates of symptomatic ICH in patients undergoing emergent stenting. [73] Similar, non-significant trends can be observed in our data as well, with emergent stenting associated with favorable clinical outcome (OR 1,57) and increased rates of ICH (OR 3,15), but not affecting mortality. Interestingly, there is a non-significant trend towards postoperative complications favoring successful recanalization (OR 3,12). We assume that this reflects the fact that both ICH and malignant infarctions are reperfusion injuries, hence a successful revascularization will theoretically increase the odds. Patients who did not receive stents in the acute setting were closely followed-up by Doppler-US and high-grade recurrent lesions were regarded as progressive, symptomatic high-grade ICA stenotic lesions even in the absence of recurrent symptoms and were preventively treated by stenting and angioplasty. We pursued this policy to prevent reocclusion, although this occurred in 10% of patients with follow-up anyway and all the reocclusions were asymptomatic. The combined rate of reocclusion and repeated revascularization in patients receiving only angioplasty in the acute setting was 45%, which is relatively high, but on the other hand all these lesions remained asymptomatic. Future prospective randomized studies should clarify the role of emergent and delayed stenting in tandem occlusion. [74] This single center retrospective analysis has some limitations. The observational and nonrandomized design is subject to methodologic and selection biases inherent in this form of study. The imaging findings were not confirmed using a core lab. There may be bias due to patients lost to follow-up and missing data in the retrospective dataset.

3. CTA AS A FOLLOW-UP IMAGING MODALITY FOR SUPRA-AORTIC STENTS

The accurate assessment of supra-aortic stenosis and restenosis is crucial for planning of stenting or reinterventions. 64-multi-slice dual energy CT angiography is a valuable imaging modality for the follow-up of patients after supra-aortic stenting including intracranial interventions even though it has its limitations. It has a high negative predictive value, but in ambiguous cases and suspected restenosis further, even invasive follow up should be carried out. With a properly performed CT angiography and adequate post processing high quality images can be obtained noninvasively to facilitate patient comfort and satisfaction. Other advantages of CT angiography are the detection of the whole supra-aortic vasculature sometimes with incidental findings. Figure 4 shows a patient's cervical and intracranial stents followed with CTA and DSA.

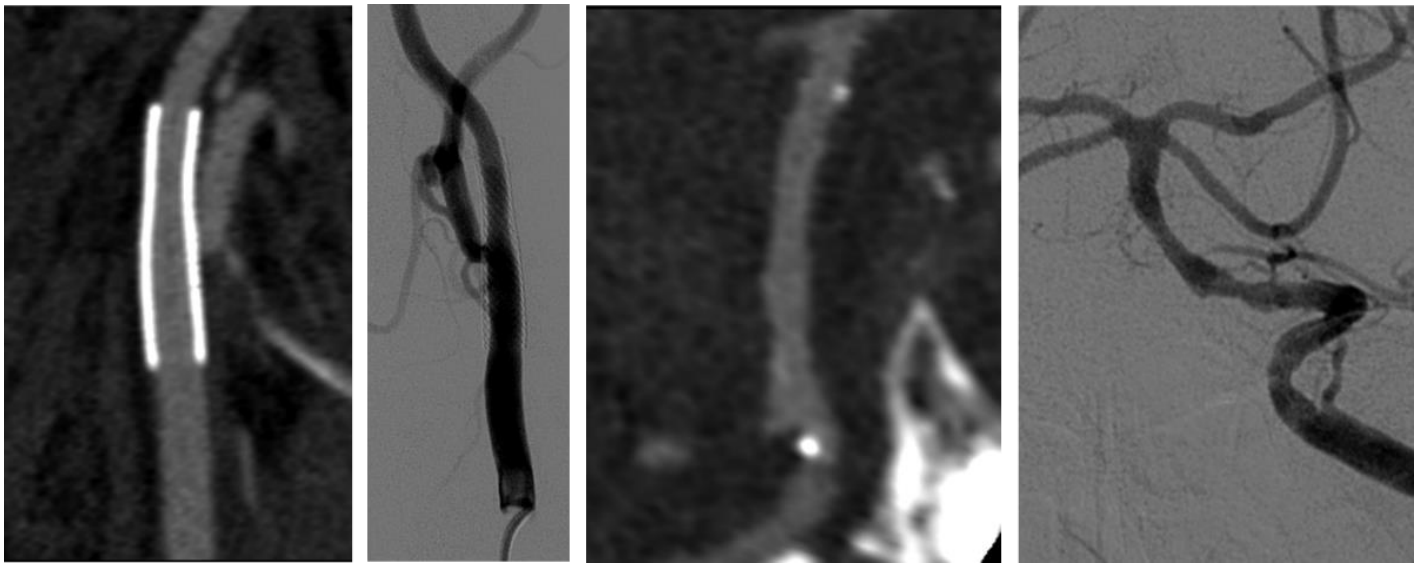

Figure 4. 55-year-old male patient with symptomatic left ICA and BA stenosis, which were treated with balloon angioplasty and stenting. After 2 years of invasive follow up we performed CT angiography, which did not show any restenosis in neither location.

SUMMARY

Stroke is the second leading cause of death and responsible for approximately 11% of total deaths. However, stroke plays an important role in the social and economic burdens because it is the major cause of long lasting disability. The development of imaging techniques has led to significant advances in diagnostic workup, treatment and prevention of stroke. Rapid and proper diagnostic procedures are indispensable for accurate diagnosis. However, identification of stroke in medical work leads to the most common misdiagnosis. [75] Newly developed recanalization techniques have significantly changed the outcome of stroke. Furthermore, management of significant stenosis preceding

cerebral artery occlusion can reduce the risk of an impending stroke. In this thesis, we investigated how to change the outcome of this relentless disease by examining these three factors (imaging, prevention and treatment), validating the imaging methods used and applying a new recanalization procedure. In the first part, we analyzed one of the most common stroke mimics, the most severe form of migraine which is the hemiplegic migraine. The neurologically symptomatic form of migraine especially when it occurs for the first time as in our case is almost impossible to distinguish from acute ischemic stroke. In our case, an event with severe symptoms and impaired consciousness led to the suspicion of a stroke. The complex MRI scan showed a significant reduction of the circulation in the left middle cerebral arterial territory, but diffusion images confirmed the integrity of the brain tissue despite the detected circulatory disturbance. Thus, intravenous thrombolysis treatment was safely avoided, and the patient's neurological symptoms resolved spontaneously. Cerebrospinal fluid 5-HIAA level during the attack confirmed the underlying migraine mechanism, as a result confirming the diagnosis of hemiplegic migraine. To the best of our knowledge concurrent imaging and cerebrospinal fluid chemistry during the attack has not been available to date. Our findings may also shed light on a detail of the pathomechanism of migraine. The presented specific case confirms the role of acute MRI in the differential diagnosis of acute diseases with severe neurological symptoms in childhood or even adulthood.

Tandem occlusive lesions in AIS have a naturally bad prognosis with or without treatment compared to other strokes, with up to 69% causing severe residual symptoms or even death. In tandem occlusions, the recanalization success rate of intravenous thrombolysis for this subgroup is also moderate compared to the overall success rate of intravenous thrombolysis in acute ischemic stroke (9-22% vs. 66%, respectively). [76] In TO cases, endovascular recanalization is particularly challenging, as safe passage through a blocked or severely narrowed lumen is more

difficult than usual and the razor-like effect of the devices that are passed through can cause further complications. An additional problem can also be that the opening of the thrombotic-atherosclerotic occlusion and the thrombectomy of the distal thromboembolism require different endovascular techniques and paradigms. Despite the exponential growth of the literature on endovascular treatment of TO, to date there is no clear recommendation for safe and effective recanalization of occluded ICA plaque in the cervical region. A key step in the recanalization of TO patients is the passage through the cervical ICA plaque. A preliminary meta-analysis on this has shown that a shorter procedural time, a higher probability of recanalization and a better outcome can be expected with an intracranial first approach. Therefore, a special technique the balloon assisted tracking technique (BAT) was used in 107 acute stroke patients with TO with the aim of minimizing additional intracranial embolization. In the second part of the thesis, we present our experience with the BAT technique. The technique in detail with a schematic drawing is described. Nevertheless, its applicability, feasibility, safety and efficacy are reported. In our study, the median ASPECTS was 8, NIHSS was 14, median onset-to-groin time was 346 minutes, and the time from puncture to passage of the guide catheter through the cervical segment was 16 minutes. The successful recanalization rate was 93%. Intraprocedural stenting was required in 37% due to high grade residual stenosis, floating thrombus or flow limiting dissection of the cervical ICA segment.

Good functional outcome (mRS 0–2) at 3 months was observed in 50%. 25% were still severely disabled (mRS 3-5) at 3 months and 24% died (mRS 6) before the follow up at 3 months.

The results of endovascular recanalization in TO patients using the BAT technique were compared with the data in the literature due to our study design. Based on our data we can conclude that:

1. The number of cases from a single trial performed under the same conditions is one of the highest.

2. Patients with TO treated with the BAT technique required periprocedural stenting less frequently.
3. In our cases, the recanalization success rate exceeded the data in the literature (93% vs. 85%).
4. The rate of good functional outcome reached and slightly exceeded that found in the literature in non-TO patients, while mortality was the same.

According to literature after preventive treatment of supra-aortic stenosis with stenting, restenosis is expected to develop in as high as 31% of patients in the first six months. It is therefore crucial to identify restenosis at an early stage, especially if it develops without clinical signs. We compared the effectiveness of possible methods of follow-up for restenosis after stenting. Evaluating our results, we found that noninvasive CT angiography has a high negative predictive value (95%) and only patients with a suspected restenosis on CT angiography should be invasively examined with DSA. In another evaluation, we compared the flow of 34 extracranial carotid stents with CT angiography and Color Doppler ultrasound scans. The comparison showed a very close concordance of results. Based on our results noninvasive carotid ultrasound is a suitable method to assess the flow of an extracranial carotid stent and the development of possible restenosis.

SUMMARY OF THE NOVEL RESULTS PRESENTED IN THIS THESIS

1. To the best of our knowledge, the presented case of an adolescent with hemiplegic migraine is the first case in Hungary in which the spasm of the branches of the large arteries supplying the cerebral area responsible for the symptoms was confirmed by imaging during an attack. The presented case points out and confirms the role of acute non-invasive vascular

imaging in the differential diagnosis of acute diseases with severe neurological symptoms in childhood or adulthood to diagnose or rule out stroke mimics and may help us understand the pathomechanism of hemiplegic migraine as well.

2. A detailed description of a novel recanalization technique (BAT technique) has been illustrated with precise drawings and examples.

3. The applicability, feasibility, efficacy and safety of a novel method known as the balloon-assisted tracking technique in the endovascular recanalization of tandem internal carotid artery occlusion in acute ischemic stroke has been demonstrated in a larger patient cohort.

4. For follow-up after supra-aortic stent implantation a properly performed CT angiography with an at least 64-section dual energy scanner, followed by adequate post processing high quality images can be obtained noninvasively to facilitate patient comfort and satisfaction, nonetheless restenosis can be ruled out with confidence.

