Aus dem Institut für Diagnostische und Interventionelle Radiologie
des Universitätsklinikums Düsseldorf

Direktor: Univ.-Prof. Dr. med. Gerald Antoch

Untersuchung des neurologischen Outcomes nach mechanischer Thrombektomie beim ischämischen Schlaganfall in Bezug auf technische, klinische und anatomische Aspekte

Habilitationsschrift
zur Erlangung der *venia legendi* für das Fach Radiologie
an der Hohen Medizinischen Fakultät
der Heinrich-Heine-Universität Düsseldorf

vorgelegt von
Dr. med. Marius Georg Kaschner

2022

Erklärung

Hiermit versichere ich an Eides statt, dass ich die vorliegende Habilitationsschrift eigenständig und ohne unerlaubte Hilfe angefertigt habe.

Ich versichere, dass bei den wissenschaftlichen Untersuchungen, die Gegenstand dieser Habilitationsschrift sind, ethische Grundsätze sowie die Grundsätze und Empfehlungen zur Sicherung guter wissenschaftlicher Praxis beachtet wurden. Die Habilitationsschrift wurde bislang keiner anderen Fakultät vorgelegt.

Düsseldorf, Januar 2022.

Dr. med. Marius Kaschner

Inhaltsverzeichnis

Abkürzungsverzeichnis

ADAPT	A Direct Aspiration First Pass Technique
ACI	Arteria cerebri interna
ACM	Arteria cerebri media
ACP	Arteria cerebri posterior
ACS	Arteria cerebelli superior
AICA	engl.: anterior inferior cerebellar artery
APH	Aperio-Hybrid-Stent-Retriever
ATE	Aspirationsthrombektomie
ASPECTS	Alberta Stroke Program Early Computed Tomography Score
AV	Arteria vertebralis
BA	Basilararterie
BI	Barthel-Index
CCT	Cranielle Computertomographie
CTA	Computertomographische Angiographie
CTP	Computertomographische Perfusion
DSA	Digitale Substraktionsangiographie
DWI	Diffusion weighted imaging
MRA	Magnetresonanzangiographie
MRT	Magnetresonanztomographie
i. a.	intraarteriell
i. v.	intravenös
mRS	modified Rankin Scale
NIHSS	National Institutes of Health Stroke Scale
OR	Odds-Ratio
PICA	engl.: posterior inferior cerebellar artery
PWI	Perfusion weighted imaging
rtPA	recombinant tissue plasminogen activator

SAB	Subarachnoidalblutung
SCA	engl.: superior cerebellar artery
SR	Stent-Retriever
TICI	thrombolysis in cerebral infarction
mTICI	modified thrombolysis in cerebral infarction
TE	Thrombektomie
UKD	Universitätsklinikum Düsseldorf

1 Einleitung

Neurointerventionelle endovaskuläre Verfahren sind heutzutage fester Bestandteil eines interdisziplinären Behandlungskonzeptes in der Therapie des ischämischen Schlaganfalls. Durch Einsatz moderner Stent-Retriever und hochflexibler Aspirationskatheter ist es möglich, die durch einen Thrombus verschlossenen Hirngefäße mittels einer sogenannten mechanischen Thrombektomie zu rekanalisieren. Stent-Retriever sind selbstexpandierende rückholbare Stents, deren Wirksamkeit zur Bergung von Thromben aus den zerebralen Hauptstammgefäßen bereits durch mehrere große randomisierte Studien (MR Clean, EXTEND IA, ESCAPE, SWIFT-PRIME und REVASCAT) belegt wurde (Ringleb *et al.* 2015). Dabei werden signifikant höhere Rekanalisationsraten als durch die alleinige systemische Lysetherapie erreicht, vor allem dann, wenn es sich um langstreckige Verschlüsse handelt. Die Tatsache, dass in Deutschland der ischämische Schlaganfall mit einer Inzidenz von circa 180/100 000 Einwohnern die häufigste Ursache für eine dauerhafte Behinderung ist, andererseits durch eine schnelle Rekanalisation des verschlossenen Hirngefäßes bei einer großen Anzahl von Patienten eine signifikante Verbesserung des Outcomes erzielt werden kann, zeigt die Notwendigkeit einer flächendeckenden endovaskulären Schlaganfallversorgung.

Thematischer Schwerpunkt dieser Arbeit ist die Darstellung der Untersuchungsergebnisse zum klinisch-neurologischen Outcome nach mechanischer Thrombektomie (TE) beim akuten ischämischen Schlaganfall in Bezug auf das klinisch-neurologische Outcome unter Betrachtung technischer, klinischer und anatomischer Aspekte. Die Arbeit umfasst die Anwendung moderner Stent-Retriever bei der TE insbesondere zur Entfernung von Blutgerinnseln aus dem Stromgebiet der Arteria cerebri media (ACM). Demgegenüber wird die Technik der alleinigen direkten Aspirationsthrombektomie mit einem flexiblen Spezialkatheter zur Rekanalisation von Verschlüssen der großen Hirngefäße betrachtet. Des Weiteren werden in dieser Arbeit Fragestellungen zu speziellen Einsatzgebieten der TE erörtert. Dazu gehören die TE bei Patienten mit nur milden Schlaganfällen und Verschluss des Hauptstammes der ACM (M1-Segment), die TE bei peripheren Verschlüssen in den sogenannten M2-Segmenten der ACM sowie die Behandlung von Stent-Thrombosen durch eine TE. Darüber hinaus werden anatomisch-funktionelle Gesichtspunkte der TE in Verbindung mit der präinterventionellen Schlaganfallbildgebung untersucht. Hier wird die Wertigkeit von Kollateralscores in der computertomographischen Gefäßbildgebung hinsichtlich der Vorhersage zum klinischen Outcome nach einer TE verglichen. Ein weiteres Thema beschäftigt sich mit den Basalganglien, die bei akuten Verschlüssen des Hauptstammes der ACM meist die ersten Strukturen sind, die irreversibel geschädigt werden. Das Ziel besteht darin, unter anderem

mithilfe bildgebender Verfahren Prädiktoren für das Überleben der Basalganglien nach erfolgreicher Rekanalisation zu identifizieren.
Abschließend werden die einzelnen Aspekte der TE in Bezug auf das klinische Outcome diskutiert.

2 Grundlagen

2.1 Epidemiologie des Schlaganfalls

Der ischämische Schlaganfall ist definiert als Episode einer neurologischen Dysfunktion, die durch einen zerebralen Infarkt verursacht wird, der durch einen Gefäßverschluss oder eine Stenose bedingt ist. In Deutschland ereignen sich circa 260 000 Schlaganfälle pro Jahr, und annähernd 66 000 Patienten (25,4 %) erleiden einen erneuten Schlaganfall (Heuschmann *et al.* 2010). Der *ischämische Schlaganfall* kommt mit circa 85 Prozent am häufigsten vor und ist durch ein akut einsetzendes fokal-neurologisches Defizit aufgrund eines Verschlusses der hirnversorgenden Gefäße definiert, wohingegen der *hämorrhagische Schlaganfall* durch eine intrazerebrale Blutung ausgelöst wird. Nach Herz-Kreislauf- und Krebserkrankungen ist der Schlaganfall aktuell die dritthäufigste Todesursache und die Hauptursache für eine erworbene Behinderung im Erwachsenenalter in Deutschland (Heuschmann *et al.* 2010; Busch *et al.* 2013). Im Jahr 2008 sind in Deutschland circa 63 000 Patienten (24,2 %) an den Folgen von Schlaganfällen verstorben. Der Schlaganfall ist die häufigste Ursache von Invalidität im Erwachsenenalter. Die Inzidenz für Schlaganfälle steigt mit zunehmendem Alter und liegt in Europa bei einem Durchschnittsalter von circa 73 Jahren (Wolfe 2009; Heuschmann *et al.* 2010). Zudem ist nach einem Erstereignis mit einem Schlaganfallrezidiv zu rechnen. Den Ergebnissen einer aktuellen Studie zufolge liegt das Ein-Jahres-Rezidivrisiko bei 7,4 Prozent und innerhalb von fünf Jahren bei 19,4 Prozent (Stahmeyer *et al.* 2019).

2.2 Klassifikationen zerebraler Ischämien

Der ischämische Schlaganfall kann unterschiedliche Ätiologien haben, wobei Arteriosklerose bedingte arterio-arterielle Embolien, Stenosen und Verschlüsse der hirnversorgenden extra- und großen intrakraniellen Gefäße sowie kardiale Embolien, mikroangiopathische Gefäßverschlüsse und Dissektionen als häufige Ursachen vorkommen. Daneben gibt es zerebrale Ischämien hämodynamisch-embolischer Genese, die eine Gefäßstenose als Ursache haben.

Zur ätiologischen Differenzierung zerebraler Ischämien hat sich die TOAST-Klassifikation etabliert, die fünf Grundtypen von Hirninfarkten unterscheidet (Adams *et al.* 1993). Dazu gehören:

- Makroangiopathien bei höhergradigen Stenosen durch arteriosklerotische Plaques oder vollständigen Verschluss einer hirnversorgenden Arterie. In der Schnittbildgebung – Computertomographie (CT) und Magnetresonanztomographie

(MRT) – zeigen sich in den abhängigen Stromgebieten Territorialinfarkte. Deutlich seltener treten hämodynamisch bedingte Infarkte, auch Grenzstrominfarkte genannt, auf.
- Mikroangiopathien entstehen bei Stenosen oder Verschlüssen aufgrund einer Lipohyalinose perforierender Hirnarteriolen, die vor allem die Basalganglien, das Marklager der Groß- und Kleinhirnhemisphären und den Hirnstamm versorgen. Ein chronischer Hypertonus und ein Diabetes mellitus sind Hauptursachen für die Mikroangiopathie. Die zerebrale Bildgebung weist lakunäre Läsionen mit einem Durchmesser $\leq$ 15 Millimeter auf, kann aber auch ohne Infarktnachweis bleiben.
- Kardiale Embolien. Zu den relevanten kardialen Embolіequellen als Ursache eines Hirninfarktes gehören Vorhofflimmern, ein mechanischer Herzklappenersatz, ein Thrombus im linken Vorhof oder Ventrikel, ein Sick-Sinus-Syndrom, ein Myokardinfarkt, der weniger als vier Wochen zurückliegt, eine dilatative Kardiomyopathie, eine infektiöse Endokarditis oder ein Vorhofmyxom. Mit einem eher niedrigen Embolierisiko gehen beispielsweise ein offenes Foramen ovale, eine Mitralklappenstenose oder ein Vorhofflattern einher. Die zerebrale Bildgebung zeigt wie bei den Makroangiopathien häufig Territorialinfarkte in unterschiedlichen zerebralen Gefäßterritorien.
- Andere Ursachen für einen Hirninfarkt kommen seltener vor. Diese umfassen nicht atheriosklerotische Arteriopathien wie eine Vaskulitis oder Dissektion, Thrombosen zerebraler venöser Blutleiter, Gerinnungsstörungen oder Mitochondriopathien. Dementsprechend sind in der Bildgebung Lokalisation und Größe des Infarktes unterschiedlich.
- Unklare Ätiologie. Zu dieser Kategorie zählen alle Hirninfarkte, bei denen keine Ursache festgestellt werden konnte oder mehrere gleichwertig konkurrierende Ursachen gefunden wurden.

Die Erfassung koexistierender Faktoren, die circa 20 Prozent der Hirninfarkte ausmachen, hat Einfluss auf die therapeutischen Maßnahmen und die Prognose. Durch eine weitere Klassifikation, die ASCOD-Klassifikation *(A – atherosclerosis/large vessel disease, S – small vessel disease, C – cardic source, O – other cause, D – dissection),* können koexistierende Ursachen des Hirninfarktes im Unterschied zur TOAST-Klassifikation nach dem Evidenzgrad des ursächlichen Zusammenhangs beschrieben und in der Therapieplanung berücksichtigt werden (Amarenco *et al.* 2013).

2.3 Pathophysiologie

• Die regionale Hirnperfusion, gemessen am regionalen zerebralen Blutfluss (rCBF), kann symptomlos zwischen 20 und 60 ml/100 g (Hirnparenchym)/Minute (min) schwanken. Die

Perfusion wird durch Autoregulation bei arteriellen Mitteldrücken zwischen 50 und 150 mmHg konstant gehalten.

• Bei einem rCBF unterhalb 15 ml/100 g/min stellen die Hirnzellen durch die Hypoxie ihre aktive Funktion ein und es kommt zum Funktionsausfall der betroffenen Gewebeanteile. Dieser Zustand der Ischämie ist zunächst reversibel und die Zellstrukturen sind noch erhalten (Penumbra), da der Energiebedarf des Strukturstoffwechsels zur Aufrechterhaltung der Zellstruktur im Gegensatz zum Funktionsstoffwechsel geringer ist.

• Bei länger anhaltender Ischämie oder Absinken des rCBF unterhalb von 8 ml/100 g/min (Infarktschwelle) kann der Strukturstoffwechsel nicht mehr aufrechterhalten werden. Die Zellstruktur wird irreversibel geschädigt und es kommt zur Nekrose des Hirnparenchyms und zur Ausbildung eines Infarktes (Winter und Hacke 1998).

Meist bildet sich im Zentrum des Ischämiegebietes ein Infarkt aus, wohingegen die Umgebung (Penumbra) bei rechtzeitiger Reperfusion mit entsprechender neurologischer Verbesserung der Funktion erhalten bleibt. Im günstigsten Fall betrifft der Infarkt ein funktionell ersetzbares Areal, sodass nach Rückbildung der Ischämie die neurologischen Ausfälle vollkommen reversibel sind.

Es gibt eine Reihe von Faktoren, die einen Einfluss auf die Ausdehnung der Ischämie- beziehungsweise Infarktzone haben. Dazu gehören an erster Stelle die Kollateralen, durch die zumindest vorrübergehend eine ausreichende Blutversorgung im Ischämieareal aufrechterhalten werden kann. Weitere relevante Faktoren sind die Ischämiezeit, eine raumfordernde Ödembildung des Infarktareals, eine Hyperthermie, ein hoher Blutglucosespiegel, bei dem es vermutlich über eine erhöhte Laktatazidose zu einer verminderten Ischämietoleranz kommt, sowie eine zerebrale Unterversorgung mit O2 durch eine schlechte Sauerstoffsättigung und eine verminderte physiologische Hämoglobinkonzentration.

2.4 Komplikationen eines zerebralen Infarktes

Bei jedem zerebralen Infarkt kommt es zu einer mehr oder weniger ausgeprägten Hirnödembildung. Hierbei lässt sich zwischen einem vasogenen Ödem infolge von Gefäßpermeabilitätsstörungen und einem zytotoxischen Ödem durch Wassereinlagerung in ischämisch geschädigte Zellen unterscheiden. Zunächst kann die Hirnparenchymschwellung durch Kompression der inneren und Ausdehnung in die äußeren Liquorräume kompensiert werden. Im weiteren Verlauf der Hirnschwellung kommt es zu einer Kompression von noch nicht geschädigtem Hirngewebe und in Abhängigkeit der Infarktlokalisation zum Liquoraufstau.

Im fortgeschrittenen Verlauf erfolgt eine Erhöhung des intrakraniellen Druckes mit Einklemmung des Hirnstammes oder Sistieren der zerebralen Perfusion mit der Folge eines letalen Ausganges von Kleinhirn- und Großhirninfarkten. Daher tritt bei jüngeren Patienten mit noch vorhandenem höheren Hirnvolumen und dadurch schmaleren Liquorräumen diese letale Komplikation früher ein. Zudem führt das Hirnödem im Infarktareal durch Kompression zu einer lokalen Erhöhung des intrakraniellen Druckes, wodurch der Perfusionsdruck, der durch die Kollateralversorgung aufrechterhalten wird, je nach Größe des Ödems unter die kritische Grenze absinken kann. Somit kann es auch zu einer deutlichen Zunahme der Ausdehnung des ursprünglichen Infarktareals kommen. Bei großen Infarkten tritt häufig eine hämorrhagische Transformation auf, bei der es sich um petechiale Einblutungen in das Infarktareal handelt. Bei der hämorrhagischen Transformation kommt es jedoch zu keiner für den klinischen Verlauf relevanten Raumforderung. Dagegen gehen kompakte Blutungen mit deutlichem raumfordernden Effekt mit einer klinischen Verschlechterung einher und können eine dekompressive Kraniotomie erforderlich machen.