ACKNOWLEDGEMENT

This project would not have been possible without the support of many people.

First of all I would like to express my deep gratitude to Dr. Zsolt Vajda, my research supervisor and mentor for his patient guidance, enthusiastic encouragement and useful critiques of my work in the last decade.

I am especially thankful to Prof. Ferenc Nagy, who has not only guided and supported me along my professional life but has been a great teacher in my personal life.

I would also like to thank Prof. Imre Repa and Dr. Marianna Moizs for their assistance and for providing the background for my work.

My grateful thanks are also extended to Dr. Gábor Bajzik, Dr. István Gubucz, Dr. Sándor Nardai and Dr. Gábor Lenzsér for their effort in participating in the publication of my paper, not regretting the time and energy to improve the quality of my manuscript.

I would also like to be grateful to the technicians of the DSA laboratory of the Neurovascular and Interventional Unit at Somogy County Moritz Kaposi Teaching Hospital (Kaposvár) for their technical support and their help with data management.

In addition, I would like to thank my wife Julia for her sympathetic ear, patience, and continuous support. Finally, I could not have completed this work without the encouragement of my son, Benjámin and daughter, Zsófia, guidance of my parents and support of my friends, Szabina and Máté.

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APPENDIX 1: CHILDHOOD SPORADIC HEMIPLEGIC MIGRAINE WITH MIDDLE CEREBRAL ARTERY HYPOPERFUSION

Ideggyógyászati Szemle (2017) 30;70(9-10): 343-348.

GYERMEKKORI SPORADIKUS HEMIPLEGIÁS MIGRÉN ARTERIA CEREBRI MEDIA HIPOPERFÚZIÓVAL

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Hungarian http://dx.doi.org/10.18071/isz.70.0343 www.elitmed.hu

A migrén egy ritka formájában, a hemiplegiás migrénben (HM) az aura során reverzibilis motoros gyengeség lép fel. A migrénnek ez a típusa gyakran gyermekkorban kezdődik, jelentőségét az első roham differenciáldiagnosztikai nehézsége adja. Jelen közleményben egy hemiplegiás migrénes gyermek esetét mutatjuk be, akinél a féloldali hullámzó intenzitású motoros tünetek és afázia miatt elsők között ischaemiás stroke gyanúja merült fel, azonban az elvégzett képalkotó vizsgálatok, az 5-hidroxi-indolacetát (5-OH-IA) -meghatározás és a roham utáni spontán, rapidan javuló klinikai kép a HM diagnózisát erősítette meg. A roham alatt elvégzett MR és MR-angiográfia nagyban elősegítette a diagnózist. A HM familiáris és sporadikus formáinak elkülönítése genetikai vizsgálatokkal lehetséges.

Kulcsszavak: *hemiplegiás migrén, TIA, MRI, MRA, 5-OH-IA*

CHILDHOOD SPORADIC TYPE OF HEMIPLEGIC MIGRAINE WITH ARTERIA CEREBRI MEDIA HYPOPERFUSION

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Ideggyogy Sz 2017;70(9–10):343–348.

Hemiplegic migraine is a rare subtype of migraine that is associated with reversible motor weakness in the aura phase. This is an uncommon form of migraine usually starting in childhood. The purpose of this case report is to highlight the differential diagnostic difficulty of the first attack. We describe a case, where the fluctuating unilateral motor weakness and aphasia suggested that the patient had ischaemic stroke. Nevertheless the brain MRI and MR angiography, the measured 5-hydroxyindole acetic acid (5-HIAA) concentration changes and the spontaneously improving clinical status proved the diagnosis of hemiplegic migraine. The MRI and MR angiography was very beneficial in establishing the correct diagnosis in this case. To distinguish between the familiar and sporadic type of hemiplegic migraine further genetic tests can be carried out.

Keywords: *hemiplegic migraine, TIA, MRI, MRA, 5-HIAA*

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Érkezett: 2017. május 7. Elfogadva: 2017. július 31.

A migrén a lakosság 10-15%-át érinti, ezzel a leggyakoribb primer fejfájás gyermek- és serdülőkorban[1]. A hemiplegiás migrén (HM) ritka formája a fejfájásoknak, mely gyakran gyermekkorban kezdődik[2]. A HM különösen ritka formája a tudatzavarral járó roham. A rohamok gyakorisága változó, jelentőségét azonban az első roham differenciáldiagnosztikai nehézsége okozza. A fejfájások érvényben lévő nemzetközi osztályozása alapján HM-ről abban az esetben beszélünk, ha a betegnek legalább két, teljesen reverzibilis motoros és szenzoros tünetekkel, valamint beszédzavarral járó

aurája jelentkezett, a tünetek közül legalább egy féloldali és a motoros tünetek nem tartanak 72 óránál tovább[2].

A családi halmozódás megléte vagy hiánya alapján a HM lehet familiáris vagy sporadikus. A genetikai vizsgálatok azonban érdemben nem segítik a HM diagnózisát, mivel a betegség genetikailag nagyon heterogén. Hátterében a mai napig három felelős gént azonosítottak. Ezek a CACNA1A, az ATP1A2 és az SCN1A gének, de ennél sokkal több, eddig ismeretlen génről lehet szó az azonos klinikai kép hátterében. A tünettani megjelenés alapján nem lehet elkülöníteni az öröklődő formát a sporadikustól, továbbá a familiáris forma eddig azonosított három altípusát sem. Így a familiáris HM diagnózisát megerősíti a pozitív genetikai vizsgálat, de negatív genetikai vizsgálat sem zárja ki a herediter formát. Egyes HM-betegeknél más, ez idáig még nem azonosított gének is érintettek lehetnek a betegség kialakulásában. Az SCN1A-mutációt hordozó beteg esetén nagyobb a valószínűsége a további neurológiai tünetek (krónikus ataxia vagy epilepszia) megjelenésének. A familiáris HM-es betegeknél a CACNA1A gén több mint 30 különböző mutációja, az ATP1A2 gén több mint 60 mutációja és az SCN1A gén mindössze négy különböző mutációja ismert[3].

A patomechanizmusban nagy valószínűséggel a kérgi úgynevezett spreading depression, vagyis az agykéreg rövid lokális idegi izgalom által kiváltott, majd tovaterjedő excitációja és az idegsejtek funkciójának ezt követő gátlása által okozott reverzibilis diszfunkciója játszik döntő szerepet. Ritka betegségről lévén szó, az irodalomban eddig összesen hozzávetőleg 200 sporadikus HM-es esetről számoltak be, a familiáris forma prevalenciája 0,003%-ra tehető[3]. Közleményünkben egy sporadikus HM miatt vizsgált gyermek esetét mutatjuk be.

Esetbemutatás

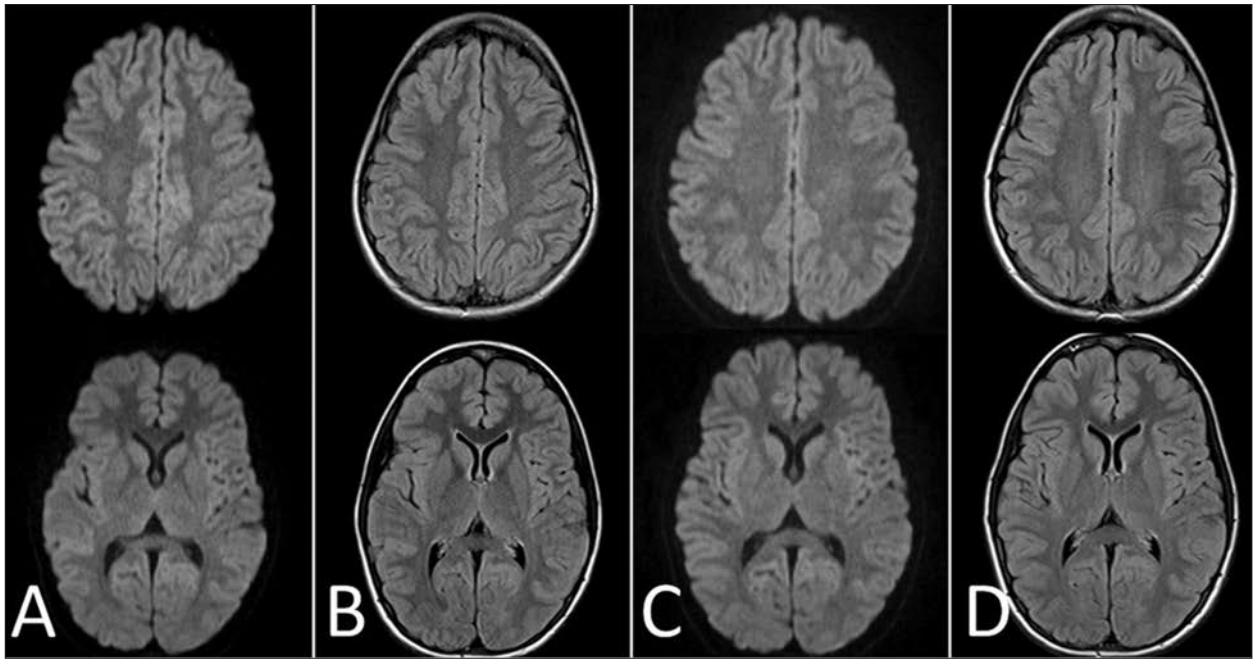
A 13 éves leány bal oldali temporalis fejfájás, ehhez társuló hányás, beszédzavar és zavartság miatt került felvételre a sürgősségi ambulanciára. A fejfájás jellege lüktető volt, közepesnél erősebb (VAS 5), időtartama több órával meghaladta az auratüneteket. A fájdalmat fény- és hangkerülés kísérte és a fizikai aktivitás rosszabbította. A fejfájására vonatkozó kérdésekre természetesen csak a tudatzavar és az afázia megszűnte utáni napokban kaptunk válaszokat a betegtől. A felvételkor készült koponya-CT-vizsgálatot követően progresszió, arcaszimmetria, a jobb oldali arcfél elmaradása és a jobb oldali végtagok enyhe fokú paresise jelentkezett, a beteg tünetei, zavartsága, beszédzavara hullámzó lefolyást mutattak. Felvételét követően neurológiai tünetei tovább progrediáltak, szenzomotoros afázia, dezorientáltság és aluszékonyság jelentkezett. Tudatállapota felvételét követően 5-6 órán keresztül somnolentia-sopor határán hullámzott. A liquor rutin laboratóriumi és mikroszkópos vizsgálata eltérést nem mutatott, valamint a liquor-ELFO során is normális fehérjekép látszott. Kezdetben a herpes encephalitis nem volt kizárható, ezért aciclovirterápiát indítottunk. Koponya-CT-vizsgálattal kóros eltérés nem igazolódott. Koponya-MR és time-of-flight (TOF) MRA készült, mely az agyállományban kóros eltérést nem bizonyított, a diffúziósúlyozott felvételeken friss ischaemiára utaló eltérés nem volt megfigyelhető **(1.A** és **B ábra)**. A TOF MRA vizsgálattal a bal oldali a. carotis interna (ICA) intracranialis szakaszának és az a. cerebri media (MCA) főtörzsének mérsékelt spasmusa ábrázolódott **(2.A ábra)**, az MCA-végágakban az ellenoldallal összehasonlítva jelentős fokú áramlási jel kiesés volt megfigyelhető **(3.A ábra)**. EEG-vizsgálattal epilepsziás működészavarra utaló aktivitás nem volt észlelhető, azonban kifejezett, bal féltekére lokalizálódó lassú aszimmetria volt látható.

A roham kezdetétől számított ötödik órától a beteg tudatállapota fokozatosan rendeződött, 24 óra elteltével neurológiai tünetei teljes mértékben megszűntek. A beteg később rákérdezésre elmondta, hogy korábban is volt már egy alkalommal jobbkéz-gyengeséggel járó fejfájásos rohama, mellyel nem fordult orvoshoz.

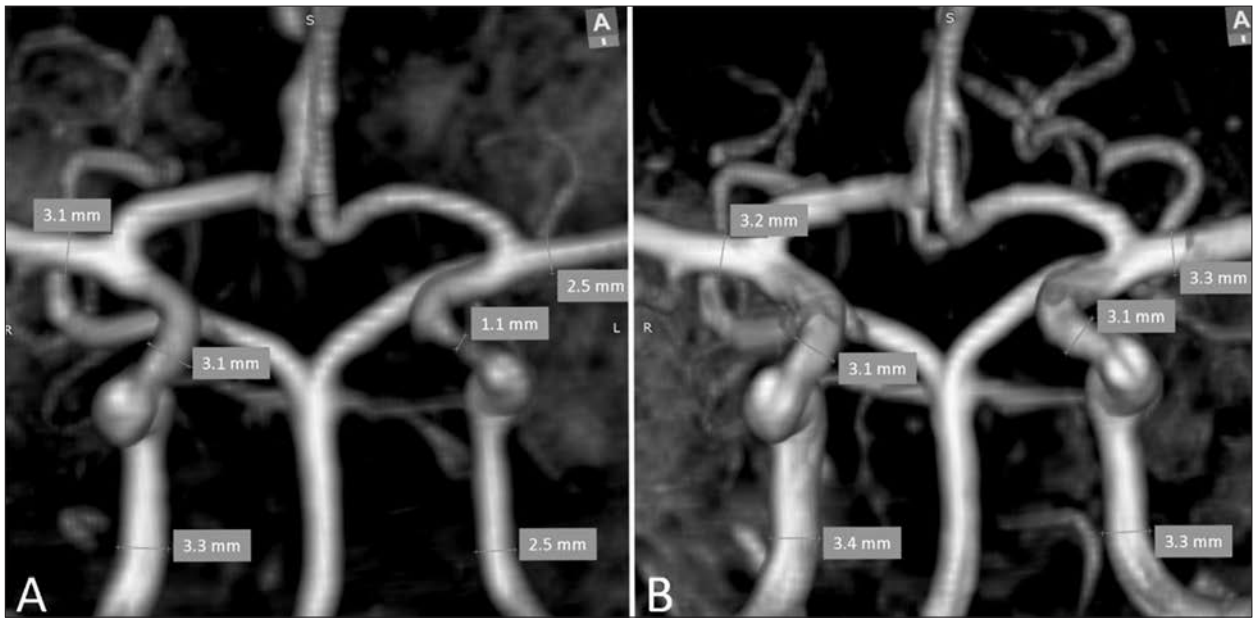
A roham alatt vett liquorból 5-OH-IA-meghatározás történt, mely a normáltartományhoz képest 10-szeres emelkedést mutatott[4]. A négy nappal később végzett kontroll-koponya-MR- és TOF MRA vizsgálat állományi károsodást továbbra sem igazolt **(1.C** és **D ábra)**, az MRA-képeken a bal oldali ICA- és MCA-ágak roham alatt látott spasmusa teljesen megszűnt (**2.B** és **3.B ábra)**.

Genetikai vizsgálatra mintát küldtünk, azonban a kézirat elkészítéséig eredményt nem kaptunk.

A beteg a sürgősségi osztályon intravénás aciclovir mellett egy alkalommal metoclopramidinjekciót, valamint Salsol, Isodex és Rindex infúziót kapott. A gyermekosztályos obszerváció során panaszai nem ismétlődtek, otthonába profilaktikus propranolol szedését, korai fájdalomcsillapítást (metamizol, ibuprofen), Magne B_6-ot, D-vitamint és Q10-et javasoltunk bő folyadékfogyasztás mellett. A követés során, az elmúlt 10 hónapban kétszer fordult elő fejfájásos epizód, amiket más panasz nem kísért, hányinger, beszédzavar nem volt, panaszai per os alkalmazott metamizolra megszűntek.



1. ábra. *A roham alatt* **(A, B)** *és a négy nappal később* **(C, D)** *készült diffúziósúlyozott* **(A, C)** *és FLAIR* **(B, D)** *MR-szekvenciák sem friss, sem szubakut állományi károsodást nem igazoltak*

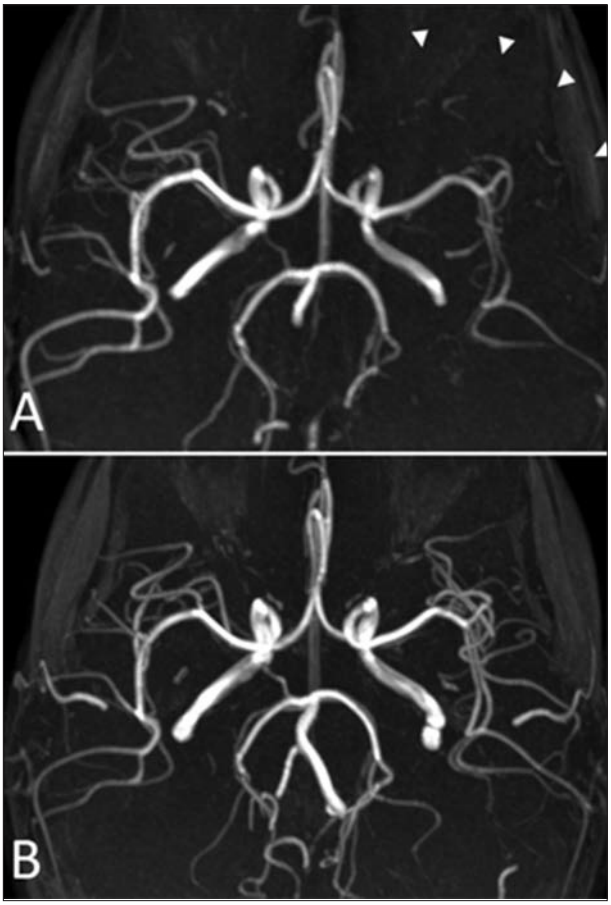


2. ábra. A *A roham alatt készült TOF MR-angiográfiás szekvencia rekonstrukciós képein a bal oldali ICA és MCA jelentős fokú spasmusa látható*. **B** *A roham utáni 4. napon készült kontroll TOF MRA vizsgálaton a spasmus teljes oldódása figyelhető meg*

Megbeszélés

A gyermekkorban első ízben jelentkező HM-roham differenciáldiagnosztikai szempontból nagy kihívást jelent, mely megkívánja a részletes laboratóriumi és képalkotó vizsgálatok végzését, valamint a tünetek változásának gondos követését.

A migrén során mért liquor 5-OH-IA szintre vonatkozó irodalmi adat meglehetősen kevés. A rendelkezésre álló tanulmányok csaknem mind-



3. ábra. A *A roham alatt készült TOF MRA képek maximum intenzitás projekciós (MIP) rekonstrukciós képein a bal oldali ICA és az MCA főtörzs spasmusa, valamint a bal oldali MCA végágakban (nyílhegyek) az áramlási jel kiesése látható, súlyos fokú perfúziós deficitre utalóan*. **B** *A négy nappal később készült kontroll TOF MRA szekvencián valamennyi ábrázolt artériában szabályos lumen és jó áramlás figyelhető meg*

egyike a rohamok között 5-OH-IA csökkenést talált[5]. Migrénes rohamok alatt viszont az 5-OH-IA szint a szérumban, a vizeletben és a liquorban is emelkedést mutatott[6, 7]. Aurával és spreading depression-nel járó migrénben a szerotoninmetabolizmus zavarának szerepe megkérdőjelezhetetlen[8–10]. Nincs adat ugyanakkor arra, hogy stroke-ban vagy gyulladásban a szerotoninnak a migrénhez hasonló kulcsszerepe volna. Mindazonáltal közleményünkben a HM diagnózisát nem az 5-OH-IA emelkedett szintjére, hanem a klinikumra alapoztuk. Az 5-OH-IA meghatározást azért végeztük el, mert mintavételkor korábbi hasonló rohamról még nem volt tudomásunk és további markereket kerestünk az ismertetett differenciáldiagnosztikai nehézségek miatt. A tünetek rendeződése után felvett részletes és célzott anamnézis derített fényt arra, hogy korábban is előfordult már egy alkalommal fejfájásos epizód, melyhez migráló neurológiai tünetek (kézzsibbadás, gyengeség, beszédzavar, zavartság) társultak. Ezek alapján a klinikai kép már teljesítette a sporadikus HM ICHD-3 szerinti diagnosztikus kritériumait[2].

Ellentmondásosak az irodalomban az aura és a spreading depression alatt az agyi nagyerek átmérőjére és vérátáramlására vonatokozó adatok is. Mind perfúziócsökkenést[5], illetve -növekedést[11] leírtak az agyi keringésben a roham alatt és után. Hiányzik azonban az irodalomból a betegség ritkasága miatt az erre vonatkozó átfogó vizsgálat. Az ellentmondó eredményeknek az is lehet a magyarázata, hogy a roham lefolyása során nagy valószínűséggel mindkét lehetőség előfordul[11]. Azt feltételezik, hogy a roham egyik triggere a szerotoninfelszabadulás lehet, mely következményes intracranialis átáramlás csökkentést eredményez. Ezt reflexes kompenzáció követ, mely az átáramlás növekedését okozza. A közleményekben szereplő eredményeket pedig az határozza meg, hogy a vizsgálatot a migrén melyik fázisában végezték. A mi esetünkben az MR-vizsgálat a korai szakaszban, még a tünetek fennállása alatt készült. Ez lehet a magyarázata a vizsgálat során látott MCA hipoperfúziójának.