Die akute zerebrale Ischämie wird in verschiedene Entwicklungsstadien eingeteilt, von denen die diversen Therapieoptionen abhängen. Kurzzeitige neurologische Defizite (einige Minuten), wie bei der transitorisch ischämischen Attacke (TIA), gehen häufig mit einer morphologisch vollständigen Rückbildung einher. Bei der TIA handelt es sich um eine vorübergehende fokal-neurologische Störung, die auf eine zerebrale Ischämie zurückzuführen ist, ohne dass in der Bildgebung ein Infarkt nachweisbar ist. Häufige Symptome sind plötzliche Sprachstörungen, halbseitige Lähmungen, Gefühlsstörungen der Extremitäten und eine Amaurosis fugax, die sich meist innerhalb einer Stunde zurückbilden. Bei über mehrere Stunden anhaltenden Ausfällen entsteht meistens ein Hirninfarkt. Dementsprechend kann vor allem in den Frühstadien einer Ischämie durch eine schnelle Gefäßrevaskularisation ein Infarkt vermieden oder zumindest das Infarktvolumen deutlich reduziert werden. Im Falle eines bereits ausgedehnten demarkierten Hirninfarktes hat die Akuttherapie das primäre Ziel, die Vitalfunktionen zu sichern, einen neuen Schlaganfall zu vermeiden und zerebrale Folgeschäden zu verringern.

2.5 Einteilung des Schweregrads der Symptome

2.5.1 National Institutes of Health Stroke Scale

Die National-Institute-of-Health-Stroke-(Schlaganfall-)Skala ist eine Methode, mit der die durch einen Schlaganfall verursachten neurologischen Symptome objektiv quantifiziert werden

können, um den Schweregrad des Schlaganfalls abzuschätzen. Dabei wird der Punktewert sowohl als Verlaufsparameter als auch zur Beurteilung der Therapiemöglichkeiten und zur Prognoseabschätzung herangezogen.
Die *National Institutes of Health Stroke Scale* (NIHSS) beinhaltet elf Fragen, die jeweils eine spezifische Fähigkeit mit einer Punktzahl zwischen 0 und 4 bewerten. Der Wert 0 entspricht einer normalen Funktion und 4 einer vollständigen Beeinträchtigung. Einige Fragen haben nur eine Skala von 0 bis 2. Je höher der Punktewert, desto schwerer ist die Beeinträchtigung für die jeweilige spezifische Fähigkeit. Durch Addieren der Punktewerte aus allen Fragen wird der NIHSS-Score mit einem maximal möglichen Punktewert von 48 berechnet (Brott *et al.* 1989; Meyer *et al.* 2002).
Bewertet werden mit den Fragen die Bewusstseinslage, das Niveau von Sprache, der Grad des Neglectes, Gesichtsfeldausfälle, Okulomotorik, Motorik von Armen und Beinen, Ataxie, Dysarthrie und Sensibilitätsstörungen.

2.5.2 Modifizierte Rankin-Skala

Die modifizierte Rankin-Skala (mRS) ist ein Messinstrument, die den Grad der neurologischen Behinderung nach einem Schlaganfall anhand einer numerischen Skala beschreibt, und wurde 1957 von Rankin eingeführt. Die heutzutage verwendete Modifikation wurde 1988 von van Swieten et al. publiziert (van Swieten *et al.* 1988).
Zudem wird die Skala für die Beschreibung des neurologischen Defizites in klinischen Studien und bei der medizinischen Qualitätssicherung verwendet.
Die sechs Abstufungen der Skala sind wie folgt definiert:

0 Kein neurologisches Defizit
1 Ischämischer Schlaganfall mit funktionell irrelevantem neurologischen Defizit
2 Leichter ischämischer Schlaganfall mit funktionell geringgradigem Defizit und/oder leichter Aphasie
3 Mittelschwerer Apoplex mit deutlichem Defizit (Hilfe im Alltag nötig, Gehen ohne Hilfe) und/oder mittelschwerer Aphasie
4 Schwerer Apoplex (Hilfe im Alltag nötig, ohne Hilfe nicht gehfähig) und/oder komplette Aphasie
5 Invalidisierender Apoplex (Bettlägerig, auf permanente pflegerische Hilfe angewiesen, inkontinent)
6 Ischämischer Schlaganfall mit tödlichem Ausgang

2.5.3 Barthel-Index

Mit dem Barthel-Index (BI) können Alltagsfunktionen systematisch erfasst und beurteilt werden (Mahoney und Barthel 1965). Dabei werden zehn unterschiedliche Tätigkeitsbereiche mit Punkten bewertet (Essen, Baden, Körperpflege, An-/Auskleiden, Stuhl-/Urinkontrolle, Toilettenbenutzung, Bett-/Stuhltransfer, Mobilität, Treppensteigen). Die minimale Punktzahl beträgt 0 (komplette Pflegebedürftigkeit), die maximal erreichbare Punktzahl ist 100 (Selbstständigkeit).

2.6 Bildgebung beim akuten ischämischen Schlaganfall

Als wesentlichste zerebrale Bildgebung in der Akutdiagnostik wird meist eine cranielle Computertomographie (CCT) durchgeführt, um eine Blutung als Ursache der Symptome auszuschließen, sodass die Standardtherapie mit i. v. rtPA-Lyse eingeleitet werden kann.
Mittels nativer CCT oder der Magnetresonanztomographie (MRT) kann anhand des ischämischen Ödems die Ausdehnung des Ischämiekerns bestimmt werden. Dabei ist die diffusionsgewichtete Bildgebung (*diffusion weighted imaging* – DWI) in der MRT deutlich sensitiver in der Darstellung des Ödems, insbesondere im vertebrobasilären Stromgebiet, als in der CCT. Der *Alberta Stroke Program Early Computed Tomography Score* (ASPECTS) wird zur systematischen Beschreibung der räumlichen Ausdehnung von Ischämien beziehungsweise der Ödemausdehnung im Stromgebiet der Arteria cerebri media (ACM) verwendet. Hierzu wird das ACM-Stromgebiet in zehn Abschnitte eingeteilt (Barber 2000). Dazu gehören der Nucleus caudatus, Nucleus lentiformis, Capsula interna, Insula und sechs Regionen des vorderen, lateralen und hinteren ACM-Kortex auf Niveau und oberhalb der Basalganglien (‚M1'–‚M6'). Die Berechnung des Scores erfolgt durch Abzug von jeweils einem Punkt für jede betroffene Region, in der eine ischämiebedingte Läsion abgrenzbar ist. Dementsprechend wird bei fehlendem Nachweis von ischämischen Läsionen ein ASPECTS-Wert von 10 vergeben. Dagegen liegt bei ischämischen Läsionen, die das gesamte Stromgebiet der ACM betreffen, ein Wert von 0 vor. Eine weitere Aufgabe der nativen CCT ist die Feststellung eventueller Komplikationen eines akuten Infarktes, wie eine raumfordernde Ödembildung oder Einblutung.
Nähere Informationen zu dem möglicherweise noch rettbarem Risikogewebe der Penumbra kann die erweiterte multiparametrische CT, die eine CT-Perfusion (CTP) beinhaltet oder das multiparametrische MRT mit DWI und Perfusions-MRT (*Perfusion weighted imaging* – PWI), liefern. Die CTP oder MR-Perfusion sind funktionelle Verfahren, mit deren Hilfe der regionale Stoffwechsel und die Durchblutung zur Differenzierung zwischen reversibler oder irreversibler

Ischämie dargestellt werden können. Als weitere standardmäßige Bildgebung wird eine intrakranielle Gefäßdiagnostik mit der Frage nach der Lokalisation des Verschlusses, dem Ausmaß leptomeningealer Kollateralisierung oder einem Zustand nach Reperfusion mittels CT-Angiographie und der MR-Angiographie durchgeführt. Unerlässlich ist auch die Darstellung der extrakraniellen hirnversorgenden Gefäße (A. carotis und Vertebralarterien) zum Ausschluss höhergradiger Stenosen oder Verschlüsse sowie zur Planung des Zugangsweges für die endovaskuläre Behandlung. Die CT-Angiographie ist ein wenig untersucherabhängiges, breit verfügbares Verfahren, wohingegen die MR-Angiographie ein ebenfalls in der Akutdiagnostik zerebraler Ischämien weitverbreitetes Verfahren mit jedoch geringerer Verfügbarkeit, höherem Zeitaufwand und größerer Empfindlichkeit gegenüber Bewegungsartefakten sowie möglichen artefaktbedingten Interpretationsproblemen bei pathologischen Gefäßbefunden darstellt. Ein Vorteil der MR-Angiographie ist, dass sie sowohl gestützt auf Kontrastmittel (KM) als auch KM-frei mit der sogenannten *Time of flight MRA* (TOF-MRA) durchgeführt werden kann (Boujan *et al*. 2018).
Die extra- und intrakranielle Doppler-/Duplex-Sonographie ist ein in der Akutdiagnostik des akuten ischämischen Schlaganfalls, bedingt durch relevante Einschränkungen, eher nachrangiges Verfahren. Zu den größten Nachteilen zählen die Untersucherabhängigkeit und die eingeschränkte Beschallbarkeit der intrakraniellen Arterien, insbesondere im distalen Abschnitt der Arteria basilaris.

2.7 Infarkttypen

2.7.1 Territorialer Hirninfarkt

Territorialinfarkte sind Infarkte der Hirnrinde meist mit Ausdehnung in das Marklager, die sich auf das Versorgungsgebiet (Territorium) der verschlossenen großen Hirnarterien oder deren Äste erstrecken. Die keilförmige Konfiguration der Infarkte ist in der Regel bei Verschluss der A. cerebri media (ACM) zu finden. Territorialinfarkte sind im Allgemeinen durch akute intrakranielle embolische Gefäßverschlüsse bedingt und entstehen deutlich seltener durch Thrombosen bei einer akuten lokalen Verschlusskrankheit. Die Unterteilung der Infarktgebiete orientiert sich an den großen Hirnarterien und ihren Versorgungsgebieten. Die paarig angelegte Arteria carotis interna (ACI) und Arteria vertebralis (AV) sowie deren Äste übernehmen die zerebrale Blutversorgung. Sie sind über den Circulus arteriosus cerebri (Circulus arteriosus Willisii) untereinander verbunden. Typische Emboliefolgen sind Verschlüsse des Hauptstammes der ACM (M1-Segment), der intrakraniellen Aufteilung der ACI (‚Karotis-T'), des Kopfes der A. basilaris und der daraus abgehenden Aa. cerebelli

superiores, der Aa. cerebri posteriores und der Thalamusperforatoren. Dissektionen betreffen am häufigsten die ACI im Abschnitt zwischen dem Karotisbulbus und dem Abgang der A. ophthalmica sowie den extrakraniellen Verlauf der AV (V1- und V3-Segment). Ursache für Verschlüsse des unteren Basilarisabschnittes sind meist Folgen der Arteriosklerose. Die mittelgroßen und kleinen Arterien sind über Anastomosen miteinander verbunden und können bei einzelnen Gefäßverschlüssen einen Kollateralkreislauf aufrechterhalten. Die von den Hauptstämmen vertikal abgehenden Basalganglienarterien (Aa. lenticulostriatae) sind Endarterien ohne Kollateralen. Bei einem Verschluss kommt es daher nach kurzer Zeit zu einer kritischen Ischämie und schließlich zum Infarkt der Basalganglien. Dementsprechend entstehen bei sich chronisch entwickelnden intrakraniellen Verschlüssen, zum Beispiel bei fortgeschrittener Arteriosklerose, seltener territoriale Infarkte, wenn sich ausreichend suffiziente Kollateralkreisläufe ausgebildet haben. Ursache für Territorialinfarkte können kardiogene, paradoxe oder arterio-arterielle Embolien sein. Paradoxe Embolien sind vom venösen in das arterielle System verschleppte Emboli des Körperkreislaufs durch einen Defekt im Bereich der Herzsepten. Neben der Arteriosklerose ist bei jüngeren Patienten eine spontane Dissektion der zervikalen Hirnarterien die häufigste Ursache arterio-arterieller Embolien. Daneben sind eine traumatische Dissektion, fibromuskuläre Dysplasien, Vaskulitiden und eine bakterielle Endokarditis als seltenere Ursachen zu finden. Als weitere Ursachen von Territorialinfarkten kommen entzündliche oder drogeninduzierte Vaskulopathien in Betracht. Bei drogeninduzierten Vaskulopathien durch Einnahme von Amphetaminen oder Kokain treten neben ischämischen Läsionen auch Blutungen auf. Angiographisch sind Kaliberschwankungen oder Gefäßabbrüche nachweisbar. Die CT und MRT als wegweisende Bildgebungsmodalitäten zeigen in > 80 Prozent Infarkte im Territorium der A. cerebri media (ACM). Des Weiteren gehören Infarkte der Stammganglien im Versorgungsgebiet der lateralen lenticulostriären Äste (Putamen, partiell Globus pallidus, Teile der Capsula interna, Capsula externa, Claustrum, Corpus des nucleus caudatus) zum ACM-Territorium. Am zweithäufigsten sind Infarkte im Territorium der A. cerebri posterior (ACP) mit Läsionen im Occipitallappen, des basalen Temporallappens, Thalamus (auch bilateral paramediane Läsionen bei anatomischer Variante eines dominanten Perforators aus dem P1-Segment). In weniger als fünf Prozent ist das Gefäßterritorium der A. cerebri anterior (ACA) betroffen mit Verteilung der Läsionen frontal, parietal sowie entsprechend des Versorgungsgebietes der medialen lenticulostriären Arterien im Caput nuclei caudati und vorderen Schenkel der Capsula interna. Infarkte des Hirnstammes sind in Abhängigkeit der Thrombusausdehnung in der Basilararterie bilateral in Tegmentum und Basis pontis sowie bei Basilarisspitzenthrombus im bilateralen paramedianen Thalamus und Mittelhirn lokalisiert. Infarkte der dorsolateralen Medulla-oblongata treten bei Verschluss der distalen, intraduralen AV (V4-Segment) auf, wohingegen die Ausdehnung der Kleinhirninfarkte von den variablen Territorien der Kleinhirnarterien

abhängt. Bei Verschluss der Arteria inferior posterior cerebelli (PICA) liegen die Läsionen in den basalen Kleinhirnhemisphären mit rostraler Ausdehnung über die Fissura horizontalis hinaus, den Tonsillen und Teilen des Vermis. Infarkte des Territoriums der A. cerebelli superior (SCA) liegen vor allem im mittleren Kleinhirnstiel und Infarkte des Territoriums der Arteria inferior anterior cerebelli (AICA) im Vermis superior, in den kranialen Anteilen der Kleinhirnhemisphären, den Lobuli quadrangulares sowie ausgedehnten Anteilen der weißen Substanz und der Kerngebiete.

Die Akuttherapie von Territorialinfarkten hat die Reperfusion von intrakraniellen Gefäßverschlüssen und hochgradigen Stenosen durch eine pharmakologische, endovaskuläre oder operative Rekanalisation zum Ziel. Sowohl die Daten der großen randomisierten Studien (National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group 1995; Hacke W. *et al.* 2004; Lees *et al.* 2010; Emberson *et al.* 2014) als auch die Daten des SITS-Registers (Wahlgren *et al.* 2007, 2008) zeigten, dass die i. v. Thrombolyse mit 0,9 mg/kg KG rtPA („recombinant tissue plasminogen activator‘) innerhalb eines 3-Stunden-Zeitfensters nach einem ischämischen Schlaganfall in einem signifikant verbesserten klinischen Ergebnis resultierte.
Die Ergebnisse der ECASS-III-Studie (Hacke *et al.* 2008) gaben dazu Anlass, dass die Zulassung für rtPA im November 2010 in Europa von einem 3-Stunden- auf ein 4,5-Stunden-Zeitintervall ausgedehnt wurde. Mittlerweile ist eine Behandlung in einem noch späteren Zeitfenster bei ausgewählten Patientengruppen nach erweiterten Bildgebungsparametern mittels multimodaler MRT und CT (z. B. Mismatch-Bildgebung in der CT-Perfusion oder MRT-Perfusion) als individueller Heilungsversuch möglich (Röther *et al.* 2002; Schellinger *et al.* 2007; Santulli 2012). Das Auslösen einer sekundären zerebralen Einblutung ist ein Hauptproblem der rekanalisierenden Fibrinolyse. Daher gilt entsprechend der Leitlinien in der Regel die Lysebehandlung bei Patienten mit schweren Infarkten (NIHSS > 25), ausgedehnten Infarktfrühzeichen und unkontrollierbarer Hypertonie (RR > 185/110 mmHg) als kontraindiziert. Die Frage, ob die systemische rtPA-Thrombolyse auch bei einem von den Zulassungskriterien abweichenden Patientenkollektiv einen Nutzen zeigt, wurde in der IST-3-Studie evaluiert (Sandercock *et al.* 2012). Insbesondere existierten keine Hinweise auf eine bestimmte obere Altersbegrenzung. Vor allem bei Patienten über 80 Jahre war der positive Effekt einer rtPA-Behandlung besonders ausgeprägt. Darüber hinaus zeigten mehrere Beobachtungsstudien die Sicherheit und Effektivität der rtPA-Therapie bei älteren Patienten (Toni *et al.* 2008; Mishra *et al.* 2010). Inwieweit bei Patienten mit einem niedrigen NIHSS (0 – 4) ein Nutzen der systemischen Thrombolyse vorliegt, wurde in einer Metaanalyse von randomisierten Studien evaluiert, in denen sich ein Therapievorteil der systemischen Lysetherapie bei gleichzeitig geringem Risikoprofil feststellen ließ (Emberson *et al.* 2014).

Demnach sollte eine kurzfristig rückläufige neurologische Symptomatik kein Ausschlusskriterium für eine rtPA-Therapie sein, sofern noch ein messbares, behinderndes Defizit besteht. Auch Patienten mit großem neurologischen Defizit (NIHSS ≥ 22) hatten keinen geringeren Nutzen der systemischen Lysetherapie, wie eine aktualisierte kombinierte Analyse der neun rtPA-Studien zeigte (Emberson *et al.* 2014).

Meist nach erfolgter systemischer Lyse, aber auch als primäre Therapie bei Patienten mit entsprechendem fokal-neurologischen Defizit, die wegen einer Antikoagulation keine systemische Thrombolyse mit rtPA erhalten können, wird eine mechanische Thrombektomie als Rekanalisationsmaßnahme durchgeführt (Steiner *et al.* 2013; Hankey *et al.* 2014). Eine ausführliche Beschreibung der mechanischen Thrombektomie erfolgt in Kapitel 2.8.

2.7.2 Hämodynamischer Hirninfarkt

Bei hämodynamischen Infarkten kommt es durch einen zu geringen Perfusionsdruck in den peripheren Hirnarterien zu einer Minderperfusion des Parenchyms, wobei Infarkte vor allem in den Grenzzonen zwischen arteriellen Versorgungsgebieten oder Endstromgebieten von penetrierenden Arteriolen auftreten.
Die im typischen Fall zugrunde liegende Pathogenese bei hämodynamischen Infarkten ist eine vollständig ausgeschöpfte Reserve der Autoregulation im minderperfundierten Areal.
Durch Abfall des arteriellen Blutdrucks oder Anstieg des Venendrucks kommt es zu einem passiven Absinken der Hirnperfusion. Ein erhöhter Sauerstoffbedarf wie bei komplexen zerebralen Leistungen kann im Sinne eines Steal-Phänomens in benachbarten Arealen zur klinisch manifesten Ischämie führen, wenn eine Steigerung der Perfusion bei bereits maximal dilatierten Widerstandsgefäßen nicht mehr möglich ist. Zunächst ist der Perfusionsdruck dort kritisch erniedrigt, wo die Versorgungswege am längsten sind, wodurch das charakteristische morphologische Schädigungsmuster der Grenzzonen- und Endstrominfarkte zustande kommt. Dabei besteht eine reversible Einschränkung der zerebralen Funktion, die weit über die Infarktzonen hinausgeht.
Dagegen treten hämodynamisch kritische Situationen seltener auf, wenn eine Obstruktion bereits über längere Zeit besteht, da in dem Fall eine Ausbildung einer suffizienten Kollateralisierung stattgefunden hat. Ursache hämodynamischer Infarkte sind meistens langsam entstandene Verschlüsse oder hochgradige Stenosen mit schlechter Kollateralisierung, selten dagegen Emboliefolgen. Zudem kann bei Erkrankungen multipler Hirnarterien, zum Beispiel durch Arteriosklerose, eine Takayasu-Arteriitis oder multiple Dissektionen, eine Kompensation durch Kollateralen vermindert sein oder vollständig ausbleiben. Neurologische Defizite können bei hämodynamischen Hirninfarkten durch Abfall

des systolischen Blutdruckes auftreten. Die zunächst reversiblen Einschränkungen der zerebralen Funktion zeigen sich in globalen neuropsychologischen Defiziten wie Konzentrationsstörung oder Adynamie. Eine Anhebung des Blutdruckes bewirkt unmittelbar eine Besserung der neurologischen Symptome. Von relevanter Bedeutung ist daher, dass ein Bedarfsbluthochdruck aufrechterhalten werden muss, da eine zu starke pharmakologische Drucksenkung weitere Hirninfarkte induziert. Hämodynamische Läsionsmuster sind in der CCT sowie noch sensitiver in der cMRT abgrenzbar und sind kortikal in der Grenzzone und als Endstrominfarkte periventrikulär und vor allem im supraventrikulären Marklager lokalisiert. Als spezielle Untersuchungsmodalität ermöglicht die CO2- oder Diamox-CT-Perfusion-Provokation die quantitative Bestimmung des Ausmaßes einer hämodynamischen Störung bis hin zur paradoxen Durchblutungsminderung bei Steal-Mechanismen. Teil der Akuttherapie ist die Aufrechterhaltung der Bedarfsperfusion in der Akutphase – zum einen indem der Blutdruck nicht gesenkt wird und zum anderen durch eine kardial tolerierbare induzierte Hypertension. Lebensbedrohliche ausgedehnte Hirninfarkte, die sich aus ‚hämodynamischen' Infarkten entwickeln, sind eher die Ausnahme. Auch wenn sich längerfristig in manchen Fällen eine spontane klinische Besserung durch eine zunehmende Adaptation der Kollateralkreisläufe einstellt, ist die Spontanprognose hämodynamischer Ischämien ungünstig. Eine endovaskuläre oder operative Rekanalisation, beispielsweise bei hochgradigen extrakraniellen Karotisstenosen oder bilateralen Vertebralisstenosen, kann dann erforderlich werden.

2.7.3 Mikroangiopathischer Hirninfarkt

Mikroangiopathische Infarkte entstehen durch eine zerebrale Mikroangiopathie, bei der es sich um eine Okklusion kleiner, langer tief in das Hirngewebe penetrierender Arterien (Aa. centrales anterolaterales) und Arteriolen mit Ausbildung subkortikal lokalisierter herdförmiger Parenchymläsionen handelt. Ätiologisch findet sich bei der zerebralen Mikroangiopathie überwiegend eine Lipohyalinose, die mit einer ausgeprägten chronischen arteriellen Hypertonie assoziiert ist. Seltener sind mikroangiopathische Veränderungen die Folge eines lange bestehenden Diabetes mellitus. Werden bei Patienten im jüngeren oder mittleren Lebensalter neuroradiologische Kriterien der Mikroangiopathie gefunden, ohne dass entsprechende Risikofaktoren vorliegen, muss jedoch eine Vaskulitis (erregerbedingt/allergisch, drogeninduziert nach Einnahme von Kokain, Amphetaminen) ausgeschlossen werden. Daneben existiert als genetische mikroangiopathische Erkrankung CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), die schon im jungen Erwachsenenalter zu Schlaganfällen führt. Die Mikroangiopathie manifestiert sich häufig durch ‚kleine' Schlaganfälle mit oft rein sensiblen

oder rein motorischen Ausfällen, die nach kurzer Zeit reversibel sind und eine relativ gute Rückbildung auch bei ausgeprägter Symptomatik haben. Selten treten eine schnell reversible Aphasie oder homonyme Gesichtsfelddefekte auf. Dagegen kommen als Folge einer Mikroangiopathie anders als bei den Territorialinfarkten Bewusstseinstrübungen oder eine forcierte Blickwendung (‚Déviation conjuguée') zur Herdseite nicht vor. Zu den charakteristischen schweren Symptomen als Folge häufig rezidivierender mikroangiopathischer Infarkte gehören neuropsychologische Defizite (‚Multiinfarktdemenz'), Affektdurchbrüche und Pseudobulbärparalysen. Bei der hypertensiven Mikroangiopathie zeigt sich in der CCT und cMRT ein Muster aus lakunären Infarkten in den Stammganglien, Thalamus, Pons und im Marklager sowie periventrikulär betont und im tiefen Marklager lokalisierte multiple rundliche, konfluierende oder diffuse, flächige Läsionen. Zudem kommt es in fortgeschrittenen Fällen zu einer globalen Hirnatrophie. Die hypertensive und diabetische Mikroangiopathie betreffen Gefäße, die in der MRA, CTA und konventionell-angiographisch nicht mehr darstellbar sind und zeigen daher typischerweise einen unauffälligen Befund. Liegen der Mikroangiopathie Vaskulitiden zugrunde, sind periphere Gefäßabbrüche und Kaliberschwankungen kleinerer Arterien in der CTA-/MRA- und DSA-Bildgebung charakteristisch. Typisch für Mikroangiopathien sind das Auftreten petechialer Mikroblutungen und postischämischer Gliosen, deren Hauptlokalisationen Stammganglien, Thalamus, Hirnstamm und Kleinhirn sind. Eine akute kausale Therapie mikroangiopathischer Hirninfarkte existiert nicht.

2.7.4 Lakunärer Hirninfarkt

Bei den erwähnten lakunären Infarkten handelt es sich um kleine, maximal 15 Millimeter messende mit Liquor gefüllte ischämische Läsionen des tiefen Marklagers, der Basalganglien und des Hirnstamms, die aus einem Astverschluss der penetrierenden Hirnarterien der A. cerebri media, A. cerebri posterior, A. basilaris und weniger häufig der A. cerebri anterior sowie der Vertebralarterien resultieren. Ätiologische Faktoren der Lakunen sind typischerweise eine Arteriosklerose oder Lipohyalinose infolge einer chronisch hypertensiven Vaskulopathie. Selten entstehen Lakunen durch Mikroembolien kardialer oder arterio-arterieller Genese oder Dissektionen der penetrierenden Arterien. Lakunen können häufig Ursprung hypertensiver Blutungen sein (Ahlhelm *et al.* 2009). Die CT-Bildgebung ist vor allem bei kleinen Lakunen wenig sensitiv. Dagegen sind Lakunen in der MRT-Bildgebung gut nachweisbar.

2.8 Grundlagen der endovaskulären Schlaganfalltherapie

2.8.1 Entwicklung der Stent-Retriever-Thrombektomie

Der zunächst rein pharmakologische Ansatz zur lokalen, intraarteriellen Therapie mit verschiedenen Thrombolytika wurde in mehreren klinischen Studien untersucht. Dazu gehörte die PROACT-Studie, in der Patienten mit Verschlüssen der proximalen A. cerebri media mit Pro-Urokinase behandelt wurden. Kathetertechniken mit mechanischer Manipulation am gefäßokkludierenden Thrombus waren nicht zugelassen. Obwohl es innerhalb von sechs Stunden nach Symptombeginn zu einer signifikanten Verbesserung des klinischen Status im Vergleich zur intraarteriellen Heparingabe kam, erhielt Pro-Urokinase keine Zulassung von der FDA (Tirschwell 2000). Es folgte die Entwicklung von unterschiedlichen mechanischen Rekanalisationssystemen, die vorerst bei Patienten, die eine Kontraindikation für die systemische rtPA-Therapie hatten, eingesetzt wurden (Smith *et al.* 2005). Besonders bei Verschluss großer Arterien beziehungsweise bei größeren Thromben führt die systemische Thrombolyse nur bedingt zu einer Rekanalisation der Gefäße. Schon die ersten klinischen Studien zeigten, dass mechanische Thrombektomieverfahren zu einer effektiveren Rekanalisation als die intravenöse Thrombolyse führten, allerdings noch ohne in einem guten klinischen Outcome zu resultieren, was auf die lange Dauer und Komplexität der Behandlung zurückzuführen war (Rha und Saver 2007).

2.8.2 Alte Thrombektomiesysteme

Das erste für die mechanische Thrombektomie verwendete Instrument, war eine Nitinol-Spirale mit der Bezeichnung *Mechanical Embolus Removal in Cerebral Ischemia* (MERCI) *Retriever* (Stryker Neurovascular, Mountain View, California), das distal des Thrombus platziert wurde, um diesen en bloc herauszuziehen. Zielgefäße waren die großen Hirnarterien wie der Hauptstamm (M1-Segment) der A. cerebri media und vertebrobasiläre Arterien. Für distal davon gelegene Thromben war das System nicht geeignet (Asadi *et al.* 2015). In die prospektive, nicht randomisierte MERCI-Studie wurden Schlaganfallpatienten mit Kontraindikation für eine systemische intravenöse Lyse eingeschlossen. Bei den Patienten wurde innerhalb von acht Stunden nach Beginn der Symptome eine mechanische Thrombektomie mit dem MERCI-Retriever durchgeführt, bei der ein Rekanalisationserfolg von 46 Prozent erzielt wurde. Die Rate an symptomatischen intrakraniellen Blutungen lag bei 7,8 Prozent. Eine Zulassung des MERCI-Retrievers in den USA erfolgte 2004 durch die FDA für Patienten mit einer Kontraindikation gegen eine systemische Lyse oder bei unwirksamer systemischer Lyse (Smith *et al.* 2005). Die nachfolgende multizentrische prospektive Multi-

MERCI-Studie war die zweite Studie zur Sicherheit und Wirksamkeit des Merci-Retrieval-Systems. Es wurden Patienten mit einem mittleren bis schweren ischämischen Schlaganfall, die für eine Therapie mit rtPA nicht geeignet waren oder bei denen eine solche unwirksam war, eingeschlossen. Die Rate an erfolgreichen Rekanalisationen betrug 57,3 Prozent unter alleiniger Verwendung des Merci-Retrieval-Systems mit einer Rate an symptomatischen intrazerebralen Blutungen von 9,8 Prozent. Bei 36 Prozent der Patienten lag drei Monate nach der Behandlung ein gutes neurologisches Ergebnis (modified Rankin Scale ≤ 2) vor (Smith *et al.* 2008). Der Penumbra-Separator ist ein weiteres Thrombektomiesystem, mit dem durch Thrombusfragmentierung und gleichzeitige Aspiration eine Revaskularisierung erreicht werden sollte. Hierzu wurde der Aspirationskatheter vor den Thrombus gebracht, der Separator durch den Aspirationskatheter in den Thrombus vorgeschoben und der Thrombus durch Vor- und Rückwärtsbewegung des Separators fragmentiert, während eine elektrische Pumpe negativen Druck erzeugte und die Fragmente über den Aspirationskatheter abgesaugt hat (Asadi *et al.* 2015). In die multizentrische prospektive Penumbra-Pivot-Studie zur Wirksamkeit und Sicherheit des Penumbra-Rekanalisationssystems (Alameda, California, USA) wurden 125 Patienten mit einem ischämischen Schlaganfall, die sich innerhalb des 8-Stunden-Zeitfensters befanden, eingeschlossen. Bei den Patienten lag eine Kontraindikation für eine i. v. Thrombolyse vor oder ging ein frustraner Therapieversuch mit i. v. Thrombolyse voraus. In dieser Studie wurde bereits eine Rekanalisationsrate von 81,6 Prozent erreicht. Die Rate an symptomatisch intrakraniellen Blutungen betrug 11,2 Prozent. Bei 25 Prozent aller Patienten konnte in der 3-Monatsverlaufskontrolle ein gutes neurologisches Ergebnis (modified Rankin Scale ≤ 2) mit einer 3-Monatsmortalität von 33 Prozent festgestellt werden (Po Sit 2009). Jedoch erzielten die ersten randomisierten Studien zur endovaskulären Schlaganfallbehandlung, die im Jahre 2013 veröffentlicht wurden, keinen klinischen Vorteil der endovaskulären Therapie gegenüber der systemischen Lyse (IMS III (Broderick *et al.* 2013), MR-RESCUE (Kidwell *et al.* 2013), SYNTHESIS (Ciccone *et al.* 2013)). Diese zeitgleich im New England Journal of Medicine publizierten Beiträge berichteten von einem fehlenden Nutzen der endovaskulären Therapie im Vergleich zur medikamentösen intravenösen Thrombolyse. Es zeigte sich jedoch schnell, dass diese drei Studien den aktuellen Fortschritt und die Möglichkeiten der endovaskulären Therapie nicht abbilden konnten: Es wurden hauptsächlich alte Methoden statt der neuen Stent-Retriever (SR) zur Rekanalisierung eingesetzt. Zum Beispiel wurden in der IMS-III-Studie nur bei einem Prozent der Patienten SR verwendet. Daneben waren die zu lange Zeitspanne vom Beginn der Symptome bis zur Rekanalisation und der Einschluss nicht geeigneter Patienten als ursächlich für die unbefriedigenden Ergebnisse anzusehen.