A bemutatott esetet a genetikai eredmények megérkezéséig sporadikus HM-nek tartjuk, mivel a részletes családi anamnézisfelvétel nem igazolt familiáris halmozódást, a beteg édesanyjánál csupán időszakosan jelentkeznek tenziós jellegű fejfájások. A bemutatott esetben a hirtelen kialakuló és progressziót mutató hemitünetek, afázia és hullámzó tudatzavar miatt a stroke gyanúja került előtérbe. Gyermekeknél tudatzavar, hemiparesis, fejfájás és zsibbadás/paraesthesia esetén megfontolást igénylő leggyakoribb állapotokat az **1. táblázatban** foglaltuk össze. Az intracranialis vérzést a koponya-CT-vizsgálat a kivizsgálás elején kizárta, azonban az ischaemiás stroke-ot egyértelműen az MR- és MRA-vizsgálattal tudtuk kizárni. Az MR-vizsgálat a T2-súlyozott és FLAIR-metódussal készült szekvenciákon strukturális állományi laesiót nem igazolt, a diffúziósúlyozott mérések (DWI) friss ischaemiára utaló diffúzibilitáscsökkenést nem mutattak, viszont a TOF MRA vizsgálat az érintett féltekét ellátó agyi nagyartériák jelentős fokú spasmusát igazolta. *Bosemani* és munkatársai egy korábban közölt, az itt bemutatotthoz hasonló eset kapcsán a migrén akut szakában kontrasztanyag adásával készült MR-perfúziós méréssel (DSC-PWI), valamint szuszceptibilitássúlyozott szekvencia (SWI) alkalmazásával kimutatták az érintett érellátási területen a szöveti hipoperfúziót, illetve a

1. táblázat. *Gyermekeknél tudatzavar, hemiparesis, fejfájás és zsibbadás/paraesthesia esetén a migrénen kívül differenciáldiagnosztikai szempontból szóba jövő leggyakoribb állapotok. A British Medical Journal (BMJ) Best Medical Practice ajánlása alapján, gyakorisági sorrendben (forrás: http://bestpractice.bmj.com/best-practice)*

Tudatzavar	Hemiparesis	Fejfájás	Zsibbadás/paraesthesia
stroke/TIA	TIA	agyrázkódás	gerincvelő-kompresszió
fejsérülés utáni állapot	vérzéses stroke	subduralis vérzés	stroke/TIA
delírium	traumás agykárosodás	ventriculoperitonealis sönt diszfunkció	brachialis vagy lumbalis plexopathia
epilepsziás roham utáni állapot	hypoglycaemia	intracranialis hypotonia	akut demyelinisatiós encephalomyelitis (ADEM)
cardialis eredetű (pangásos szívelégtelenség, kamrai ritmuszavarok)	odd-paresis (postictalis bénulás)	epiduralis vérzés	Guillain–Barré-szindróma (GBS)
hyperglycaemia	subduralis vérzés	agyhártyagyulladás	nehézfém-mérgezés
hypoglycaemia	subarachnoidealis vérzés	agyvelőgyulladás	egyéb (étel-) mérgezés
hypernatraemia	hematomyelia	cerebralis tumor	rheumatoid arthritis
hyponatraemia	háti/ágyéki gerincsérülés	intermittáló hydrocephalus	SLE
dehidráció (volumhiány)	nyakigerinc-sérülés	pseudotumor cerebri	granulomatosis (Wegener-szindróma)
hypothermia	agyvelőgyulladás	subarachnoidealis vérzés	mikroszkopikus polyangitis
hypoxia	agytályog	ischaemiás stroke	parciális epilepsziás roham
hypercapnia	poliovírus	agyállományi vérzés	intravascularis lymphoma
hepaticus encephalopathia	Guillain–Barré-szindróma (GBS)	érdisszekció	neuro-Behcet-kór
uraemia	transzverzális myelitis (TM)	vénás sinusthrombosis	
akut szisztémás infekció	akut hypokalemia	agyalapimirigy-bevérzés	
akut pszichózis	gyógyszer indukálta neuropathia		hypertoniás encephalopathia
alkoholhatás	toxin indukálta diszfunkció		
gyógyszerhatás	kompartmentszindróma		
gyógyszermegvonás	gerincvelő-kompresszió		
tüdőembolia			

vénás oldalon a lassult keringést és emelkedett deoxihemoglobin-szintet, de korai ischaemiás eltérések a DWI-szekvencián nem voltak megfigyelhetőek[12]. Sajnos esetünkben az akutan végzett MR-vizsgálat nem tartalmazott perfúziós és SWI-méréseket, a diffúziósúlyozott felvételeken korai ischaemiás eltéréseket mi sem tudtunk igazolni. A fentiek alapján valószínű kórlefolyásnak a migrénes aura kezdeti szakaszában az érintett oldali ICA- és MCA-ágakban súlyos fokú vasospasmus kialakulása, ennek következtében az érintett félteke perfúziójának kritikus szint alá csökkenése és következményesen neurológiai góctünetek megjelenése tartható[12, 13]. Mivel az agyszöveti hipoperfúzió nem csökkent az ischaemiás állománykárosodás szempontjából kritikus határérték (12–20 ml/100 g agyszövet/perc) alá, így sem az akut, sem a napokkal később elvégzett kontroll-MR-vizsgálat nem mutatott strukturális állománydefektust.

Ismereteink szerint a bemutatott beteg az első olyan magyarországi HM-eset, akinél roham alatti képalkotással sikerült igazolni tünetekért felelős agyi területet ellátó nagyartériák ágainak spasmusát. A bemutatott eset megerősíti az akut MR-vizsgálat szerepét a gyermekkori, súlyos neurológiai tünetekkel járó akut kórképek differenciáldiagnosztikájában, de segítségünkre lehet a HM betegség patomechanizmusának megértésében is.

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Appendix 2: Endovascular Recanalization of Tandem Internal Carotid Occlusions Using the Balloon-assisted Tracking Technique

Clinical Neuroradiology (2021) doi: 10.1007/s00062-021-01078-2.

Clin Neuroradiol
https://doi.org/10.1007/s00062-021-01078-2

ORIGINAL ARTICLE

Endovascular Recanalization of Tandem Internal Carotid Occlusions Using the Balloon-assisted Tracking Technique.

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Received: 24 April 2021 / Accepted: 24 July 2021

Abstract

Purpose Tandem occlusive lesions are responsible for up to 20% of acute ischemic stroke cases and are associated with poor prognosis if complete recanalization cannot be achieved. Endovascular recanalization might be challenging due to difficulties in the safe passage of the occluded plaque at the origin of the internal carotid artery (ICA). The balloon-assisted tracking technique (BAT), where a partially deflated balloon is exposed out of the catheter tip to facilitate its passage through stenosed or spastic arterial segments was introduced by interventional cardiologists and the applicability of the technique has been recently proposed in the field of neurointervention as well. Here we describe our experience using the BAT technique in the endovascular recanalization of tandem occlusive lesions.

Methods Procedures were performed from June 2013 to December 2020 in a single center. Baseline clinical and imaging data, procedural and follow-up details and clinical outcomes were retrospectively collected.

Results In this study 107 patients, median age 66 years, median admission NIHSS 14 and median ASPECTS 8 were included. Successful recanalization of the ICA using the BAT technique was achieved in 100 (93%) and successful intracranial revascularization in 88 (82%) patients. There were no complications attributable to the BAT technique. Intraprocedural complications occurred in 9 (8%) patients. Emergent stenting was performed in 40 (37%) at the end of the procedure. Postprocedural adverse events (intracerebral hemorrhage [ICH], malignant infarction) occurred in 6 (5%) patients. Good clinical outcome at 3 months (modified Rankin scale [mRS] 0–2) was 54 (50%) and mortality 26 (24%). Delayed stent placement during follow-up occurred in 21 cases.

Conclusion Application of BAT technique in tandem occlusions appears feasible, safe, and efficient. Further evaluation of this technique is awaited.

Keywords Stroke · Stent · Technique · Thrombectomy · Intervention

Availability of Data and Material Questions regarding details not seen in the manuscript should be addressed to Zsolt Vajda M.D., Ph.D., the corresponding author, who maintains the clinical research files and provides access to the data upon reasonable request.

Code availability Not applicable.

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Published online: 21 September 2021

Introduction

Tandem occlusion (TO) of the internal carotid artery (ICA) is characterized by proximal occlusion of ICA, either due to acute thrombosis of an unstable atherosclerotic plaque or dissection, resulting in the embolic blockage of the ICA terminus (ICA-T) and/or the main trunk (M1 segment) of the middle cerebral artery (MCA). The condition is responsible for up to 20% of acute ischemic stroke (AIS) cases [1], responds poorly to IV thrombolysis [2] and is associated with poor prognosis without timely and successful recanalization [3]. Despite the high incidence and large clinical impact, the initial large, randomized trials showing the efficiency of endovascular treatment (EVT) of large vessel occlusion (LVO) in acute ischemic stroke either did not report key technical and clinical results from this subgroup or entirely excluded these patients from the analysis [4]. This is likely explained at least in part by the fact that tandem occlusions challenge the surgeon with a thrombotic-atherosclerotic (occluded plaque at the origin of the ICA) and a thromboembolic (distal ICA and/or MCA occlusion) pathology at the same time, each requiring different endovascular techniques and paradigms. Successful penetration of the thrombosed plaque at the origin of the ICA with a large lumen catheter is the first and key step in the procedure to provide sufficient back-up for the intracranial recanalization and to aspirate thrombotic material from the cervical ICA segment, if necessary. Elongated supra-aortic arteries, angulated origin of the ICA and the stiff and often calcified plaque make the penetration of the ICA lumen difficult with risk of vessel perforation, whereas iatrogenic dissection of the ICA and penetration of a false lumen with a large catheter can render the intervention unsuccessful right at the beginning of the procedure.

Although the literature on the endovascular treatment of TO in AIS is rapidly expanding, data on the safe and efficient maneuvers for the recanalization of the occluded ICA plaque are still sparse. The balloon-assisted tracking technique (BAT), where a partially deflated balloon is exposed out of the catheter tip to facilitate its passage through stenosed or spastic arterial segments was introduced by interventional cardiologists [5], and recent case studies proposed the applicability of the technique in the field of neurointerventions as well [6–8].

In the present study we report our experience with the BAT technique in the endovascular recanalization of 107 AIS patients with tandem occlusion.

Methods

Study Design and Patient Selection

A retrospective analysis of patients treated with tandem ICA-MCA occlusion between June 2013 and December 2020 at the Neurovascular Unit of the Moritz Kaposi Teaching Hospital, Kaposvár, Hungary was performed. Consecutive patients were included matching the following criteria: AIS explained by occlusion of an intracranial segment (carotid-T or MCA) of the anterior circulation and additional ipsilateral proximal ICA occlusion of atherosclerotic origin (i.e. tandem occlusion) verified by CT angiography and eligible for endovascular recanalization according to the guidelines set forth by the American Heart Association/American Stroke Association for the management of patients with AIS and the Society of Neurointerventional Surgery [9]. Only cases with complete (100%) occlusion of the proximal ICA were included in the analysis. Patients with ICA dissections were excluded due to the different nature of disease. In all included patients endovascular recanalization of the occluded ICA was performed on an emergency basis using the BAT technique described below.

A head CT scan was performed at admission and immediately postprocedurally. Neurological status at admission including National Institutes of Health Stroke Scale (NIHSS) score and i.v. lysis eligibility was assessed by a stroke neurologist. Functional outcome defined by the modified Rankin scale (mRS) was assessed at least 3 months after the intervention by outpatient visit or telephone interview.