2.8.3 Stent-Retriever

Die Einführung des Stent-Retrievers (SR) eröffnete neue Möglichkeiten in der endovaskulären Therapie des akuten ischämischen Schlaganfalls. Der erste publizierte Fall, bei dem bei einer Thrombektomie (TE) ein SR verwendet wurde, stammt aus dem Jahr 2008 (Pérez *et al.* 2012). Der Solitaire-Stent wurde ursprünglich zur endovaskulären Behandlung intrakranieller Aneurysmen konzipiert und später als erster SR von der FDA für die mechanische Rekanalisation bei Verschlüssen intrakranieller Gefäße freigegeben (Hameed *et al.* 2017). Dieses selbstexpandierende, an einem Führungsdraht fixierte Stent-ähnliche Thrombektomiesystem wird über einen Mikrokatheter über die Leistenarterien bis in das Hirngefäß vorgeschoben, am Thrombus entlanggeführt und über dem Thrombus entfaltet. Der Thrombus verhakt sich in den Stent-Maschen und wird zusammen mit dem SR unter Aspiration des Führungskatheters aus dem Gefäß herausgezogen (**Abb. 1–3**). In den Jahren darauf folgte die Entwicklung weiterer SR anderer Hersteller, die auf vergleichbare Weise funktionieren. Eine Auswahl der bekanntesten SR sind der Trevo (Concentric Medical), IRIIS Plus and OptiCell (MindFrame, Irvine, USA), Aperio (Acandis, Pforzheim, Germany), ReVive (Micrus, Codman and Shurtleff, Raynham, USA) und pREset (phenox).

Die deutlich höheren Rekanalisationsraten von SR gegenüber dem Merci-Device wurden schon früh in zwei randomisierten Studien belegt (Nogueira 2012; Saver *et al.* 2012).
Die erste größere prospektiv randomisierte Studie, die die höhere Wirksamkeit der TE gegenüber der i. v. Lysetherapie nachweisen konnte, war die MR-Clean-Studie (Fransen *et al.* 2014) mit 500 randomisierten Patienten, von denen 233 einer endovaskulären Therapie zugeführt wurden. Einschlusskriterien waren der bildgebende Nachweis eines Gefäßverschlusses im vorderen Stromgebiet der intrakraniellen Gefäße (A. carotis interna, A. cerebri media, A. cerebri anterior) und die Möglichkeit der endovaskulären Behandlung innerhalb von sechs Stunden nach Symptombeginn. Der mittlere NIHSS betrug 17, wobei auch Patienten mit niedrigem neurologischen Defizit eingeschlossen wurden (NIHSS 2–42). Der mediane ASPECT-Score betrug 9. Nach durchschnittlich 85 Minuten erhielten 87 Prozent der Patienten eine Thrombolyse mit rtPA. Bei 92 Prozent der Patienten lag ein distaler Karotisverschluss oder proximaler Media-(M1-)Verschluss vor. Der primäre Endpunkt der Studie war die Wahrscheinlichkeit einer Verbesserung des Punktewertes (Shift-Analyse) auf der modifizierten Rankin-Skala (mRS), nach der das Ausmaß der Behinderung erfasst wurde. Dabei ergab sich ein adjustierter Odds-Ratio (OR) von 1,67 (95%CI 1,21–2,30) zum Vorteil der TE. In der endovaskulären Gruppe erreichten 33,6 Prozent der Patienten ein gutes klinisches Ergebnis gegenüber 19,1 Prozent in der Kontrollgruppe (‚number needed to treat' [NNT]: 7) (Berkhemer 2015). Zwischen den interventionell behandelten Patienten und der

Kontrollgruppe lagen die Raten an symptomatischen intrakraniellen Blutungen nach ECASS II (definiert als intrakranielle Blutungen mit einer neurologischen Verschlechterung um $\geq$ 4 Punkte auf der NIHSS) bei 7,7 vs. 6,4 Prozent und die Mortalitätsraten bei 21 vs. 20 Prozent in einem vergleichbaren Bereich.
Nach Auswertung der MR-CLEAN-Ergebnisse wurden mehrere andere Studien (EXTENDIA (Campbell *et al.* 2015), REVASCAT (Jovin *et al.* 2015), SWIFT PRIME (Saver *et al.* 2015), ESCAPE (Goyal *et al.* 2015) letztlich aufgrund des Nachweises des deutlichen klinischen Nutzens der mechanischen TE abgebrochen.

2.8.4 Bewertung des Rekanalisationserfolges

Der Erfolg der endovaskulären Rekanalisation nach Behandlung des verschlossenen Gefäßes wird durch die TICI-(*thrombolysis in cerebral infarction*-)Skala beurteilt. Die Bewertung der Hirndurchblutung basiert auf der Darstellung des behandelten verschlossenen Gefäßes und der distalen Äste in den angiographischen Aufnahmen. Die TICI-Klassifikation dient der Prognoseeinschätzung des funktionellen Outcomes.

Die ursprüngliche TICI-Klassifikation beinhaltet folgende Abstufungen:

TICI 0	= Keine Perfusion
TICI 1	= Penetration des Thrombus mit minimaler Perfusion
TICI 2a	= Partielle Füllung (< 2/3) des abhängigen Gefäßterritoriums
TICI 2b	= Komplette Füllung des abhängigen Gefäßterritoriums mit verlangsamter Füllung
TICI 3	= Komplette Perfusion (Higashida und Furlan 2003)

In der in Stroke 2013 publizierten Konsensusschrift von drei Arbeitsgruppen wurde eine modifizierte TICI-Skala empfohlen, die *modified thrombolysis in cerebral infarction* (mTICI) genannt wurde (Zaidat *et al.* 2013). Diese sollte die TICI-2-Bewertung mit Unterteilung der Perfusion in weniger als die Hälfte (TICI 2a) und mehr als die Hälfte des betroffenen Gefäßareales (TICI 2b) vereinfachen.

Eine weitere Modifikation der TICI-Skala beinhaltet eine Erweiterung der TICI-2-Abstufung zu TICI 2c (fast vollständige Perfusion mit residuellem Verschluss einiger kortikaler Äste oder verlangsamtem Fluss) und soll eine genauere Aussage des funktionellen Outcomes ermöglichen (Almekhlafi *et al*. 2014).

2.8.5 Neue Studien zum Einsatz der Stent-Retriever-Thrombektomie im erweiterten Zeitfenster

Der Nutzen der mechanischen Rekanalisation beim ischämischen Schlaganfall innerhalb von sechs Stunden nach Beginn der Symptome konnte wie zuvor beschrieben bereits in zahlreichen Studien nachgewiesen werden. Dagegen liegen bisher nur wenige Daten über den Nutzen einer mechanischen Rekanalisation bei einem Symptombeginn von mehr als sechs Stunden vor. Die Ergebnisse einzelner nicht randomisierter Studien lassen jedoch darauf schließen, dass Patienten mit einer ausgeprägten Penumbra auch noch nach diesem Zeitraum von der mechanischen Rekanalisation profitieren können.

Diese Annahme wurde in der 2018 publizierten randomisierten DAWN-Studie (*DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention with Trevo*) untersucht (Nogueira *et al.* 2017).
Darin wird die mechanische Rekanalisation, die mit der standardmäßigen Leitlinientherapie kombiniert wird, mit einer ausschließlich standardmäßigen Leitlinientherapie bei Schlaganfallpatienten mit Symptombeginn 6 bis 24 Stunden vor der Therapie verglichen.

In die Studie wurden Patienten mit einem Verschluss der intrakraniellen A. carotis interna oder der proximalen A. cerebri media eingeschlossen, bei denen 6 bis 24 Stunden zuvor keine neurologischen Symptome vorlagen und die eine Diskrepanz zwischen der Schwere des klinischen Defizits und des Infarktvolumens, das per Diffusionsbildgebung oder Perfusions-CT ermittelt wurde, aufwiesen. Dafür wurden drei altersabhängige Konstellationen festgelegt: Alter über 80 Jahre, ein NIHSS-Wert von 10 oder mehr Punkten und ein Infarktvolumen unter 21 ml; Alter unter 80 Jahre, ein NIHSS-Wert von 10 oder mehr Punkten und ein Infarktvolumen unter 31 ml; Alter unter 80 Jahre, ein NIHSS-Wert von 20 oder mehr Punkten und ein Infarktvolumen zwischen 31 und 51 ml. Die Patienten wurden entweder mit einer Thrombektomie (TE) und anschließender Standardbehandlung oder lediglich mit der Standardtherapie behandelt. Die primären Endpunkte waren der durchschnittliche Wert für die Behinderung auf der *Utility-Weighted Modified Rankin Scale* (0 = Tod bis 10 = keine Symptome) und die Rate von auf der modifizierten Rankin-Skala (mRS: 0 = keine Symptome bis 6 = Tod) funktionell unabhängigen Patienten nach 90 Tagen (mRS von 0 bis 2).
Der TE-Gruppe wurden 107 Patienten mit einem medianen NIHSS von 17 Punkten und 99 Patienten der Kontrollgruppe zugeordnet. In der TE-Gruppe betrug das durchschnittliche Alter 69,4 Jahre, 23 Prozent der Patienten waren über 80 Jahre alt. Beim Erwachen hatten 63 Prozent der Patienten Schlaganfallsymptome, bei 27 Prozent war der Beginn der Symptomatik unklar. Das mediane Infarktvolumen wurde anhand der Bildgebung mit 7,6 ml berechnet. Bei 78 Prozent lag ein Verschluss der A. cerebri media- und bei 20 Prozent ein Verschluss der A.

carotis interna vor. Die mediane Zeit bis zur Randomisierung betrug 13 Stunden. Der durchschnittliche Wert auf der Utility-weighted modifizierten Rankin-Skala erreichte nach 90 Tagen einen signifikant höheren Wert von 5,5 in der TE- gegenüber 3,4 in der Kontrollgruppe. Eine deutlich höhere Rate an funktioneller Unabhängigkeit nach 90 Tagen war mit 49 Prozent in der TE- gegenüber 13 Prozent in der Kontrollgruppe zu verzeichnen. Die Raten symptomatischer intrakranieller Blutungen in der TE- und in der Kontrollgruppe mit 6 Prozent gegenüber 3 Prozent und die Raten für die 90-Tage-Sterblichkeit mit 19 Prozent gegenüber 18 Prozent wiesen keine signifikanten Unterschiede auf.

Untersuchungsgegenstand der DEFUSE-3-Studie (*Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3*) war ebenfalls die Wirksamkeit einer TE bei Patienten mit einem ischämischen Schlaganfall mit Verschlüssen der großen Gefäße der vorderen Zirkulation nach Auftreten der Symptome jenseits von sechs Stunden (Albers *et al.* 2018). Die Studie war zu einem Zeitpunkt begonnen worden, als die Ergebnisse der DAWN-Studie noch nicht bekannt waren und unterscheidet sich von dieser zudem durch einen anderen Ansatz der Patientenselektion. In diese randomisierte Studie wurden Patienten mit einem Verschluss der distalen A. carotis interna oder der proximalen A. cerebri media (ACM) eingeschlossen, bei denen 6 bis 16 Stunden zuvor keine neurologischen Symptome vorlagen. Weitere Einschlusskriterien waren ein in der initialen zerebralen Bildgebung nachgewiesenes Infarktvolumen von weniger als 70 ml sowie ein Verhältnis von > 1,8 zwischen ischämischem Volumen in der Perfusionsbildgebung und dem Infarktvolumen. Auch für diese Studie wurden die Patienten entweder mit einer TE behandelt mit anschließender Standardbehandlung oder erhielten ausschließlich die Standardtherapie auf der Stroke Unit. Der primäre Endpunkt war der Punktewert auf der modifizierten Rankin-Skala (0 = keine Symptome, 6 = Tod). Von den 182 Patienten mit einem mittleren Alter von 70 Jahren wurden 92 Patienten der TE-Gruppe zugeordnet und 90 Patienten einer konservativen Therapie zugeführt. Bei etwa 50 Prozent der Patienten trat der Schlaganfall beim Erwachen auf. Der mediane NIHSS-Score lag bei 16 Punkten. Ein Karotis-Verschluss lag bei 35 Prozent und ein Verschluss der ACM bei 65 Prozent der Patienten vor. Das präinterventionelle mediane Volumen des Infarktkerns betrug 9,4 ml und das Volumen der Perfusionsläsion 114,7 ml, was durch eine CT-Perfusionsbildgebung oder ein Diffusions- und Perfusionskernspintomogramm ermittelt wurde. Das postinterventionelle mediane Volumen des Infarktkerns nach 24 Stunden lag bei 35 ml. Die mediane Zeit vom Beginn der Schlaganfallsymptome bis zur Bildgebung betrug 10 Stunden, vom Beginn der Leistenpunktion bis zur Reperfusion 38 Minuten. Die Rate für eine funktionelle Unabhängigkeit nach 90 Tagen (entsprechend einem Punktewert zwischen 0 und 2 auf der modifizierten Rankin-Skala – mRS) war mit 45 Prozent für die endovaskuläre Therapie signifikant höher – verglichen mit 17 Prozent für die konservative Behandlung (Risk ratio 2,67; 95 % Konfidenzintervall [KI], 1,60 bis 4,48; $p < 0,001$). Die endovaskuläre Therapie

mit Standardtherapie war mit einer Verbesserung des mRS nach 90 Tagen gegenüber der alleinigen Standardtherapie assoziiert (Odds ratio 2,77; 95 % KI, zwischen 1,63 und 4,70; p < 0,001). Die Mortalität nach 90 Tagen betrug 14 Prozent in der endovaskulären Gruppe und 26 Prozent in der Standardtherapiegruppe (p = 0,05). Symptomatische intrakranielle Blutungen traten in beiden Gruppen vergleichbar häufig auf (7 % endovaskulär und 4 % Standardtherapie, p = 0,75).
Zusammenfassend haben sowohl die DAWN- als auch die DEFUSE-3-Studie einen Vorteil der endovaskulären gegenüber der Standardtherapie für das funktionelle neurologische Ergebnis im späten Zeitfenster gezeigt.

Auf Grundlage der für die Versorgungspraxis wegweisenden Ergebnisse der genannten Studien zur interventionellen Rekanalisationstherapie bei Patienten mit akutem ischämischen Schlaganfall wurde 2015 getrennt zur Gesamtleitlinie ‚Akuttherapie des ischämischen Schlaganfalls' (AWMF_Register Nr. 030-046) die Leitlinie ‚Akuttherapie des ischämischen Schlaganfalls – Ergänzung 2015 – Rekanalisierende Therapie' publiziert, die folgende Empfehlungen zu den Rekanalisationsverfahren enthält:
- Schnelle Indikationsstellung zur mechanischen TE bei Patienten mit akutem ischämischen Schlaganfall durch sofortige nicht invasive Gefäßdiagnostik (CTA, MRA)
- Empfehlung zur TE bei Patienten mit akutem ischämischen Schlaganfall im vorderen Kreislauf und relevantem neurologischen Defizit innerhalb von sechs Stunden nach Symptombeginn zusammen mit intravenöser Thrombolyse (wenn nicht kontraindiziert und innerhalb des zugelassenen Zeitfensters)
- Nachgewiesener Nutzen der TE jenseits von sechs Stunden nach Beginn der klinischen Symptome bei selektierten Patienten, bei denen durch erweiterte Bildgebungsparameter (z. B. Mismatch-Bildgebung, Kollateraldarstellung) rettbares Risikogewebe identifiziert wurde
- Keine Verzögerung der TE durch die i. v. rtPA-Lyse; ein möglicher rtPA-Effekt vor der TE soll nicht abgewartet werden
- Geforderter Zeitrahmen, in dem nach Indikationsstellung die TE durchgeführt werden soll: maximal 90 Minuten zwischen Eintreffen in der Klinik und Leistenpunktion (door-to-groin time) und maximal 30 Minuten zwischen Leistenpunktion und TE
- Mindestens 75 Prozent der Patienten sollte ein Reperfusionsgrad von TICI 2b/3 nach TE erreichen
- Krankenhäuser ohne Möglichkeit einer TE: unmittelbarer Transfer in ein neuroendovaskuläres TE-Zentrum nach Beginn der i. v. rtPA-Lyse (‚Bridging-Konzept')
- Stent-Retriever als bevorzugte Verwendung für TE; Einsatz anderer TE-Systeme entsprechend der Einschätzung des Interventionalisten hinsichtlich vergleichbarer Effektivität und Sicherheit möglich

- Empfehlung zur Erstlinientherapie bei Kontraindikation für die intravenöse Thrombolyse
- Behandlung akuter Basilarisverschlüsse mit TE und intravenöser Thrombolyse; keine fest definierte Obergrenze des Zeitraums, in dem TE stattfinden soll
- Art der Sedierung (Analgosedierung, Intubationsnarkose) abhängig von individueller Situation; Zeitverzögerung sollte unbedingt vermieden werden
- Thrombektomie bei Patienten mit ausgedehnten Infarktzeichen in der radiologischen Bildgebung (ASPECTS < 6): Nutzen, sofern Hinweise auf noch rettbares Hirngewebe mit relevantem Ausmaß bestehen (wie Mismatch in der Perfusionsbildgebung)
- Keine obere Altersgrenze für TE
- Thrombektomie ist als technisch anspruchsvolles interventionelles Verfahren Zentren mit ausgebildeten Interventionalisten vorbehalten; entsprechende Erfahrung sollte anhand von Daten zur Qualitätssicherung (z. B. Zeit bis Bildgebung, Zeit bis Leistenpunktion, Rekanalisationsrate) nachgewiesen werden (Ringleb *et al*. 2015)

Die Deutsche Gesellschaft für Neurologie (DGN) e.V. und die Deutsche Schlaganfall-Gesellschaft (DSG) veröffentlichten 2021 die aktualisierte und erweiterte S2e-Leitlinie zur Akuttherapie des ischämischen Schlaganfalls (Ringleb P. *et al.* 2021).
Hinsichtlich der rekanalisierenden Maßnahmen sind als wesentliche Punkte die Durchführung einer Gefäßdiagnostik (vom Aortenbogen aufwärts) sowie die TE nach erweiterter Bildgebung (z. B. Perfusionsuntersuchung mit MRT oder CT) bei Patienten mit relevanten Verschlüssen im vorderen Kreislauf, bei denen das Zeitintervall von sechs Stunden nach Beginn der Symptome überschritten wurde, hervorzuheben. Die Bildgebung der extrakraniellen und intrakraniellen hirnversorgenden Gefäße ist erforderlich, um die Indikation zu einer endovaskulären Schlaganfalltherapie stellen zu können. Die erweiterte Bildgebung erlaubt, Patienten mit rettbarem Risikogewebe zu detektieren (z. B. Darstellung eines kleinen Infarktkerns, Mismatch, Kollateraldarstellung), die noch von einer TE im erweiterten Zeitintervall profitieren können.

2.8.6 Stent-Retriever-Thrombektomie im hinteren Kreislauf – Basilarisverschlüsse

Vertebrobasiläre Verschlüsse sind ebenfalls der Thrombektomie (TE) mit Stent-Retrievern zugänglich. Weil die Basilaristhrombose mit einer hohen Letalität und Morbidität verbunden ist, empfiehlt die Deutsche Gesellschaft für Neurologie bereits in der Ergänzung der Leitlinie von 2015 ‚Akuttherapie des ischämischen Schlaganfalls – rekanalisierende Therapie' die mechanische Rekanalisation (Ringleb et al. 2015). Auch wenn die Daten des derzeit durchgeführten randomisierten BASICS-Registers (Basilar Artery International Cooperation

Study, NCT01717755) bei Verschluss der A. basilaris keine Überlegenheit der TE gegenüber der i. v. Thrombolyse nachweisen konnten, geben Metaanalysen und nicht randomisierte Fallstudien Hinweise auf die Wirksamkeit der mechanischen TE bei Basilarisverschlüssen (van der Hoeven *et al*. 2013; Kumar *et al*. 2015; Sheng und Tong 2019). Mangels alternativer Behandlungsoptionen spielt die Zeit zwischen Behandlungsbeginn und Auftreten der Symptome eine eher untergeordnete Rolle.

2.8.7 Verschiedene Techniken der mechanischen Thrombektomie mit Stent-Retrievern

Gegenstand der aktuellen Forschung ist, die optimale mechanische Rekanalisationstechnik mit Stent-Retrievern (SR) in Kombination mit verschiedenen Kathetermaterialien zu finden. Prinzipiell kann zwischen zwei Techniken der TE mit SR unterschieden werden: die alleinige Verwendung eines SR mit Flussblockade durch einen Katheter mit proximalem Okklusionsballon und die TE mit einem SR und lokaler Aspiration unter Verwendung eines distalen Aspirationskatheters, die mit einem proximalen Okklusionsballon unterstützt werden kann.

2.8.7.1 Stent-Retriever-Thrombektomie mit Ballonkatheter

Zunächst wird in der Regel über die Leistenarterie ein Führungskatheter mit an der Spitze integriertem Ballon bis in die Arteria carotis interna oder Arteria vertebralis vorgebracht. Anschließend wird über einen Mikrokatheter der SR in Position des Thrombus gebracht und dort freigesetzt. Bevor er mit dem Thrombus wieder zurück in den Führungskatheter gezogen wird, wird der Ballon inflatiert, um eine Flussblockade in dem Gefäß zu erzeugen und damit den Gegenstrom Richtung Thrombus zu reduzieren. Zusätzlich kann ein Sog am Führungskatheter angelegt werden, um einen retrograden Fluss zu erreichen und so Embolien durch abgerissene Fragmente zu verhindern.

2.8.7.2 Stent-Retriever-Thrombektomie mit lokaler Aspiration

Daneben gibt es die Methode der lokalen Aspiration (Abb. 1). Hier wird ebenfalls ein Führungskatheter in dem jeweiligen hirnversorgenden Gefäß (Arteria carotis interna oder Arteria vertebralis) platziert. Zusätzlich wird ein zweiter großlumiger flexibler Aspirationskatheter, der unter Sog bis an das Blutgerinnsel herangeführt wird, verwendet, um so ein Abschwemmen von Thrombusmaterial zu verhindern. Durch diesen wird koaxial der

Mikrokatheter mit dem SR positioniert. Die lokale Aspiration kann in zwei Varianten durchgeführt werden: Bei der sogenannte Solumbra-Technik wird der SR unter lokaler Aspiration mit dem Thrombus vollständig in den Aspirationskatheter zurückgezogen (Munich *et al.* 2019). Bei der sogenannten SAVE-(*Stent retriever assisted vacuum locked extraction*-)Technik wird der SR zu circa zwei Dritteln hinter den Thrombus gelegt und der Aspirationskatheter an das proximale Thrombusende unter negativem Druck angedockt, bis der Aspirationskatheter durch den Thrombus blockiert ist und ein Vakuum entstanden ist (wedge position). Danach wird die gesamte Einheit aus Aspirationskatheter und SR mit Thrombus in den Führungskatheter, an dem ebenfalls ein negativer Druck zur Kontrolle von Thrombusfragmenten angelegt wird, zurückgezogen (Maus *et al.* 2017). Alternativ kann auch ein Führungskatheter mit Ballon verwendet werden, um maximale Flusskontrolle zu erhalten, wie in der retrospektiven PROTECT-Vergleichsstudie beschrieben (Maegerlein *et al.* 2018). Prinzipiell ist die Verwendung eines Führungskatheters mit Ballons in der Anwendung technisch aufwendiger und mit der Gefahr einer Gefäßdissektion durch den inflatierten Ballon verbunden, weshalb die Technik eine intensive Übung und Erfahrung voraussetzt.

2.8.8 Primäre Aspirationsthrombektomie

Eine weitere angewandte Methode, Thromben mechanisch aus Hirnarterien zu entfernen, ist die direkte Thrombusaspiration über hochflexible intrakranielle Katheter ohne die Anwendung von Stent-Retrievern (SR). Bei Versagen der Methode kann auf den Einsatz von SR gewechselt werden. Diese Technik wurde unter dem Begriff ADAPT (*A Direct Aspiration First Pass Technique*) bekannt (Turk *et al.* 2014). In der ersten publizierten randomisierten Studie, in der die direkte Aspirationsthrombektomie (ATE) mit der Stent-Retriever-Thrombektomie (SRTE) verglichen wurde, konnte keine Überlegenheit der Aspirationstechnik gezeigt werden (Lapergue *et al.* 2017). Danach folgte als weitere randomisierte Studie die Compass-Studie (Turk *et al.* 2019). Diese hatte als primären Endpunkt die Nichtunterlegenheit der ADAPT-Methode gegenüber der SRTE beim funktionellen Therapieergebnis (Anteil der Patienten mit funktioneller Unabhängigkeit [Score auf der modifizierten Rankin-Scala 0–2]) zum Ziel. Die Behandlung musste in beiden Interventionsgruppen innerhalb von sechs Stunden nach Symptombeginn erfolgen. Der Anteil der Patienten mit einem guten funktionellen Therapieergebnis betrug 52 Prozent in der Gruppe mit primärer ATE und 50 Prozent in der Gruppe mit primärer SRTE ($p_{\text{non-inferiority}} = 0{,}0014$). Auch sekundäre Endpunkte wie die Rate einer erfolgreichen Reperfusion (*modified thrombolysis in cerebral infarction*, mTICI 2b) war mit 83 Prozent bei der primären ATE gegenüber 81 Prozent mit primärer SRTE vergleichbar ($p = 0{,}75$). Zudem scheinen beide Methoden mit einer Rate an symptomatischen intrakraniellen Blutungen (mit einer neurologischen Verschlechterung um $\geq$ 4 NIHSS-Punkte)

von 6 Prozent für die primäre Aspiration und 6 Prozent für die primäre SRTE vergleichbar sicher zu sein.

Wie die aufgeführten Studien zeigen, stellt die Grundlage der modernen Schlaganfalltherapie in einem dafür geeigneten Teil der Fälle die Thrombektomie (TE) dar. Die Indikation zur TE wird zunehmend ausgeweitet, sodass eine immer größere Anzahl von Schlaganfallpatienten mit dieser Therapieform behandelt wird. In den meisten Fällen wird die TE mit Stent-Retrievern mit den zuvor beschriebenen Techniken durchgeführt. Ziel der Behandlung ist es, die für die jeweilige Situation optimale Technik oder die Kombinationen von Methoden zur schnellen und effektiven TE ohne Thrombusfragmentverschleppung zu finden und diejenigen Patienten zu identifizieren, die von einer TE profitieren werden.

3. Eigene Arbeiten

3.1 Überblick

Aufbauend auf den bisherigen in den vorausgegangenen Kapiteln dargestellten Erkenntnissen wurde in den folgenden aufgeführten Arbeiten das klinisch-neurologische Outcome nach mechanischer Thrombektomie (TE) bei Gefäßverschlüssen des vorderen Kreislaufs in Hinblick auf technische, klinische und anatomische Aspekte untersucht.

In zwei Arbeiten wurde die Frage nach der Effizient und Sicherheit von zwei modernen Stent-Retriever-Modellen, zu denen zum Zeitpunkt der Untersuchung nur wenige publizierte Daten aus der klinischen Anwendung vorlagen, hinsichtlich Rekanalisationsraten, klinischem Outcome und Komplikationen validiert. Als eine der technischen Besonderheiten wurde das Marker-Konzept zur Sichtbarkeit des Stent-Retrievers unter Röntgendurchleuchtung vorgestellt (Kapitel 3.2.1 und 3.2.2).

Als alternatives TE-Verfahren wurde in einer Arbeit die Technik der alleinigen lokalen Thrombusaspiration über einen Katheter ohne Verwendung eines Stent-Retrievers mit der Frage nach Rekanalisationserfolg, klinischem Outcome und der möglichen Gefahr einer höheren Rate an Thrombusverschleppung gegenüber der Stent-Retriever-TE untersucht (Kapitel 3.3.1).

Spezielle Indikationen zur mechanischen TE unter klinischen, anatomischen und technischen Gesichtspunkten wurden in drei weiteren Arbeiten thematisiert. In einer Arbeit zu den klinischen Aspekten der TE liegt der Fokus auf der Frage, ob Patienten mit einem Hauptstammverschluss der ACM und nur geringer Schlaganfallschwere hinsichtlich des Nutzen-Risiko-Verhältnisses von einer TE profitieren (Kapitel 3.4.1).

In Bezug auf die besonderen technisch-anatomischen Aspekte der TE bei M2-Segment-Verschlüssen werden in zwei Arbeiten (Kapitel 3.4.2 und 3.4.3) der Nutzen der TE in Abhängigkeit des Verschlusses bestimmter M2-Territorien beurteilt sowie ein Vergleich der Ergebnisse einer TE von M1-Hauptstammverschlüssen gegenüber M2-Segment-Verschlüssen hinsichtlich des technischen und klinischen Erfolges durchgeführt. Insbesondere wird der Frage nach einer möglichen höheren Komplikationsrate der TE in den M2-Segmenten nachgegangen. Anknüpfend an die vorausgehende Arbeit zur alleinigen lokalen Thrombusaspiration wird im Rahmen einer Studie zur Sicherheit von Flow-Divertern (FD) die

Eignung der alleinigen lokalen Thrombusaspiration zur Behandlung eines ischämischen Schlaganfalls durch eine Stent-Thrombose nach FD-Implantation diskutiert (Kapitel 3.4.4).

In zwei Arbeiten wurden anatomisch-funktionelle Aspekte des ischämischen Schlaganfalls beleuchtet. In einer Arbeit wurde der Stellenwert von CTA-Kollateralscores in der präinterventionellen bildgebenden Diagnostik zur Prognose des klinischen Langzeit-Outcomes nach einer TE evaluiert (Kapitel 3.6.1). Die Beobachtung, dass die Basalganglien auch nach längerer Ischämiezeit nach erfolgreicher Rekanalisation von Verschlüssen der ACM intakt bleiben können, führte zu der Frage nach prädiktiven Faktoren für das Überleben der Basalganglien, die in einer weiteren Arbeit untersucht wurde (Kapitel 3.6.2).

3.2 Effizienz und Sicherheit der mechanischen Thrombektomie am Beispiel moderner Stent-Retriever

3.2.1 Monozentrische Studie zur einjährigen Erfahrung mit dem Aperio-Stent-Retriever bei akuten thrombotischen Verschlüssen der großen Hirngefäße im vorderen Kreislauf

Marius Georg Kaschner, Daniel Weiss, Christian Rubbert, John-Ih Lee, Michael Gliem, Sebastian Jander, Vivien Ivan, Bastian Kraus, Bernd Turowski, Julian Caspers (2019). *One-year single-center experience with the Aperio thrombectomy device in large vessel occlusion in the anterior circulation: safety, efficacy, and clinical outcome.* Neurol Sci 40: 1443–1451.

In dieser Arbeit wurden die Sicherheit und Effizienz des Aperio-Stent-Retrievers (Aperio) bei Thrombektomien untersucht und die Ergebnisse mit den Daten aus Studien zu etablierten Stent-Retrievern (SR) verglichen. Es wurden die Daten von 82 Patienten mit Verschlüssen der großen Gefäße der vorderen Gefäßzirkulation ausgewertet, die zwischen Januar und Dezember 2017 mittels SR-Thrombektomie behandelt wurden. Dazu wurden unter anderem die Lokalisation des Verschlusses, die Rekanalisationsraten, die Dauer der Intervention, die Komplikationsraten und das klinische Outcome erfasst. Die Thrombektomie (TE) wurde unter Durchleuchtung mit dem Aperio in lokaler Aspirationstechnik durchgeführt, bei der ein Aspirationskatheter vor den proximalen Anteil des mit dem SR überdeckten Thrombus gebracht und unter Sog in diesen hineingezogen wurde. Der Aperio (APERIO® Thrombectomy Device, Acandis, Pforzheim, Germany) hat ein sogenanntes Hybrid-Design aus kleinen geschlossenen Zellen, durch die eine gute Wandadaptation erreicht werden soll, und großen Zellen mit integrierten Ankerelementen, durch die ein Abrutschen der Thromben aus dem SR verhindert werden soll (Abb. 2).

Das mediane Durchschnittsalter der zu circa 60 Prozent weiblichen Patienten betrug 77 Jahre (SD: 12) bei einem medianen NIHSS von 14, einem medianen mRS von 5 und medianen ASPECT von 10 als präinterventionelle Ausgangssituation. In den meisten Fällen (76 %) lag ein isolierter Verschluss des M1-Segmentes vor. Eine intravenöse Thrombolyse wurde bei 53 Patienten (64,6 %) verabreicht. Eine entsprechend der TICI-Klassifikation erfolgreiche Rekanalisation mit mehr als 50-prozentiger Reperfusion des Mediastromgebietes (TICI 2b–3) wurde in 85,3 Prozent der Behandlungsfälle erreicht. Der Rekanalisationserfolg lag bereits nach dem ersten SR-Manöver bei 43,9 Prozent. Von den für die zur Nachbeobachtung zur Verfügung stehenden 68 Patienten zeigten 41 Prozent nach drei Monaten gemessen an der mRS-Skala ein sehr gutes bis gutes Behandlungsergebnis, was bedeutet, dass kein neurologisches Defizit oder nur geringe funktionelle Einschränkungen vorlagen (mRS 0–2). Im frühen Krankheitsverlauf sind 17 Prozent der Patienten verstorben, jedoch stand kein Todesfall mit der Intervention selbst in Zusammenhang. Symptomatische Infarkteinblutungen traten in 7 Prozent der Fälle auf. Intrakranielle Blutungen während der Intervention kamen nicht vor. Nur in einem Fall (1,2 %) wurden Thrombusfragmente beim SR-Manöver in andere Gefäßterritorien abgeschwemmt. Bereits nach dem ersten SR-Manöver zeigte sich eine hohe Rate an vollständiger Rekanalisation sowie mehr als 50-prozentiger Rekanalisation des Mediaterritoriums. Korrelierend dazu fand sich eine hohe Rate an sehr gutem (mRS 0) und gutem (mRS 1–2) funktionellen neurologischen Outcome. Diese Ergebnisse sind vergleichbar mit den Daten aus randomisierten größeren SR-Studien (ENDOSTROKE (Singer *et al.* 2013), HERMES (Goyal *et al.* 2016), SEER (Campbell *et al.* 2016), TRACK, (Zaidat *et al.* 2017), ASTER (Lapergue *et al.* 2017)). Sowohl die hohe Rekanalisationsrate als auch die äußerst niedrige Rate von Embolien in zuvor nicht betroffene Regionen durch Thrombusabschwemmung bei der Extraktion sprechen für die hohe Funktionalität und Effizienz des SR in Kombination mit der lokalen Aspirationstechnik. Des Weiteren beweisen das Ausbleiben von interventionsbezogenen Komplikationen und Todesfällen eine hohe Sicherheit des TE-Verfahrens mit dem Aperio.