Data Collection

Recorded baseline data included age, sex, history of hypertension, atrial fibrillation, diabetes and dyslipidemia. Admission clinical parameters such as CT ASPECTS score, NIHSS score, ictus to needle time, occlusion site, use of recombinant tissue plasminogen activator (rtPA) administration were also retrieved. The CT imaging data were reviewed by the radiologist on call and the interventionalist performing the treatment in all cases and ASPECTS values were determined by consensus. eASPECTS, an automated software for determining ASPECTS (Brainomix Limited, Oxford, UK) was installed in our hospital in June 2017, from this point, the results of the software were also considered in the determination of ASPECTS. Digital subtraction angiography (DSA) images of the procedures included in the study were reviewed by the first and the senior author and occlusion levels as well as recanalization TICI grades were determined by consensus.

Regarding procedural and technical data, groin to ICA occlusion passage time, groin to definitive intracranial re-

canalization (defined as TICI grade 2b–3) time, intracranial recanalization technique (ADAPT or SOLUMBRA), bail-out intracranial stenting and the implantation of an ICA stent were recorded. In the case of stent implantation, the applied antiplatelet medication was recorded.

The registered technical success and outcome parameters were the following: rate of successful proximal ICA recanalization, rate of definitive intracranial revascularization, TICI grade, procedural complications (ICA dissection, perforation, SAH), postprocedural adverse events (parenchymal reperfusion hematoma or space-occupying infarction) and mRS score at 3 months postprocedure.

Ethics approval for retrospective patient data retrieval was granted by the Institutional Review Board (IKEB/02163-000/2020). Written informed consent was waived due to the retrospective nature of the study. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Balloon-assisted Tracking Technique

Interventions were carried out on a monoplane angiosuite (Axiom Artis, Siemens, Erlangen, Germany) under anesthesiology standby including conscious sedation or general anesthesia if necessary. The right or left common femoral artery was accessed by an 8 F introducer sheath and 5000IU unfractionated heparin was administered. No antiplatelet therapy was administered beforehand in these cases. An 8F guiding catheter (Guider Softip, Boston Scientific, Marlborough, MA, USA) was advanced into the common carotid artery (CCA) on the affected side. The ICA occlusion was then confirmed with a prolonged run after contrast injection through the guide catheter. The runs were repeated in various projections until the tiny stump of the occluded ICA could be clearly visualized, when possible. The recanalization of the occluded ICA was performed through the guide-catheter using a slightly shaped hydrophilic 0.014″ microguidewire supported by a low profile 4 mm PTCA balloon catheter (Ryujin, Terumo Corporation, Shibuya, Japan). For crossing the ICA occlusion, a neuro microguidewire (Traxcess, Microvention, Aliso Viejo, CA, USA), Portal (Phenox GmbH, Bochum, Germany) or Chikai Black (Asahi Intecc, Seto-shi, Japan) was used in 81 out of the 107 cases (76%) or a PTCA guidewire (CHOICE Extra Support or PT GRAPHIX, Boston Scientific) was used in 26 out of the 107 (24%) cases, depending on the lesion and on the operator's preference. In 39 cases (36%) additional wires were used for crossing the ICA occlusion, maintaining stability or replacing the crooked wire. The wire was carefully advanced through the occluded plaque with special attention to keep the wire in a true intraluminal position by navigating it through the tiny stump of the ICA identified on initial angiographic series. This was followed by angioplasty of the plaque using the undersized 4 mm balloon catheter, following i.v. administration of atropine if necessary. The balloon was partially deflated thereafter and the guide catheter was advanced to partially cover it, with the half-deflated balloon protruding out from the catheter tip, forming a streamlined outline of the balloon-catheter tip complex, so that the rim of the catheter tip cannot

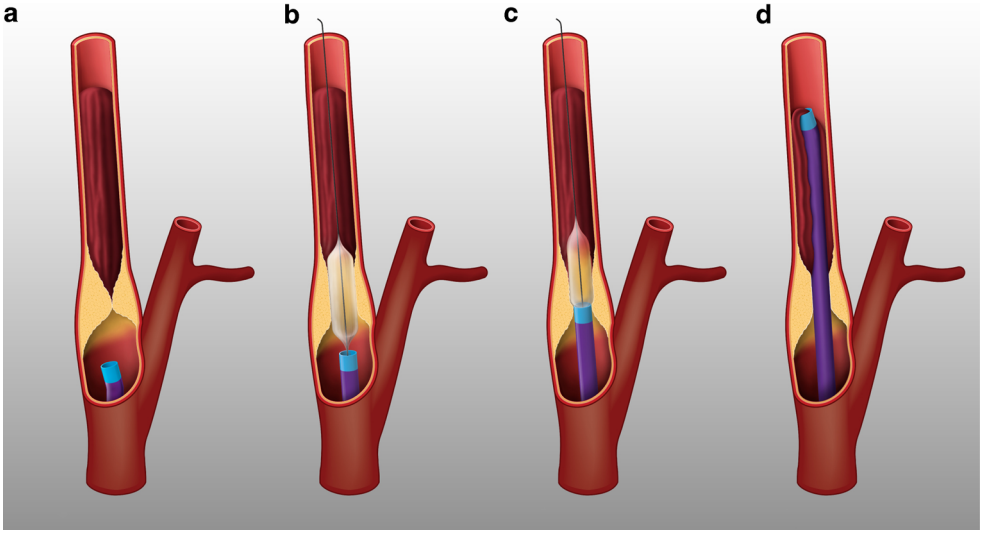

Fig. 1 Schematic drawing illustrating key steps of the application of the balloon-assisted tracking technique in the recanalization of an occluded plaque at the origin of the internal carotid artery (ICA). **a** A guide catheter is positioned in front of the ICA stump. **b** A 0.014″ micro-guidewire is carefully passed through the ICA stump and angioplasty is performed with an undersized, low-profile balloon. **c** The guide catheter is then tracked by the partially deflated balloon over the plaque into the occluded lumen of the ICA. The protruding balloon acts as a stylet preventing contact between the irregular plaque surface and the catheter rim. **d** Finally, the balloon and microwire are removed and the thrombus is extracted by aspiration

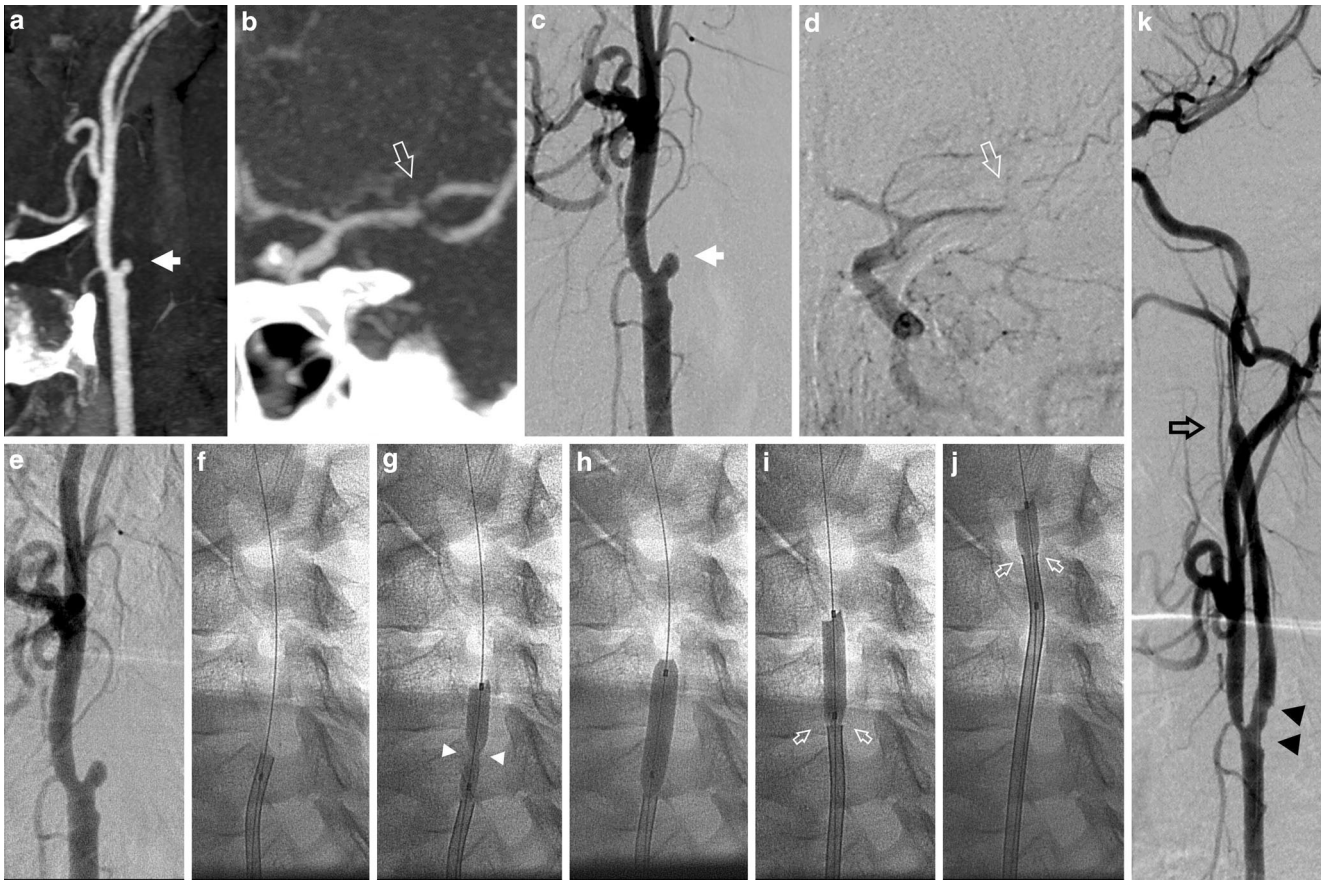

Fig. 2 Demonstrative case of the balloon-assisted tracking technique showing the recanalization of a left-sided tandem ICA-MCA occlusion in a middle-aged patient with acute onset severe left hemispheric symptoms. **a** Preoperative CTA reveals proximal occlusion of the left ICA with a small, rounded stump (*white arrow*) and a filling defect in the left M1 bifurcation (**b**, *open white arrow*) with apparently good filling of the distal MCA branches. **c** Subtraction angiography confirms the ICA occlusion but shows a complete flow arrest at the M1 bifurcation (**d**, *open white arrow*). The field-of-view position on panels **f**,**g** demonstrating the BAT technique corresponds to that of panel **e**. **f** The procedure begins with the careful penetration of the ICA stump with a 0.014″ microguidewire. The large lumen 8F soft tip guide catheter is then moved to the very end of the stump for sufficient back-up. **g** A low-profile coronary PTCA balloon with a diameter of 4 mm is positioned across the plaque followed by angioplasty by careful manual inflation of the balloon. The occlusion point (*white arrowheads*) is easily recognized. After complete inflation (**h**) the balloon is deflated passively (i.e., the syringe is detached from the conus) and the guide catheter is advanced over the balloon and then they are moved carefully together into the ICA (**i**,**j**). The partially deflated balloon forms a streamlined stylet (*white open arrows* on **i** and **j**), preventing the rim of the catheter to get in contact with the irregular surface of the plaque, precluding thereby shaving off plaque debris or plaque dissection. The balloon is deflated completely thereafter and is removed together with the microwire. The ICA lumen is then recanalized by careful manual aspiration through the guide catheter and the recanalization of the MCA is performed by ADAPT technique. **k** Selective injection of the left CCA at the end of the procedure shows the complete recanalization of the ICA and MCA. The *black open arrow* indicates the highest level to which the balloon-guide catheter complex was advanced. The recanalized plaque shows a smooth surface (*black arrowheads*), without signs of dissection, floating thrombus, or high-grade residual stenosis, therefore stent implantation was not pursued at the acute stage. The total time from the selective diagnostic run of the CCA to the complete recanalization (from panel **c** to panel **k**) was 8 min