3.2.2 Der neue fluoroskopisch vollständig sichtbare Aperio-Hybrid-Stent-Retriever – effizient und sicher? Erste Erfahrungen in einer multizentrischen Studie

Marius Kaschner, Thorsten Lichtenstein, Daniel Weiss, Bernd Turowski, Lukas Goertz, Claudia Kluner, Marc Schlamann, Christian Mathys, Christoph Kabbasch (2020). *The New Fully Radiopaque Aperio Hybrid Stent-Retriever: Efficient and Safe? An Early Multicenter Experience.* World Neurosurg 141: e278–e288.

Diese Arbeit war die erste klinische retrospektive Studie, in der die Sicherheit und Effizienz des neuen Aperio-Hybrid-(APH-)Stent-Retrievers (APERIO® Hybrid Thrombectomy Device, Acandis, Pforzheim, Germany), des Nachfolgermodells des Aperio, bei Thrombektomien (TE) der intrakraniellen Hirngefäße untersucht wurden und die Ergebnisse mit den Daten aus Studien zu etablierten Stent-Retrievern verglichen wurden. Der APH ist ein selbstexpandierender nitinolbeschichteter Stent-Retriever (SR) mit dem bekannten hybriden Zelldesign, der eine effektive Interaktion mit dem Thrombus ermöglicht. Zusätzlich hat der APH eine verbesserte Sichtbarkeit über die gesamte Länge des SR unter fluoroskopischer Darstellung durch einen integrierten Markierungsdraht (Abb. 2). Die TE wurden mit dem APH unter lokaler Aspiration unter Durchleuchtung bei 48 Patienten (männlich: 46 %) mit akutem ischämischen Schlaganfall der vorderen oder hinteren Zirkulation durchgeführt. Dazu wurden unter anderem die Sichtbarkeit des APH unter Durchleuchtung, die Rekanalisationsraten, periprozedurale Komplikationen und das frühe neurologische Outcome bei Entlassung erfasst. Das Durchschnittsalter betrug 73 Jahre (SD 15), der mediane NIHSS 15 (2–36), 52 Prozent der Patienten erhielten eine zusätzliche intravenöse Thrombolyse mit rtPA. Durchschnittlich wurden mit dem APH drei (SD 3) SR-Manöver bei einer medianen Zeit von der Leistenpunktion bis zur endgültigen Rekanalisation von 54 Minuten (SD 33) durchgeführt. Eine erfolgreiche Rekanalisation mit vollständiger und mindestens über 50-prozentiger Reperfusion des Mediastromgebietes (mTICI $\geq$ 2b) wurde in 95,8 Prozent der Fälle erreicht, mit bereits 60,4 Prozent exzellentem Rekanalisationserfolg (mTICI $\geq$ 2c) nach dem ersten SR-Manöver. Dreiunddreißig Prozent (15/46) der für die Nachbeobachtung zur Verfügung stehenden Patienten zeigten bereits bei Entlassung und 36,7 Prozent (11/30) in der 3-Monatsverlaufskontrolle ein sehr gutes bis gutes Behandlungsergebnis, ohne neurologisches Defizit oder mit nur geringen funktionellen Einschränkungen (mRS 0–2). Im frühen Krankheitsverlauf verstarben 21,7 Prozent der Patienten. Todesfälle oder behandlungsbedürftige Komplikationen in Zusammenhang mit der Intervention oder dem verwendeten APH sind nicht aufgetreten. Symptomatische postinterventionelle Infarkteinblutungen traten in 6,3 Prozent der Fälle auf. Intrakranielle prozedurale Blutungen kamen nicht vor. Eine Verschleppung von Thrombusfragmenten in andere Gefäßterritorien trat in keinem Fall auf. Die fluoroskopische Sichtbarkeit wurde in 98 Prozent von den Interventionalisten als gut bis sehr gut bewertet. In drei Fällen (6,3 %) wurden eine erschwerte Zuführung und Freisetzbarkeit des APH festgestellt.

Der APH wurde konzipiert, um die Sichtbarkeit unter Durchleuchtung zu verbessern. Durch Einflechten röntgendichter Drähte in den Stent ist das Device über die gesamte Länge sichtbar und liefert Informationen über die Thrombusposition in Relation zum SR. So kann ein Versagen des Thrombektomiemanövers in einem früheren Stadium entdeckt werden,

zum Beispiel bei fehlender Stent-Thrombus-Integration, wenn der Stent am Thrombus vorbeigleitet. Zudem soll die volle Sichtbarkeit zur Sicherheit der Prozedur beitragen, beispielsweise indem eine Streckung des Gefäßbaums ohne relative Bewegung des SR zu diesem auf eine erhöhte Spannung mit dem Risiko eines Gefäßschadens hinweist. Diese Studie hat gezeigt, dass die neue SR-Konstruktion zu einer deutlich verbesserten Sichtbarkeit des APH im klinischen Einsatz geführt hat. Das hybride Zelldesign wurde beibehalten. Die sehr guten Rekanalisationsraten von circa 95 Prozent und die sehr niedrige Rate an Embolien durch Thrombusfragmentation weisen auf eine effiziente Interaktion des APH mit dem Thrombus hin. Die ausgebliebenen interventionsbedingten Komplikationen bestätigten das hohe Sicherheitsprofil moderner SR sowie des Thrombektomieverfahrens.

3.3 Alternative Thrombektomie-Verfahren

3.3.1 Direkte Aspirationsthrombektomie (ADAPT) als Erstlinientherapie beim ischämischen Schlaganfall – mit Literaturüberblick

Marius G. Kaschner, Christian Rubbert, Julian Caspers, Jennifer Karsten, Bastian Kraus, John-Ih Lee, Michael Gliem, Sebastian Jander, Bernd Turowski (2019). *A Retrospective Single-Center Case Series of Direct Aspiration Thrombectomy as First-Line Approach in Ischemic Stroke and Review of the Literature.* J Stroke Cerebrovasc Dis 28: 640–648.

Nachdem die erste randomisierte ASTER-Studie keine Überlegenheit der alleinigen Aspirationsthrombektomie (ATE) als Erstlinien-Rekanalisationsversuch, die unter dem Namen ADAPT (*a direct aspiration first pass technique)* bekannt wurde, zeigen konnte, blieb die Frage bestehen, ob die ATE ein der Stent-Retriever-Thrombektomie (SRTE) zumindest gleichwertiges Verfahren hinsichtlich Rekanalisationsraten, klinischem Outcome und prozeduraler Sicherheit darstellt, (Lapergue *et al.* 2017). In Bezug auf diese Fragestellung wurden in dieser retrospektiven monozentrischen Studie die Ergebnisse von 40 Patienten mit einem ischämischen Schlaganfall durch M1- und M2-Segment-Verschluss der A. cerebri media ausgewertet, die durch eine ATE als Erstlinienversuch im Zeitraum eines Jahres – von 2016 bis 2017 – im Universitätsklinikum Düsseldorf (UKD) endovaskulär behandelt wurden. Es wurden Rekanalisationsraten (*modified thrombolysis in cerebral infarction* – mTICI), periprozedurale Komplikationen und das frühe neurologische Outcome (modified Rankin Scale – mRS) erfasst. Das durchschnittliche Patientenalter lag bei 67,5 Jahren, 28 Prozent der Patienten waren männlich. Der mediane *National Institutes of Health Stroke Scale* (NIHSS) lag vor der Behandlung bei 12 und verbesserte sich nach der Behandlung auf 3. Vor der

Intervention erhielten 70 Prozent der Patienten eine intravenöse Thrombolyse mit rtPA. Bei der ATE wurde ein hochflexibler Aspirationskatheter direkt an den proximalen Thrombusanteil herangeführt beziehungsweise im Fall stark gewundener Arterien über einen Mikrodraht- und Mikrokatheter gestützt vorgeschoben. Unter manueller Aspiration wurde der Aspirationskatheter in den Führungskatheter zurückgezogen. Das Manöver wurde bis zu dreimal wiederholt. Wenn keine erfolgreiche Rekanalisation (mTICI $\geq$ 2b) erreicht werden konnte, wurde als ‚Rettungsmanöver' ein Stent-Retriever (SR) verwendet. Mit der alleinigen ATE konnte in 85 Prozent der Fälle eine Rekanalisationrate mit mTICI 2b–3 erreicht werden. In den Fällen, in denen eine alleinige TE durchgeführt wurde, wurde weiches rotes Thrombusmaterial geborgen, wohingegen bei den sechs Thrombektomie-Patienten, bei denen zusätzlich ein SR verwendet werden musste, weiße feste Thromben gefunden wurden.
Die durchschnittliche Zeit von der Leistenpunktion bis zur Rekanalisation betrug für die alleinige ATE 20,7 Minuten (SD 8,4). Wenn zusätzliche SR-Manöver notwendig wurden (ATE + SR), erhöhte sich die Dauer auf 50,6 Minuten (SD 15,2). Prozedurale Komplikationen sind in keinem der Behandlungsfälle mit alleiniger ATE aufgetreten. Bei einem Patienten in der ATE + SR-Gruppe kam es zu einer Embolie durch Thrombusfragmente in zuvor unbeteiligte Gefäßterritorien. Eine postprozedurale Infarkteinblutung trat bei insgesamt 7,5 Prozent der Patienten auf, davon bei 5,8 Prozent in der ATE und bei einem Patienten (16,7 %) in der ATE + SR-Gruppe. In der ATE-Gruppe erreichten 55,8 Prozent der Patienten ein gutes bis sehr gutes neurologisches Outcome (mRS 0–2). Die Gesamtmortalität des behandelten Patientenkollektivs war mit 2,5 Prozent niedrig.
Diese Studie gibt Hinweise darauf, dass die ATE mit manueller Aspiration als Erstlinien-Rekanalisationsversuch bei Verschlüssen der A. cerebri media zu guten Reperfusionsergebnissen führen kann. Aufgrund des Ausbleibens prozeduraler Komplikationen, insbesondere von Subarachnoidalblutungen, stellte sich die ATE in dem untersuchten Patientenkollektiv als sicheres Verfahren dar.

3.4 Spezielle Indikationen zur mechanischen Thrombektomie unter klinischen, anatomischen und technischen Gesichtspunkten

3.4.1 Mechanische Thrombektomie bei Patienten mit Hauptstammverschlüssen der Arteria cerebri media und niedrigem NIHSS-Score

Marius Georg Kaschner, Julian Caspers, Christian Rubbert, Raul Lande, Bastian Kraus, John-Ih Lee, Michael Gliem, Sebastian Jander, Bernd Turowski (2018). *Mechanical*

thrombenctomy in MCA-mainstem occlusion in patients with low NIHSS scores. Interv Neuroradiol 24: 398–404.

Während sich der Nutzen der Thrombektomie (TE) bei Hauptstammverschlüssen der A. cerebri media (M1-Segment) für Patienten mit schwerem neurologischen Defizit bei einem ischämischen Schlaganfall bestätigte, ist die Evidenz für Patienten mit nur geringen Symptomen gering, die sich in einem niedrigen NIHSS-(*National Institutes of Health Stroke Scale*-)Wert widerspiegeln. Auch die großen randomisierten Multicenterstudien haben Patienten mit niedrigem NIHSS eingeschlossen, wie MR CLEAN (NIHSS 2–42) und EXTEND-IA (NIHSS 0–42), jedoch hatte die Mehrzahl der Patienten einen im Mittel hohen NIHSS-Wert von 15–17 (Berkhemer *et al.* 2015; Campbell *et al.* 2015; Goyal *et al.* 2015; Jovin *et al.* 2015; Saver *et al.* 2015). Damit gibt es aus den randomisierten Studien wenige Daten für Patienten mit niedrigem NIHSS.

In diese retrospektive monozentrische Studie wurden 1081 Patienten mit einem M1-Verschluss eingeschlossen, die zwischen Februar 2012 und November 2017 in der Neuroradiologischen Abteilung des UKD behandelt wurden und von denen 30 Patienten einen NIHSS $\leq$ 5 hatten. Die Entscheidung zur TE wurde für jeden Patienten im Konsensus zwischen Neurologie und Neuroradiologie, insbesondere in Abhängigkeit des interventionellen Risikos und der Wahrscheinlichkeit einer Rekanalisation des Thrombus durch eine alleinige intravenöse (i. v.) Thrombolyse, getroffen. Die TE wurde unter Analgesie als Stent-Retriever-TE mit distaler lokaler Aspiration durchgeführt. Die Lokalisation des Verschlusses wurde mittels Computertomographie-Angiographie (CTA) und in manchen Fällen mit einem sogenannten ‚Wake-up-Stroke' mit einer Magnetresonanzangiographie (MRA) veranschaulicht. Die Thrombuslänge wurde anhand der CTA gemessen. Zudem wurde die Kollateralisierung mittels CT-Perfusion und CTA-Kollateralscore dargestellt. Der Tan-CTA-Kollateralscore bewertet die Kollateralisierung des Mediastromgebietes auf einer Skala, die von 0–3 (0 = komplett fehlende Gefäßkontrastierung bis 3 = vollständige Gefäßkontrastierung) reicht. Rekanalisationsraten (*modified thrombolysis in cerebral infarction* – mTICI), Interventionszeiten (von Leistenpunktion bis zur angiographischen Abschlussserie), periprozedurale Komplikationen, das frühe neurologische Outcome (*modified Rankin Scale* – mRS) und das Infarktausmaß (gemäß des *Alberta stroke program early CT score – ASPECTS*) wurden erfasst. Das durchschnittliche Patientenalter der zu circa 57 Prozent weiblichen Patienten lag bei 72 Jahren (SD 11). Vor der Intervention erhielten 24 der 30 Patienten (80 %) eine i. v. Thrombolyse. Isolierte M1-Verschlüsse lagen bei 53 Prozent vor, zu je 17 Prozent ergaben sich kombinierte M1- und M2-Verschlüsse oder ACI- und M1-Verschlüsse und zu 13 Prozent Karotis-T-Verschlüsse. Die mediane Thrombuslänge betrug 14 Millimeter. Mit

einem Median des Kollateralstatus von 3 lag eine gute Kollateralisierung vor. Eine gute bis sehr gute Rekanalisation (mTICI 2b–3) wurde in 96,7 Prozent der Fälle erreicht, davon waren 66,7 Prozent sehr gute Rekanalisationsergebnisse (mTICI 2c–3). Die durchschnittliche Interventionszeit betrug im Median 244 Minuten. Sowohl der mediane NIHSS als auch der mediane mRS verbesserten sich bereits im kurzfristigen postinterventionellen Verlauf (Median: 9 Tage) statistisch signifikant von 4 auf 1 beziehungsweise von 2 auf 1. Der mediane ASPECTS vor Intervention betrug 10 und verringerte sich auf 9 nach der Intervention. Bei 16,7 Prozent traten postinterventionell nicht symptomatische kleine oder konfluierende petechiale Hämorrhagien auf. In einem Fall (3,3 %) kam es zu einem substanziellen raumfordernden Reperfusionshämatom der Basalganglien mit neurologischer Verschlechterung. Todesfälle traten nicht auf.
In der vorliegenden Studie zeigte sich nur ein geringer Effekt der i. v. Lyse bei M1-Segment-Verschlüssen. Die initiale i. v. Lyse hat bei allen 24 Patienten, die diese vor der TE erhalten haben, eine unzureichende Wirkung aufgewiesen, wie sich durch den angiographisch nachweisbaren Thrombus vor dem ersten TE-Durchgang zeigte. Bei zwei Patienten kam es mit in der CTA nachgewiesener guter Kollateralisierung und fast vollständiger Rückbildung der Symptome nach i. v. Lyse nach mehreren Stunden zu einer progredienten neurologischen Verschlechterung. In dem vorliegenden Patientenkollektiv korrelierte mit statistischer Signifikanz der präinterventionelle Kollateralstatus in der CTA mit dem Ausmaß der Änderung zwischen prä- und postinterventionellem ASPECTS (r_2 0.53, $p < 0,005$). Das bedeutet, dass bei Patienten mit einer besseren Kollateralisierung vor der TE ein geringerer Abfall zwischen prä- und postinterventionellem ASPECTS vorlag, was einer geringeren Infarktausprägung nach erfolgreicher TE entsprach. Insgesamt konnte in dem behandelten Patientenkollektiv durch die TE eine hohe Rekanalisationsrate mit gutem funktionellen Outcome (medianer mRS: 1) und geringem Interventionsrisiko erreicht werden.