get in contact with the irregular plaque surface, then the guide catheter was gently advanced with the half-inflated balloon acting as a "stylet" through the ruptured plaque and occluded cervical segment of ICA to prevent the razor effect of the rim of the guide catheter [8]. The balloon was then slowly deflated and removed together with the microguidewire. The 8F guiding catheter was detached from the hemostatic valve and carefully moved and torqued back and forth under gentle manual aspiration using a 50 ml perfusor syringe, removing thereby the thrombotic material in the cervical ICA segment. Extra care was taken during this step to prevent the vessel wall being sucked in by the tip of the catheter to prevent dissection. The hemostatic valve was then reattached and stent-retriever or direct aspiration thrombectomy of the carotid-T or MCA was performed in the usual technique. During distal thrombectomy the guide catheter was kept in the newly opened proximal ICA causing flow arrest and acting as dilator on the ICA plaque as described by Dotter et al. [10].

Following the successful recanalization of the dependent intracranial arteries, the 8F guide catheter was retrieved into the CCA under continuous manual aspiration with the

microguidewire left in the distal segment of the ICA to maintain access and an angiogram was done to evaluate the reopened ICA plaque. In cases of high-grade recoiling, an additional angioplasty was performed using a 6 mm balloon. Stent implantation was performed only in the case of flow-limiting residual stenosis, immediate reocclusion after repeated angioplasty, visible floating thrombus on the plaque or flow-limiting dissection. A schematic drawing of the BAT maneuver is shown in Fig. 1 and an illustrative case using the technique is presented in Fig. 2.

Follow-up and Delayed Stent Implantation

All patients who only went through angioplasty without stent implantation were tightly reassessed using Doppler US within the first 4–6 weeks following the intervention and in case of a high grade and/or progressing recurrent stenotic lesion, elective carotid stenting was performed in a second session when the patient's clinical and functional status allowed further treatment (mRS 0–2).

Anticoagulation/Antiaggregation Medication

All patients received 5000 IU sodium heparin IV at the beginning of the procedure. When emergent stenting was not necessary, antiaggregation medication was withheld for 3 days following the procedure and a single antiplatelet therapy (SAPT) with a daily dose of 100 mg acetylsalicylic acid p.o. was initiated thereafter. If stent implantation was necessary, 500 mg acetylsalicylic acid was administered IV at the end of the procedure and was maintained with a daily dose of 100 mg p.o. from the following day. A head CT was performed the day after the procedure and a loading dose of 300 mg clopidogrel p.o. was additionally administered in the absence of intracranial hemorrhage and/or large subacute infarction. In cases of intracranial hemorrhage not requiring surgical treatment or a large subacute infarction, p.o. clopidogrel was first initiated at the 5th postprocedural day. Oral dual antiplatelet therapy with 100 mg acetylsalicylic acid and 75 mg of clopidogrel was maintained for 6 months and clopidogrel monotherapy was continued thereafter.

Statistical Analysis

Continuous variables were reported as median with range and categorical variables as number and percentage. Categorical variables were compared using the χ^2-test or Fisher's exact test for small cell values, p values <0.05 were interpreted as statistically significant. Analyses were performed using SPSS, Version 26.0 (IBM, Armonk, NY, USA).

Results

Between June 2013 and December 2020, 592 patients with AIS were treated by endovascular recanalization. Tandem occlusion of the ICA and MCA was the primary pathomechanism in 113 (19%) cases. Of these patients 6 (5%) were excluded from the analysis because of having proximal ICA dissection as pathomechanism. The remaining 107 (77, 72% male, median age 66 years, range 45–87 years) cases with atherosclerotic origin were included in the study. The median (IQR, range) for ASPECTS and NIHSS on admission were 8 (2, 3–10) and 14 (6, 3–22), respectively.

Median onset-to-groin time was 346min (158–1405min), median total procedural time was 51min (10–178min) and the median time from groin puncture to the passage of the 8F guide catheter into the cervical segment of the ICA through the thrombosed plaque was 16min (5–108min).

Successful recanalization of the cervical ICA could be achieved in 100 (93%) cases. Details of the unsuccessful 7 (7%) cases were: in two patients (2%) the occluded ICA plaque could not be passed even after multiple attempts; in one patient (1%) the mid segment of the cervical ICA and in one patient (1%) the terminal segment of the ICA was perforated with guidewire and active extravasation could not be sealed with a balloon, so the ICA had to be reoccluded with coils; in three cases (3%) the microguidewire penetrated into the subintimal space during the ICA recanalization attempt and no re-entry could be achieved at any level even after multiple attempts.

Successful intracranial recanalization, defined as TICI2b-3 was achieved in 88 (82%) patients, thereof TICI2b in 50 (46.7%) and TICI3 in 38 (35.5%) cases. Bail-out stenting of the intracranial ICA and/or the MCA using a bare-metal coronary stent was required in 3 (3%) cases. Attempts of intracranial revascularization following the successful recanalization of the cervical ICA failed in 12 (11%) patients, resulting in TICI0 in 1 (1%) and TICI2a in 11 (10%) cases.

Intraprocedural stent implantation in the proximal ICA followed by balloon angioplasty was performed in 40 (37%) patients due to high-grade (>70%) residual stenotic lesion resistant to angioplasty, flow limiting dissection and/or visible floating thrombus on the recanalized ICA plaque. Wallstent (Boston Scientific) was used in 80% (32/40) and Roadsaver (Terumo) stent in the remaining 20% (8/40) of these emergent stenting cases. Regular US follow-up of patients with emergent stenting was available in 20 (50%) cases and revealed complete stent patency, without high-grade in-stent restenosis in 19 (98%) of the patients. Delayed occlusion of the stent implanted in the acute setting occluded in 1 (2%) of the case, and the single ICA stent reocclusion case was asymptomatic.

Out of the 60 cases without emergent stent implantation, 7 (12%) patients died during the acute postoperative period and 11 (18%) patients were lost to follow-up after discharge. Out of the 42 (70%) patients with regular US follow-up of the recanalized ICA, 6 (10%) reoccluded without any newly developed neurological deficit and 21 (35%) received delayed stent placement due to asymptomatic, but progressive high-grade restenosis (>70%) in a second session, giving a combined rate of reocclusion and revascularization of 45% (27/60).

The combined rate of emergent and delayed stenting was 61% (61/100).

Intraprocedural complications occurred in 9 (8%) patients: subarachnoid hemorrhage Fisher grade 1 in 7 (6%) cases, intracranial vessel perforation resulting in Fisher grade 4 subarachnoid hemorrhage in 1 (1%) case and termination of the procedure due to extracranial vessel perforation in 1 (1%) case. None of the complications were related to the BAT technique.

In two cases (2%), embolization into new vascular territories occurred. In both procedures, the proximal ICA occlusion was passed as described, then selective ICA injection revealed a proximal MCA occlusion, which was recanalized with a stent-retriever using the SOLUMBRA technique, resulting in TICI2a and TICI2b recanalization of the affected vascular territories; however, peripheral emboli in the ipsilateral anterior cerebral artery were seen in both cases. Clinical follow-up 3 months later revealed mRS 1 and mRS 0 in the patients with TICI2a and TICI2b recanalization, respectively.

The rate of postprocedural adverse events was 6 (5%). Intracerebral hemorrhage (ICH) developed in 4 (4%) cases (type 1 and 2 in 2 and 2 cases, respectively). A non-significant trend could be observed towards developing an ICH following emergent stent implantation ($p = 0.407$, OR = 3.15, 95% CI = 0.35–27.94).

Space-occupying infarction of the affected brain area developed in 2 (2%) patients, requiring craniectomy in 1 (1%) case. The development of ICH and space-occupying infarction was not significantly associated with differences in adequate reperfusion: 67% (4/6) versus 33% (2/6) in patients with successful versus unsuccessful recanalization, but the odds of developing a postprocedural adverse event were higher in patients with successful revascularization ($p = 0.148$, OR = 3.12, 95%CI = 0.68–14.29).

Good functional outcome (mRS 0–2) at 3 months was observed in 54 (50%) patients, 27 (25%) patients were still severely disabled (mRS 3–5) at 3 months and 26 (24%) patients died (mRS 6) before the follow up at 3 months. Successful intracranial recanalization was significantly associated with good clinical outcome (mRS 0–2): 59% (52/88) in the TICI2b-3 group versus 11% (2/19) in the TICI0-2a group, ($p < 0.001$, OR = 12.28, 95% CI = 2.67–56.45). Emergent stenting versus angioplasty did not significantly influence the rate of favorable clinical results, although there was a trend towards good clinical outcome in stented group (mRS 0–2 in the emergent stenting group: 58%, 23/40; mRS 0–2 in angioplasty group 52%, 31/60; $p = 0.261$, OR = 1.57, 95% CI = 0.71–3.46). Mortality was

Table 1 Summary of demographic, baseline medical, neurological, imaging, procedural and follow-up data

Number of patients (*n*)	107
Baseline characteristics	
Age (years) (median, range)	66 (45–87)
Male (*n*, %)	77 (72%)
Left hemispheric stroke (*n*, %)	62 (58%)
Arterial hypertension (*n*, %)	79 (74%)
Atrial fibrillation (*n*, %)	5 (5%)
Diabetes mellitus *n* (%)	31 (29%)
Dyslipidemia/obesity *n* (%)	7 (7%)
NIHSS baseline (median, *IQR*, range)	14, *6* (3–22)
IVT *n* (%)	47 (44%)
ASPECTS baseline (median, *IQR*, range)	8, *2* (3–10)
Occlusion site	
CCA-ICA-MCA *n* (%)	2 (2%)
ICA-MCA *n* (%)	104 (97%)
ICA-ACA *n* (%)	1 (1%)
Time intervals, procedural data	
Onset to groin (min, median, range)	346 (158–1405)
Groin to ICA passage (min, median, range)	16 (5–108)
Groin to complete revascularization (min, median, range)	51 (10–178)
Unsuccessful reperfusion (TICI 0-2a) n (%)	*12 (11%)*
TICI 0 flow n (%)	*1 (1%)*
TICI 1 flow n (%)	*0*
TICI 2a flow n (%)	*11 (10%)*
Successful reperfusion ICA/intracranial (TICI 2b-3) *n* (%)	100 (93%)/88 (82%)
TICI 2B flow n (%)	**50 (46.7%)**
TICI 3 flow n (%)	**38 (35.5%)**
Intraprocedural ICA stent implantation *n* (%)	40 (37%)
Intraprocedural complications *n* (%)	9 (8%)
Postprocedural adverse events *n* (%)	6 (5%)
Clinical outcome	
mRS ≤ 2 after 90 days *n* (%)	54 (50%)
Mortality after 90 days *n* (%)	26 (24%)
Delayed proximal ICA revascularization with stent implantation *n* (%)	21 (31%)
Delayed reocclusion/stent thrombosis *n* (%)	6 (10%)/1(2%)

NIHSS National Institutes of Health Stroke Scale, *IVT* intravenous lysis therapy, *ASPECTS* Alberta stroke programme early CT score, *CCA* common carotid artery, *ICA* internal carotid artery, *MCA* middle cerebral artery, *ACA* anterior cerebral artery, *TICI* thrombolysis in cerebral infarction, *mRS* modified Rankin Scale

not affected by emergent stenting ($p = 0.737$, OR = 1.17, 95% CI = 0.46–2.95).