3.4.2 Mechanische Thrombektomie bei Patienten mit M2-Segment-Verschlüssen unter Berücksichtigung der Gefäßterritorien

Vivien Lorena Ivan, Christian Rubbert, Julian Caspers, John-Ih Lee, Michael Gliem, Sebastian Jander, Bernd Turowski, **Marius Kaschner** (2020). *Mechanical thrombectomy in acute middle cerebral artery M2 segment occlusion with regard to vessel involvement.* Neurol Sci 41: 3165–3173.

Die Thrombektomie (TE) des akuten Schlaganfalls bei Verschluss der M2-Segmente beinhaltet zumindest theoretisch ein potenziell erhöhtes Komplikationsrisiko gegenüber der

M1-Segment-TE durch den technisch schwierigeren Zugang in peripheren Gefäßabschnitten aufgrund des geringeren Gefäßdurchmessers, des kurvigeren Gefäßverlaufes und – insbesondere bei älteren Patienten – einer erhöhten Fragilität der Gefäßwand. Dennoch gibt es relevante Argumente für eine TE in den M2-Segmenten, da insbesondere bei Thromben der proximalen M2-Segmente Perfusionsausfälle großer Territorien auftreten, die mit einem relevanten neurologischen Defizit einhergehen. Die bisherige Studienlage ist uneinheitlich. Randomisierte Studien liegen nicht vor. Jedoch konnten mehrere nicht randomisierte Studien einen Nutzen der M2-TE zeigen. Ziel dieser retrospektiven Studie war es, die Wirksamkeit der M2-TE in Abhängigkeit einzelner Gefäßterritorien hinsichtlich der Erhaltung des ischämischen Hirnparenchyms und des frühen klinischen Outcomes zu beurteilen. In dieser Arbeit werden die Ergebnisse von 57 Patienten vorgestellt, die mit einem akuten ischämischen Schlaganfall durch Verschluss eines oder mehrerer M2-Äste zwischen Januar 2012 und Dezember 2017 in der Neuroradiologie des UKD durch eine Stent-Retriever-TE behandelt wurden. Als M2-Segment-Verschluss wurden alle Verschlüsse von M2-Segmenten ab der Aufteilung des M1-Segmentes definiert. Die Patienten wurden in drei Gruppen von Verschlussmustern unterteilt. Gruppe A umfasste Patienten mit Verschluss der Äste der Zentralregion (Aa. praecentralis, centralis, postcentralis), Gruppe B mit Verschluss der Gefäße der Zentralregion und frontalen Äste (Aa. frontobasalis, Aa. frontoopercularis) und Gruppe C mit Verschluss der Äste der Zentralregion und der parietalen und/oder temporalen Gefäße (Aa. parietalis posterior, temporooccipitalis und gyri angularis). Darüber hinaus wurden die Verschlüsse in proximale Verschlüsse (M2-Truncus ab der Mediahauptstammaufteilung) oder in Verschlüsse der distalen M2-Äste (nach Aufteilung der Trunci) unterteilt. Rekanalisationsraten (*modified hrombolysis in cerebral infarction – mTICI*), Interventionszeiten, Komplikationen (symptomatische intrakranielle Blutungen, Embolien in neue Gefäßterritorien, Dissektionen), das frühe neurologische Outcome (*modified Rankin Scale* – mRS) sowie das Infarktausmaß (*Alberta stroke program early CT score – ASPECTS*) wurden erfasst. Das durchschnittliche Patientenalter der 57 Patienten (60 % weiblich) lag bei 73 Jahren (SD 13,3 Jahre). In 75,4 Prozent der Fälle haben die Patienten vor der Intervention eine intravenöse Thrombolyse erhalten. Einen Verschluss der Zentralregion hatten 14 Patienten, 24 Patienten einen Verschluss der Zentralregion und frontalen Äste, 19 Patienten einen kombinierten Verschluss der zentralen, parietalen und temporalen Äste. Die Patienten hatten hinsichtlich Infarktausmaß und klinisch-neurologischem Zustand eine vergleichbare Ausgangssituation. Der Median des ASPECTS lag in allen drei Gruppen (A, B, C) präinterventionell bei 10, der NIHSS im Median bei 12 vs. 10 vs. 11 und der mediane mRS bei 4 vs. 5 vs. 5 – jeweils ohne signifikante Unterschiede. Bemerkenswerte Differenzen vom Symptombeginn des Schlaganfalls bis zur Leistenpunktion sowie hinsichtlich der Interventionsdauer (Mittel 68 $\pm$ 42 Minuten) bestanden nicht zwischen den Gruppen. Bei allen

Patienten wurde eine Stent-Retriever-TE in lokaler Aspirationstechnik mit einem Aspirationskatheter durchgeführt. Eine erfolgreiche partielle oder komplette Reperfusion (mTICI 2b–3) wurde bei 49 Patienten (86 %) ohne signifikante Unterschiede zwischen den einzelnen Gruppen erreicht. Im frühen klinischen Verlauf verbesserte sich zum Zeitpunkt der Entlassung der mediane mRS erheblich von 5 auf 4 ($p < 0,001$) und der mediane NIHSS statistisch signifikant von 11 auf 5 ($p < 0,001$). Ein gutes klinisches Outcome (mRS $\leq$ 2) wurde tendenziell häufiger bei alleinigem Verschluss der zentralen Äste erreicht, jedoch ohne statistische Signifikanz zwischen den Gruppen. Auch das Outcome zwischen den Patientengruppen mit proximalen und distalen M2-Segment-Verschlüssen unterschied sich nicht erkennbar (Median mRS proximal: 4 vs. distal: 4, $p = 0,81$; Median NIHSS proximal: 6 vs. distal: 5, $p = 0.53$). Der mediane postinterventionelle ASPECTS zeigte einen statistisch bemerkenswerten Abfall von 10 auf 7 ohne beachtlichen Unterschied zwischen den einzelnen Verschlussmustern (A, B, C) oder der Verschlusslokalisation (proximal vs. distal). Symptomatische intrakranielle Blutungen innerhalb von 24 Stunden nach der Intervention traten in 10,5 Prozent der Fälle auf. Außer Embolien in neue Gefäßterritorien in 5,4 Prozent der Fälle ergaben sich keine weiteren prozeduralen therapeutisch relevanten Komplikationen. Zwischen den untersuchten Gruppen wurden keine signifikanten Unterschiede für Komplikationen beobachtet.

3.4.3 Vergleich des klinischen Outcomes, der Effektivität und Sicherheit zwischen Thrombektomien im M1- gegenüber dem M2-Segment

Daniel Weiss, Christian Rubbert, Vivien Lorena Ivan, John-Ih Lee, Sebastian Jander, Michael Gliem, Julian Caspers, Bernd Turowski, **Marius Kaschner** (2022). *Thrombectomy in stroke patients with acute occlusion of the M1 compared to the M2-segment: safety, efficacy, and clinical outcome.* Neuroradiol J 27: 19714009211067403. doi: 10.1177/19714009211067403. Epub ahead of print. PMID: 35083935.

Bisher gibt es nur wenige Ergebnisse aus Studien zu einem direkten Vergleich der Thrombektomie (TE) im M1- gegenüber dem M2-Segment, in denen das mögliche höhere Interventionsrisiko einer TE in M2-Segmenten verglichen mit dem M1-Segment untersucht wurde. Die nachfolgend vorgestellte Arbeit hatte zum Ziel, die Daten aus dem eigenen Institut zur TE von M1-Verschlüssen mit denen von Patienten nach TE von M2-Verschlüssen retrospektiv hinsichtlich des klinischen Outcomes und des prozeduralen Komplikationsrisikos zu vergleichen. In dieser Arbeit werden die Ergebnisse von 141 Patienten mit einem akuten ischämischen Schlaganfall durch einen M1-Verschluss gegenüber 33 Patienten mit einem M2-

Verschluss, die in der Neuroradiologie des UKD zwischen Juni 2016 und Mai 2018 durch eine Stent-Retriever-TE in lokaler Aspirationstechnik behandelt wurden, vorgestellt. Acht Patienten mit einem M2-Verschluss wurden initial mit einer alleinigen Aspirations-TE behandelt. Dreiunddreißig Patienten hatten einen Verschluss des M2-Truncus (proximaler Verschluss, pM2), und 11 Patienten hatten einen M2-Ast-Verschluss ab der Aufteilung der Trunci in die M2-Äste oder noch weiter peripher gelegener M2-Äste (distaler M2-Verschluss, dM2). Rekanalisationsraten (mTICI-Skala), Interventionszeiten, behandlungsbedürftige periprozedurale und postinterventionelle Komplikationen (Dissektionen, Gefäßperforationen oder Embolien in neue Gefäßterritorien, Infarkteinblutungen), das frühe neurologische Outcome (*modified Rankin Scale* – mRS-Skala) sowie das Infarktausmaß (gemäß des Alberta stroke program early CT score – ASPECTS) wurden erfasst. Das durchschnittliche Alter der Patienten mit M1-Verschluss lag bei 76 Jahren (SD 13), das der Patienten mit proximalem M2-Verschluss bei 77 Jahren (SD 11) und das der Patienten mit distalem M2-Verschluss bei 70 Jahren (SD 14). Signifikante Unterschiede des medianen präinterventionellen NIHSS zwischen der M1-TE-Gruppe und der pM2- und dM2-TE-Gruppe lagen nicht vor. Der Ausgangs-NIHSS in der M1-Gruppe war erwartungsgemäß am höchsten (NIHSS 14), da in diesem Fall das gesamte nachgeschaltete Mediastromgebiet von der Minderperfusion betroffen ist. Jedoch waren auch die Patienten mit proximalen und distalen M2-Verschlüssen relativ schwer betroffen (NIHSS 10 bzw. 8), da zum einen bei proximalen M2-Verschlüssen ebenfalls ausgedehnte Areale nicht perfundiert werden und zum anderen bei peripheren Verschlüssen funktionell bedeutende Areale betroffen sein können. Der präinterventionelle ASPECTS betrug 10 in der M1-TE-Gruppe und in den M2-TE-Gruppen. Die Zeit zwischen dem Beginn der neurologischen Symptome und der Leistenpunktion betrug in der M1-TE-Gruppe durchschnittlich 128 Minuten (SD 77), in der pM2-TE-Gruppe 137 Minuten (SD 52) und für die dM2-Gruppe 146 Minuten (SD 93). Die Interventionsdauer lag bei 225 Minuten (SD 80) in der M1-TE-Gruppe gegenüber 257 Minuten (SD 114) in der pM2-TE-Gruppe und bei 221 Minuten (SD 104) in der dM2-TE-Gruppe ohne signifikanten Gruppenunterschied. In 63,2 Prozent der Fälle haben die Patienten vor der Intervention eine systemische Lyse erhalten. Eine erfolgreiche Rekanalisation (mTICI 2b–3) wurde bei 87 Prozent in der M1-TE-Gruppe, bei 95,5 Prozent in der pM2-Gruppe und bei 81,8 Prozent in der dM2-TE-Gruppe erreicht. Die Rate für ein gutes neurologisches Outcome (mRS 0–2) nach 90 Tagen lag bei 42,6 Prozent in der M1-TE-Gruppe, bei 63,6 Prozent in der pM2-TE-Gruppe sowie bei 45,5 Prozent in der dM2-TE-Gruppe. Sie wies zwischen den Gruppen keinen signifikanten Unterschied auf. In der M2-TE-Gruppe ließ sich kein signifikanter Unterschied zwischen proximalen Verschlüssen und distalen Verschlüssen hinsichtlich des klinischen Outcomes nach TE feststellen. Der NIHSS verbesserte sich in der M1-Gruppe bei Entlassung im Median um 6 Punkte, in der pM2-Gruppe um 6 Punkte und in der dM2-Gruppe um 5 Punkte ohne Signifikanz zwischen den Gruppen.

Der postinterventionelle ASPECTS zeigte ein medianes Absinken zum Ausgangswert um 4 Punkte in der M1-TE-Gruppe, um 3 Punkte in der pM2-TE-Gruppe und um 2 in der dM2-TE-Gruppe ohne signifikanten Unterschied zwischen den Gruppen. Die Rate an symptomatischen intrazerebralen Infarkteinblutungen waren in der M1-TE-Gruppe und der M2-TE-Gruppe ebenfalls vergleichbar niedrig (M1: 7,1 %, pM2: 4,5 %, dM2: 9,1 %). Es zeigte sich eine vergleichbare Rate an nicht symptomatischen Subarachnoidalblutungen mit 10,6 Prozent in der M1-TE-Gruppe, 9,1 Prozent in der pM2-TE-Gruppe und 0 Prozent in der dM2-TE-Gruppe. Behandlungsbedürftige Dissektionen, Gefäßperforationen oder Embolien in neue Gefäßterritorien traten nicht auf. Somit konnte in der vorliegenden Arbeit keine erhöhte prozedurale oder postinterventionelle Komplikationsrate bei der M2-TE gegenüber der M1-TE festgestellt werden. Auch der Vergleich zwischen M1-TE und der TE in peripheren M2-Abschnitten ergab keine signifikant höhere Komplikationsrate. Hinsichtlich des neurologischen Status gemessen am Rückgang des NIHSS profitierten neben den Patienten mit M1-Verschluss sowohl die Patienten mit proximalem als auch mit peripherem M2-Verschluss deutlich von der TE. Zusammenfassend stellte sich die M2-TE in dem vorliegenden Patientenkollektiv als zur M1-TE vergleichbar sichere und effektive Methode dar.

3.4.4 Thrombektomie zur Behandlung thrombotischer Komplikationen nach Flow-Diverter-Implantation

Marius G. Kaschner, Athanasios Petridis, Bernd Turowski. *Single-center experience with the new-generation Derivo embolization device for ruptured and unruptured intracranial aneurysms (2020).* J Neurosurg Sci. 64: 353–363.

Die endovaskuläre Behandlung von intrakraniellen Aneurysmen mit flussmodulierenden Implantaten, den sogenannten Flow-Divertern, wird bei Aneurysmen mit komplexer Anatomie wie fusiformer, dysplastischer oder disseziierender Aneurysmen in zunehmendem Maße durchgeführt. Bei dem Flow-Diverter (FD) handelt es sich um einen Stent mit geringer Porengröße, der endovaskulär in das Trägergefäß implantiert wird und den Blutfluss an dem Aneurysma vorbeileitet. Dadurch kommt es zu einer graduellen Thrombosierung des Aneurysmas. Dagegen bleiben diejenigen Gefäßäste des Trägergefäßes, von denen das Aneurysma ausgeht und die von dem FD überdeckt werden, aufgrund des bestehenden Flussgradienten perfundiert. Flow-Diverter werden sowohl in der elektiven Aneurysmabehandlung eingesetzt als auch bei der Behandlung des hämorrhagischen Schlaganfalls durch eine Aneurysmablutung. Eine Hauptkomplikation bei der Aneurysmabehandlung mit FD stellen thromboembolische Ereignisse und – als eine