A summary of demographic, baseline medical, neurological, imaging, procedural and follow-up data are given in Table 1.

Discussion

Although there is a rapid expansion in the literature on the treatment of tandem occlusions in acute ischemic stroke recently, key aspects including distal-to-proximal versus proximal-to-distal recanalization approach, placement versus non-placement of a stent in the acute setting, perioperative and postoperative antithrombotic medication and the role of embolic protection devices are still debated. The pathophysiology of the disease is a combination of several distinct vascular and hemostatic pathologies: atherothrombosis, artery-to-artery thromboembolism and less frequently dissection [11]. In severe atherosclerotic carotid disease, a progressive high-grade stenotic lesion at the origin of the ICA will gradually slow down the flow in the cervical segment; however, apart from a truly isolated ICA combined with a high-grade stenotic lesion at the ECA origin, flow in the intracranial ICA segment is maintained through the circle of Willis (COW) and the ECA-to-ICA collaterals, most importantly the ethmoidal-ophthalmic and meningo-ophthalmic collateral pathways. In the moment of occlusion of the ICA plaque, as a consequence of the rupture of the unstable thinned fibrotic cap and subsequent thrombosis of the already filiform lumen, the cervical segment of the ICA begins to fill up with large amount of fresh thrombotic material, followed by one of three possible sequences: (i) the ICA fills up with thrombus up to the inflow of the most proximal ECA or COW collateral, through which the arterial supply of the dependent intracranial arteries is maintained uninterrupted, resulting in an asymptomatic ICA occlusion, with a prevalence of 16% according to a meta-analysis of data from 4406 patients [12]; (ii) until the cervical ICA segment is not completely thrombosed, the growing occlusive thrombus at the origin of the ICA can be flushed distally, leading to an intracranial large-vessel occlusion. In this case, an M1 or ICA-T lesion is seen on angiography, together with a preocclusive filiform stenosis at the origin of the ICA. This scenario might result in the so-called pseudo-occlusion phenomenon on CTA [13]; (iii) thrombotic occlusion of the atherosclerotic lesion at the ICA origin, with the angiographic image of a tiny stump at the ICA origin and absence of flow in the cervical segment and the dependent intracranial branches. This third pathology can be de facto named tandem occlusion and only patients having this type of lesion were included in the present study. The key steps of the recanalization are the safe passage of the ICA plaque with the microwire avoiding perforation and dissection, and the access of the cervical ICA segment with a large lumen catheter for aspiration and further intracranial recanalization. In our opinion, emergent implantation of a stent in the ICA origin to facilitate access to the cervical and intracranial segments before removing the bulk of the thrombotic material from the cervical ICA might be counterproductive and in cases of heavily calcified plaques and/or extensive supra-aortic elongation, the struts of a partially wall-adapted stent can indeed hamper the access to the ICA and can result in serious difficulties at the withdrawal of a stent-retriever during the intracranial recanalization.

There is no consensus in the literature regarding the extracranial versus intracranial first approach. A recent meta-analysis of data from the German Stroke Registry (GSR) with endovascular treatment of 607 AIS patients with tandem lesions found significantly shorter procedural times (53.5 versus 72.0 min) and a higher nonsignificant probability of successful reperfusion defined as mTICI2b/3 (92.1% versus 86.1%) and good clinical outcome (45.8% versus 33.0%) using the intracranial first approach [19]. In the present work, the BAT technique allowed the exquisite use of the extracranial first approach in all the cases, with a median total procedural time of 51 min combined with a good clinical outcome rate of 50%. Interestingly, the better clinical outcome in our cohort was achieved with poorer reperfusion success rate (86.1% in GSR versus 82% in our cohort). A possible explanation would be the higher rates of periprocedural complications in the GSR extracranial-first cohort (24% versus 8%), although it should be noted that only severe complications are reported in our cohort, whereas minor complications, such as vasospasm and high proportion of not detailed (other) complications are included in the GSR data, limiting the possibilities of comparison.

In the present series, the large lumen guiding catheter could safely be inserted into the occluded cervical ICA segment over the thrombosed plaque using the BAT technique in all cases, without the need for a stent implantation. The primary angioplasty of the ICA plaque is done with a 4 mm balloon, which is only slightly larger than the catheter, resulting in recoiling of the plaque and the proximal ICA around the perimeter of the catheter, providing flow arrest and thereby an inherent proximal protection against embolization during intracranial thrombectomy/aspiration, eliminating the need of an embolic protection device. For the same reason, balloon guide catheters were not used, as in our experience the additional benefit of embolic protection is offset by poorer navigability due to the stiffness of these catheters in elongated vessels.

Tortuosity of the cervical ICA is commonly encountered, especially in older patients, usually involving the proximal segment with angles ranging from 90° up to 140–150°. The use of an atraumatic technique during the recanalization of

these vessels of paramount importance. In these cases, we tracked the half-deflated balloon on a longer distance with the guiding catheter, using it practically as a streamlined stylet together with the micro guidewire, slightly straightening the tortuous, kinked ICA segment. Additionally, careful torquation of the guiding catheter with an angulated tip allowed the operator to adapt the outline the microwire-balloon guiding catheter structure to follow as much as possible the course of the ICA. Accordingly, none the unsuccessful ICA recanalization attempts were attributed to the elongation of the ICA.

Using the BAT technique, tiny emboli in new territories were detected only in 2 patients, both of them recovering to mRS 0–1 at the 3 months clinical follow-up.

In selecting the appropriate catheter for the recanalization of the occluded ICA, the operator must balance between stability that is especially important in cases of extensive supra-aortic elongation, found mostly in older patients and requires a certain degree of rigidity of the proximal segment of the catheter for good maneuverability through the thrombosed and often stiff and calcified ICA plaque and an atraumatic distal tip, as the wall of the collapsed cervical ICA becomes more prone to injury in response to mechanical manipulation, easily resulting in iatrogenic dissection, which may completely block further recanalization efforts. In the presented patient cohort, the 8F guide catheter Guider Softip (Boston Scientific) provided a good combination of proximal stability and atraumatic distal tip. The emergence of large-bore aspiration catheters, e.g. ACE68 (Penumbra Inc., Alameda, CA, USA) or SOFIA Plus 6F (Microvention) and the evidence supporting the safety and efficacy of first-line thrombectomy with contact aspiration (ASTER trial) [20] has changed the standard practice for intracranial revascularization. The design of large-bore aspiration catheters with numerous transition zones in the shaft facilitates stability and pushability in the proximal portion and trackability through tortuous vessels in the distal segment and the main purpose of these catheters is to deliver aspiration vacuum to the distal tip of the catheter; however, in order to remain atraumatic, the distal tip of these catheters is prone to external compression, which at least in our hands, substantially limits their ability to penetrate the rigid atherosclerotic plaque at the ICA origin.

During the advancement of the catheter over the plaque, the half-deflated balloon hangs out of the catheter tip like a streamlined stylet, facilitating the passage over the irregular surfaced plaque and preventing the razor-like effect of the rim of the catheter on the vessel wall, minimizing the risk of iatrogenic dissection [8]. Accordingly, there were no procedural complications attributable to the BAT technique in the present series.

Potential disadvantages of the BAT technique should however be noted. In cases of plaque dissection, unnoticed by the operator prior to the angioplasty, the inflation of the balloon can lead to progression of the intimal tear, rendering further recanalization attempts impossible and extreme cases can result in vessel perforation and serious extravasation. On the other hand, the undersized balloon, and the narrow diameter of the guiding catheter relative to the terminal CCA and proximal ICA might prove insufficient to efficiently prevent distal embolization following the recanalization of the occluded proximal plaque. In our experience, a steep learning curve can be achieved with the technique, bypassing the abovementioned potential disadvantages.

Following the successful recanalization of the ICA and the intracranial arteries, the large lumen catheter is withdrawn into the CCA while access is maintained by a microwire left behind in the ICA and the status of the recanalized ICA origin is assessed. Stent implantation is deemed mandatory only in the case of acute or imminent reocclusion, flow-limiting dissection or large apposed thrombus on the plaque surface and was performed in 37% of the patients in the present series, which is lower compared to the 54% reported in the STRATIS EVT registry [14]. There was no significant difference in good clinical outcome and mortality between patients treated with emergent stenting versus angioplasty alone, supporting the findings of a recent meta-analysis [15]. Another recent meta-analysis found a non-significant trend in good clinical outcome favoring emergent stenting over angioplasty with a cumulative OR of 1.43, albeit combined with a trend towards increased rates of symptomatic ICH in patients undergoing emergent stenting [16]. Similar, non-significant trends can be observed in our data as well, with emergent stenting associated with favorable clinical outcome (OR 1.57) and increased rates of ICH (OR 3.15), but not affecting mortality. Interestingly, there is a non-significant trend towards postoperative complications favoring successful recanalization (OR 3.12). We assume that this reflects the fact that both ICH and malignant infarctions are reperfusion injuries, hence a successful revascularization will theoretically increase the odds.

Patients who did not receive stents in the acute setting were closely followed-up by Doppler-US and high-grade recurrent lesions were regarded as progressive, symptomatic high-grade ICA stenotic lesions even in the absence of recurrent symptoms and were preventively treated by stent angioplasty. We pursued this policy to prevent reocclusion, although this occurred in 10% of patients with follow-up anyway and all the reocclusions were asymptomatic. The combined rate of reocclusion and revascularization in patients receiving only angioplasty in the acute setting was 45%, which is relatively high, but on the other hand all these lesions remained asymptomatic. Future prospective randomized studies should clarify the role of emergent and delayed stenting in tandem occlusion [17, 18].

This single center retrospective analysis has some limitations. The observational and nonrandomized design is subject to methodologic and selection biases inherent in this form of study. The imaging findings were not confirmed using a core lab. There may be bias due to patients lost to follow-up and missing data in the retrospective dataset.

Conclusion

In this retrospective single center series of 107 acute ischemic stroke patients with tandem occlusion, the efficacy and safety of the balloon-assisted tracking technique in the endovascular recanalization has been demonstrated in a larger patient cohort. Our data show that the balloon-assisted tracking technique can be effectively applied in this patient population with an otherwise poor prognosis. The technique proved very efficient in attaining short recanalization times without the need of antegrade stent implantation at the beginning of the procedure, with good safety margin and very favorable long-term clinical outcomes. Our follow-up clinical and imaging data confirm the results of recent meta-analyses reporting non-significant trends for better functional outcome but also increased rates of ICH associated with emergent stenting. According to our results, long-term patency of the recanalized ICA is better maintained with emergent or delayed stenting; however, patients who did not receive stents also remained asymptomatic during the follow-up, even in cases of high-grade recurrent stenosis or reocclusion. These encouraging pilot results await confirmation from further experience and prospective randomized studies.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. The research was conducted as part of a doctoral program at the Doctoral School of the University of Pécs, Faculty of Health Sciences, Hungary.

Author Contribution All authors made a significant contribution to the study and to manuscript preparation. CN, JH, FN and ZV contributed to study conception and design, CN, JH, GBG, IG, SN, GL, MF and GBK contributed to data acquisition and MM and IR contributed to data interpretation and analysis. CN and ZV drafted the manuscript, GL, MF, GBK, MM, IR and FN critically revised the paper, and IR contributed significantly to the intellectual content. CN, MM, IR, FN and ZV approved the final version of the manuscript.

Declarations

Conflict of interest C. Nagy, J. Héger, G. Balogh, I. Gubucz, S. Nardai, G. Lenzsér, G. Bajzik, M. Fehér, M. Moizs, I. Repa, F. Nagy and Z. Vajda declare that they have no competing interests.

Ethical standards This retrospective analysis was conducted with approval of the Moritz Kaposi Teaching Hospital Institutional Review Board (IKEB/02163-000/2020). Consent to participate: informed consent for the study was waived due to the retrospective nature of the study; however, patients or a family member gave informed consent for the endovascular procedures. Consent for publication: publication has been approved by all co-authors.

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APPENDIX 3: DIAGNOSTIC VALUE OF DUAL-ENERGY CT ANGIOGRAPHY IN THE ASSESSMENT OF SUPRA-AORTIC IN-STENT RESTENOTIC LESIONS: COMPARISON WITH DOPPLER US FINDINGS

Interventional Neuroradiology (2017) 23: Suppl. 1 Paper: P607, 1 p.

Feasibility and diagnostic value of CT angiography after supraaortic stenting including intracranial interventions

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Introduction

Our retrospective study aimed to determine whether the **64-slice dual energy CT angiography** after intravenous contrast medium administration is suitable for the evaluation of luminal patency and **in-stent restenosis** after supraaortic **percutan transluminal angioplasty and stenting** involving intracranial and extracranial atherosclerotic lesions, which stenoses are an established risk factor for stroke. Supraaortic stenting has been shown to increase the therapeutic value of balloon angioplasty for the treatment of these arterial lesions. The main drawback of stent placement is the mandatory initiation of dual antiplatelet therapy besides the occurrence of in-stent restenosis. The major cause of in-stent restenosis is neointimal hyperplasia. The occurance of in-stent restenosis can be as high as 10,6% in the extracranial internal carotid artery, 31% in the intracranial arteries and 15.9% in the orifice of the vertebral arteries. The extracranial internal carotid artery is the vessel where color-coded duplex sonography can visualize the vessel lumen for adequate screening and follow up after interventions, nevertheless ultrasound may have limitations due to anatomical anomalies or technical difficulties. Besides the extracranial internal carotid artery is the less prone to restenosis. For intracranial and vertebral orifice stents conventional DSA is the current criterion standard follow up examination. In a high-volume neurointerventional department the risk of neurologic complications during conventional DSA is close to zero, still the complication rate can range as high as 0,3% due to its invasive nature. Promising new noninvasive alternative tool could be the cone beam CT after intravenous contrast medium administration performed in an angio suite equipped with flat-detector. The downside of this method is the lack of bolus tracking and the accessability, which can be a limitation for the method to unfold. Using MR imaging exact depiction of the stent lumen and exact measurement of the in-stent restenosis is not possible. A non-invasive alternative method for assessment of the stented supraaortic vessels would be highly desired. The purpose of our study was to **assess the diagnostic value of 64-multi-slice dual energy CT angiography in the follow-up of supraaortic stenting including intracranial interventions**. Nevertheless our aim was to estimate the feasibility of this non-invasive tool instead of cathether based examinations.

Materials and Methods

At our institution in the period of 33 months, from September 2014 to May 2017 54 consecutive patients (23 female, 31 male) with 72 stents had a supraaortic dual energy CT angiography. All CT examinations were done without adverse events following contrast media application and without other complications. Multi-slice CT angiographs were performed in the caudocranial direction with a Siemens Flash Dual Source 64-slice scanner (Siemens, Erlangen, Germany) ranging from the aortic valve to the skullcap. Data acquisition consisted of 64 × 0,6 mm collimation, 100/140 kV (dual energy), 270/270 mAs, a helical pitch of 0,7 and a 0,28 s gantry rotation time. Axial images were reconstructed with a slice width of 1 mm and a reconstruction increment of 1 mm using a sharp kernel. Using care bolus-tracking, 70-80 ml of contrast medium (Iomeron 350, Bracco, Milan) followed by a 30-40 ml saline bolus were administered via power injector with an injection rate of 4-5 ml/s. Centered on the stents, parallel and perpendicular to the stents' centerline reconstructions were performed under a smaller field of view with advanced imaging software (SyngoVia Workstation, Siemens, Erlangen, Germany). Mean multiplanar reconstructions (MPR), maximum intensity projections (MIP) were reconstructed with a 1 mm slice thickness and an increment of 1 mm. Curved planar reformations (CPR) were performed with a 1 mm slice thickness. Images were transferred to a picture archiving and communication system (PACS). The CT angiography follow-up after angioplasty ranged from 1 month to 91 months, average 28 ± 23 months (mean ± SD) after stent implantation. To determine the percent of residual or restenosis the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method was used. All stents were classified as patent or re-stenotic. A stenosis of at least 70% according to the NASCET criteria was considered restenotic. All measurements were obtained perpendicular to the center line of the stented segment. Stent patency was evaluated by two experienced neuroradiologists using curved multiplanar reformations and different planes of maximal intensity projection images.

Results

54 consecutive patients with 72 stents (47 cercival carotid, one brachiocephalic trunk, 5 subclavien, 11 ostial vertebral and 8 intracranial) were evaluated. In 21 (29%) stents the CT angiography suspected a restenosis. In 11 instances, these patients with suspected restenosis underwent catheter based angiography. 5 patients had significant restenosis, 6 did not.
In an other group of patients twenty conventional digital subtraction angiographies were performed after the CT angiography. The sensitivity of CT angiography was 67% and the specificity was 91%. The **negative predictive value was much stronger than the positive predictive value (95%, 50% respectively)**.
Thirty-four patients underwent extracranial carotid artery stenting in our study group. In this group results obtained from CT angiography were compared with duplex ultrasonography which has gained wide acceptance to estimate restenosis rate. More than 70% of these cases with suspected restenosis found on ultrasonography was confirmed with CT angiography and in only four cases additional invasive procedures had to be done to confirm the diagnosis. CDUS has a sensitivity of 92% and a specificity of 62%, and has a strong negative predictive value.

Conclusion

The accurate assessment of supraaortic stenosis and restenosis is crucial for planning of stenting or reinterventions. 64-multi-slice dual energy CT angiography is a valuable imaging modality for the follow-up of patients after supraaortic stenting including intracranial interventions even though it has its limitations. It has a high negative predictive value, but in ambiguous cases and suspected restenosis further, even invasive follow up should be carried out. With a properly performed CT angiography and adequate post processing high quality images can be obtained noninvasively to facilitate patient comfort and satisfaction. Other advantages of CT angiography is the detection of the whole supraaortic vasculature sometimes with incidental findings.

Figure 1. Case 1 (A-E) 59 year-old male with right ACA territory stroke caused by right ACA occlusion. The left ACA A2 segment was severly stenosed. This soliter left ACA A2 high-grade stenosis was treated with balloon angioplasty and stent placement. After 1 year of close invasive imaging the patient was followed with CT angiography. CT angiography showed no restenosis.
Case 2 (F-I) 55 year-old male patient with symptomatic left ICA and BA stenosis, which were treated with balloon angioplasty and stenting. After 2 years of invasive follow up we performed CT angiography, which did not show any restenosis in neither locations.

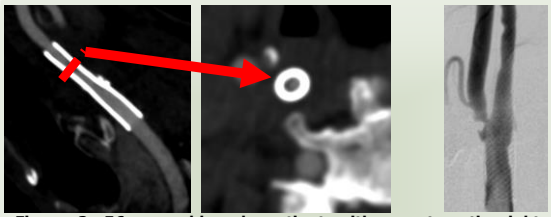

Figure 2. 56 year-old male patient with symptomatic right ICA stenosis treated with carotid artery stenting and angioplasty. Follow up US showed increased velocity in the stented segment of the cervical ICA. CT angiography suggested in-stent restenosis 18 months after stent placement. DSA did not confirm significant restenosis

Vascular risk factors	
Hypertension	64 (89%)
Diabetes	22 (31%)
Hyperlipidemia	56 (78%)
Male/female:	23/31
Symptomatic stenosis	48 (67%)
Asymptomatic stenosi	24 (33%)

Treated vessels:	
Cervical ICA	47 (65%)
Orifice VA	11 (15%)
Intracraniali stent	8 (11%)
Subclavien stent	5 (7%)
Brachiocephalic trunk	1 (1%)

Table 1.: Patient demographics and stent location

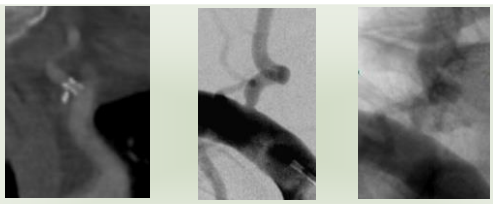

Figure 3. 69 year-old patient with a symptomatic left VA orifice stenosis was stented, CT angiography and DSA follow up showed no restenosis.

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Financial disclosure: The participation of C. Nagy on WFITN 2017 was sponsored by Vascular Venture Kft., Hungary

7. sz. melléklet

DOKTORI ÉRTEKEZÉS BENYÚJTÁSA ÉS NYILATKOZAT A DOLGOZAT EREDETISÉGÉRŐL

Alulírott

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„Diagnostic and therapeutic aspects of neuroradiology in acute ischemic stroke affecting the anterior circulation"

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Dátum: Pécs, 2022. június 7.

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