schwerwiegende Komplikation – der thrombotische Verschluss des FD mit Folge eines ischämischen Schlaganfalls dar. In der vorliegenden Arbeit wurden die Effektivität und Sicherheit des Flow-Diverters ‚Derivo Embolization Device' in der Behandlung rupturierter (41 %) und nicht rupturierter intrakranieller Aneurysmen (59 % [inzidentell, symptomatisch, Re-Behandlung]) des vorderen und hinteren Kreislaufs untersucht. Dazu wurden die Daten von 32 Patienten ausgewertet, die im Zeitraum zwischen November 2015 und Dezember 2018 an insgesamt 39 Aneurysmen in der Neuroradiologie des UKD behandelt wurden. Bei der DSA-Kontrolle der behandelten Aneurysmen nach sechs Monaten zeigten sich bei 73,1 Prozent vollständige und bei 3,8 Prozent subtotale Verschlüsse der Aneurysmen. Intraprozedurale Komplikationen bei der technischen Durchführung der FD-Implantation traten nicht auf. Die Rate an periinterventionellen Komplikationen mit transienter Behinderung lag bei 18,7 Prozent und an persistierender neurologischer Einschränkung bei 6,2 Prozent. Die Komplikationen umfassten bei einem Patienten eine fatale Re-Blutung als Folge einer nach Ausschöpfen aller technisch-interventionellen und pharmakologischen Maßnahmen nicht zu beherrschenden persistierenden Inflammation der Aneurysmawand. Bei einem weiteren Patienten mit rupturiertem Aneurysma trat als Folge der Subarachnoidalblutung (SAB) ein territorialer Infarkt durch Vasospasmus und Verschluss der Thalamusperforatoren durch den FD auf. Zwei Patienten entwickelten ein postoperatives Delirium. Thromboembolische Ereignisse mit fokal-neurologischen Symptomen eines ischämischen Schlaganfalls durch Mikroembolien traten bei zwei Patienten auf. In einem Fall war das Einbringen eines Einzel-Coils in ein linksseitiges ACI-Aneurysma vor der FD-Implantation Ursache der angiographisch nicht sichtbar gewesenen Mikroembolien, die sich in der MRT in Form von Mikroinfarkten zeigten und sich als persistierende Aphasie manifestierten. Bei dem zweiten Patienten war eine Thromboembolie aus dem durch Coiling vorbehandelten linksseitigen ACI-Aneurysma ursächlich für eine transiente postinterventionelle Aphasie (mRS 0 nach 48 h). Diese war in der abschließenden angiographischen Kontrollserie nicht mehr sichtbar gewesen, da sie zu diesem Zeitpunkt bereits durch körpereigene Lyse nicht mehr vorhanden war. Bei einem Patienten kam es 12 und 18 Monate nach Behandlung eines rupturierten vertebrobasilären, disseziierenden Aneurysmas jeweils nach geplantem Absetzen der doppelten Thrombozytenaggregationshemmung (TAH) zu einem thrombotischen Verschluss des FD, der sich durch eine akute Hemiparese manifestierte. Bei den Ereignissen wurde als Ursache des Verschlusses eine unzureichende Endothelialisierung des FD-Lumens angenommen, die sich später durch einen persistierenden Zufluss aus der kontralateralen A. vertebralis erklären ließ. Dadurch kam es vermutlich nach Absetzen der TAH zu einer Thrombusbildung an dem frei liegenden Metall des FD. Nach Bestätigung eines Verschlusses des FD in der MR-Angiographie wurde bei beiden Ereignissen eine alleinige Aspirationsthrombektomie (ATE) mit vollständiger Rekanalisation (TICI 3) durchgeführt. Der Zufluss über die rechte Vertebralarterie

wurde nach der zweiten Thrombektomie durch ein endovaskuläres Coiling verschlossen. Durch die TE konnte ein gutes neurologisches Outcome mit einer geringen residuellen Parese (mRS 2) erzielt werden. Die Studie zeigte, dass lokale und emboligene thromboembolische Komplikationen mit unterschiedlichem Schweregrad typische Komplikationen bei der FD-Behandlung sind. Die alleinige ATE mit einem großlumigen flexiblen Katheter stellte sich im Fall des FD-Verschlusses als sichere und effektive Behandlungsoption dar.

3.6 Anatomisch-funktionelle Aspekte beim ischämischen Schlaganfall

3.6.1 Systematische Evaluation von Computertomographie-Angiographie-Kollateralscores zur Vorhersage des Langzeitergebnisses nach mechanischer Thrombektomie beim akuten Schlaganfall

Daniel Weiss, Bastian Kraus, Christian Rubbert, **Marius Kaschner**, Sebastian Jander, Michael Gliem, John-Ih Lee, Carl-Albrecht Haensch, Bernd Turowski, Julian Caspers (2019). *Systematic evaluation of computed tomography angiography collateral scores for estimation of long-term outcome after mechanical thrombectomy in acute ischaemic stroke.* Neuroradiol J 32: 277–286.

Ein vorrangiges Ziel der Forschung zur endovaskulären Schlaganfallbehandlung besteht darin, Wege zu finden, ein funktionell gutes klinisches Outcome verlässlich vorhersagen zu können, um diejenigen Patienten zu identifizieren, die von der Intervention einen Nutzen haben. Die bereits erwähnten aktuellen Studien zeigen, dass auch zwölf Stunden nach Beginn der Schlaganfallsymptome Patienten von einer Thrombektomie (TE) bei zerebralem Gefäßverschluss profitieren können. Jedoch ist der entscheidende Prognosefaktor zur Abschätzung des Outcomes die verbleibende Blutversorgung des betroffenen Hirngewebes durch Kollateralen. Das Ziel dieser Studie war die systematische Analyse von vier etablierten computertomographischen Angiographie-(CTA-)basierten Kollateralscores zur Vorhersage des funktionellen Outcomes nach einer TE. In die Studie wurden 48 prospektive Patienten eingeschlossen, die zwischen Juni 2016 und Juni 2017 durch eine TE bei Gefäßverschluss der vorderen Zirkulation behandelt worden waren. Zu den weiteren Einschlusskriterien gehörte das Vorliegen einer technisch ausreichenden CTA und eine 3-Monatsverlaufskontrolle mittels modifizierter Rankin-Scala (mRS). Das Durchschnittsalter betrug 75 Jahre (SD 14), 53,6 Prozent der Patienten waren weiblich. Das Stromgebiet der A. cerebri media (M1-Segment) war mit 73,8 Prozent am häufigsten von Gefäßverschlüssen betroffen. Der mittlere ASPECT-Score lag bei 10 (IQR 10–18). Bei den meisten Patienten konnte eine erfolgreiche Reperfusion nach TE erreicht werden (TICI 2–3: 89,3 %, TICI 3: 36,9 %).

Der modified Tan-Score, Miteff-Score, Maas-Score und das Opercular-Index-Score-Verhältnis wurden anhand der präinterventionellen CTA durch zwei Radiologen untersucht. Die Kollateralscores wurden hinsichtlich der Interrater-Reliability der Korrelation mit der 3-Monats-modifizierten Rankin-Scale sowie der Fähigkeit zwischen Patienten mit gutem (*modified Rankin Scale 2*) und schlechtem Outcome (*modified Rankin Scale* 3) zu differenzieren, mittels weighted Kappa überprüft. Eine Korrelation zwischen dem relativen Blutvolumen und dem relativen Blutfluss wurde bei Patienten mit vorhandener CT-Perfusionsbildgebung (CTP) durchgeführt. Eine sehr gute Interrater-Reliability konnte für den modified Tan-Score (k = 0,86), Miteff-Score (k = 0,81) und das Opercular-Index-Score-Verhältnis (k = 0,91) sowie eine substanzielle Reliabilität für den Maas-Score festgestellt werden (k = 0,77). Es konnten zudem statistisch signifikante Gruppenunterschiede zwischen Patienten mit gutem und schlechtem Outcome für Maas-Score, Miteff-Score und das Opercular-Index-Score-Verhältnis ermittelt werden. Dabei waren Miteff (OR 2,08 [0,82–5,26]) und Maas (5,01 [1,25–20,04]) statistisch signifikante Prädiktoren für ein gutes Outcome in der binären logistischen Regressionsanalyse. Alle Kollateralscores korrelierten signifikant mit dem mittleren zerebralen Blutvolumen und relativen Blutfluss, wobei das mittlere relative zerebrale Blutvolumen eine hohe und statistisch signifikante Korrelation mit dem funktionellen Outcome zeigte, die über denen aller Kollateralscores lag. Diese Arbeit zeigte, dass CTA-Kollateralscores ein nützliches Werkzeug zur Abschätzung der Kollateralisierung und damit zur Vorhersage des funktionellen Outcomes nach einer TE beim akuten Schlaganfall sind. Jedoch sollte – wenn möglich – der CTP gegenüber der Einphasen-CTA der Vorzug gegeben werden.

3.6.2 Prädiktoren für den Erhalt der Basalganglien nach mechanischer Thrombektomie bei akuten Verschlüssen des Hauptstammes der A. cerebri media beim ischämischen Schlaganfall

Marius Georg Kaschner, Raul Lande, Christian Rubbert, Julian Caspers, John-Ih Lee, Michael Gliem, Sebastian Jander, Bernd Turowski (2019). *Predictors for basal ganglia viability after mechanical thrombectomy in proximal middle cerebral artery occlusion.* Clin Imaging 57: 1–6.

Bei einem ischämischen Schlaganfall mit akutem Verschluss des Hauptstammes der A. cerebri media (ACM), bei dem die lenticulostriären Arterien (LA) vollständig vom Thrombus überdeckt sind, kommt es in den meisten Fällen zu einer relativ schnellen Infarzierung der Basalganglien (BG). Dies liegt daran, dass die LA die einzige bekannte Blutversorgung der BG sind und die BG somit nur eine kurze Ischämiezeit tolerieren. Dennoch wurde in dem untersuchten Patientenkollektiv in einer Vielzahl von Fällen ein vollständiger oder zumindest

teilweiser Erhalt der BG nach erfolgreicher Rekanalisation durch eine Thrombektomie (TE) des Gefäßverschlusses beobachtet. Ziel der Studie war es, Prädiktoren zu identifizieren, die mit dem Erhalt der BG trotz längerer Ischämiezeit nach dem Gefäßverschluss korrelieren. In dieser monozentrischen Studie wurden retrospektiv zwischen November 2009 und Oktober 2016 alle Patienten mit einem akuten Schlaganfall eingeschlossen, die als Einschlusskriterien einen in der CT-Angiographie (CTA) und in der digitalen Substraktionsangiographie (DSA) bestätigten Verschluss des Hauptstammes der ACM mit vollständiger Überdeckung der LA hatten, um so eine residuelle Blutversorgung der BG vor der TE auszuschließen. Zudem konnten durch die DSA das Vorliegen eventueller Varianten der Blutversorgung der BG ausgeschlossen werden. Die Schlaganfallbildgebung umfasste neben der CTA eine native cranielle Computertomographie (CCT) und die CT-Perfusionsbildgebung (CTP). Für die betroffenen BG-Anteile, die ausschließlich durch die LA versorgt werden (Globus pallidus und Putamen), wurden in der CTP das relative cerebrale Blutvolumen (rCBV), der relative cerebrale Blutfluss (rCBF) durch Verhältnisbildung zur nicht betroffenen kontralateralen Seite bestimmt sowie die maximale Transitzeit (Tmax) und die mittlere Transitzeit (MTT) berechnet. Der Erhalt der entsprechenden BG-Anteile nach Rekanalisation wurde durch eine CCT beurteilt. Dazu wurden die nicht infarzierten BG-Anteile und das übrige Hirnparenchym des Mediastromgebietes in die folgenden sechs Muster eingeteilt:

Putamen (P)
Globus pallidus (GP)
Globus pallidus und Putamen (GP + P)
Putamen und Parenchym (PM = weiße Substanz und Kortex); (P + PM)
Globus pallidus und Parenchym (GP + PM)
Globus pallidus, Putamen und Parenchym (GP + P + PM)

Die Kollateralversorgung des Mediastromgebietes wurde durch den Tan-CTA-Kollateralscore auf einer Skala von 0 = keine Kollateralen bis 3 = 100-%-Füllung der Kollateralen bestimmt (Tan *et al.* 2009). Insgesamt erfüllten 92 Patienten, die mit einer TE in lokaler Aspirationstechnik behandelt wurden, die Einschlusskriterien. In 86,9 Prozent der Fälle wurde eine erfolgreiche Reperfusion (TICI 2b–3) erreicht. Es konnte eine signifikante Korrelation zwischen einem höheren Wert beim Kollateralscore und dem Erhalt der BG-Anteile sowie des Parenchyms des ACM-Territoriums hinsichtlich aller sechs entsprechend definierten Muster festgestellt werden. Die größte positive Korrelation zwischen dem Kollateralscore und dem Erhalt der BG zeigte sich für die Kombination aus GP und PM (OR 3,006, p = 0,003) und für die Kombination aus GP, P und PM (OR: 2,76; p = 0,007). Zudem bestand eine signifikante Korrelation zwischen einem höheren Kollateralscore-Wert und dem Erhalt des

Hirnparenchyms des ACM-Gebietes außerhalb der Basalganglien (Regressionskoeffizient: 0,247, R^2: 0,385, p = 0,000). In zwölf Prozent der Fälle trat im postinterventionellen Verlauf eine symptomatische intrakranielle Blutung auf. Eine hämorrhagische Transformation (PH1-PH2 nach ECASS) des Parenchyms des ACM-Gebietes korrelierte statistisch signifikant ($p < 0,05$) mit weniger erhaltenen BG-Anteilen. In der univariaten und multivariaten Analyse der Perfusionsparameter rCBV-Verhältnis, rCBF-Verhältnis, Tmax und MTT ergab sich eine signifikante Korrelation für das rCBV-Verhältnis als Prädiktor für den Erhalt des Globus pallidus in Kombination mit dem Hirnparenchym des ACM-Gebietes (univariat: OR = 3,160; p = 0,014; multivariat: OR 6,058, p = 0,021). Zusammenfassend konnte in dieser Arbeit gezeigt werden, dass trotz eines über einen längeren Zeitraum bestehenden initialen Verschlusses der LA die BG nach erfolgreicher Rekanalisation des Hauptstammes der ACM erhalten bleiben können. Bis auf das Globus pallidus, das zusätzlich über die Heubnersche Arterie und die A. choroidea anterior versorgt wird, sowie das Caput nuclei caudati, das ebenfalls aus der Heubnerschen Arterie versorgt wird, haben die BG keine angiographisch nachweisbaren Kollateralen und scheinen ausschließlich durch die LA versorgt zu werden, sodass es in den meisten Fällen bei Verschluss der LA zu einer ausgedehnten Infarzierung der BG kommt. Dennoch stellte sich in dieser Studie heraus, dass das Putamen von einer guten Kollateralisierung des Parenchyms des ACM-Gebietes profitiert, obwohl es bis auf den vorderen Anteil keine angiographisch nachweisbaren Kollateralen besitzt. Daher wird in dieser Arbeit die Hypothese aufgestellt, dass angiographisch nicht sichtbare unspezifische tiefe Kollateralen der BG existieren, die durch eine allgemeine gute Parenchymkollateralisierung unterstützt werden. Ein weiteres Indiz dafür ist, dass Defekte des Hirnparenchyms im ACM-Gebiet durch Einblutungen mit einer erhöhten Infarzierung der BG korrelieren. Dadurch stehen theoretisch weniger Kollateralen für die BG zur Verfügung. Ein höheres rCBV-Verhältnis war ebenfalls prädiktiv für den Erhalt der Basalganglien, nahm jedoch gegenüber der Kollateralisierung eine untergeordnete Rolle ein.

4. Zusammenfassende Diskussion

Die interventionelle Behandlung des ischämischen Schlaganfalls gehört heutzutage zusammen mit der medikamentösen rtPA-Lysetherapie zur Standardbehandlung bei Verschluss der großen hirnversorgenden Gefäße des vorderen Hirnkreislaufs. Die Einführung der erstmals im Jahr 2008 eingesetzten Stent-Retriever revolutionierte die Therapie des ischämischen Schlaganfalls. Die Überlegenheit der endovaskulären Behandlung gegenüber der alleinigen Lysetherapie sowie gegenüber älteren mechanischen Systemen wurde im Jahr 2015 in fünf umfassenden randomisierten Studien belegt. Seitdem gibt es eine Vielzahl unterschiedlicher Stent-Retriever (SR) verschiedener Hersteller auf dem Markt, die letztendlich alle prinzipiell die gleiche Funktionsweise haben. Ziel bei der Weiterentwicklung von SR ist es, eine optimale Verankerung zwischen SR und Thrombus herzustellen, die auch bei kurviger Gefäßanatomie erhalten bleibt, um den Thrombus vollständig, möglichst nach einem SR-Durchzug und im Ganzen, aus dem Gefäß zu extrahieren. Zudem wird versucht, eine optimale Visualisierung der SR unter Röntgendurchleuchtung zu erreichen und sie flexibel und atraumatisch zu gestalten.
In dieser Arbeit wurden stellvertretend für modernste Stent-Retriever der Aperio (AP) und Aperio Hybrid (APH) hinsichtlich deren Effektivität bei der Thrombusentfernung, der Sicherheit und des neurologischen Outcomes der Patienten untersucht. Hinweise auf die Effektivität des hybriden Zelldesigns, sich fest mit dem Thrombus zu verbinden, um diesen aus dem Gefäß zu bergen, sind die erzielten hohen Rekanalisationsraten (TICI-Score 2b–3) von 85,3 bis 95,8 Prozent. Letztendlich gibt aber eine hohe Rekanalisationsrate noch keine ausreichende Information über die klinische Wirksamkeit der TE-Behandlung. Hier spielt die erreichte funktionelle Unabhängigkeit (Punktewert 0–2 auf der mRS-Skala) eine entscheidende Rolle zur Beurteilung des funktionell-neurologischen Erfolges der TE. Mit einer Rate von 37 bis 41 Prozent an Patienten mit einem mRS von 0–2 konnte in der vorliegenden Arbeit der klinische Erfolg für die TE-Behandlung mit den hier untersuchten modernen SR bestätigt werden. Das Ausbleiben von symptomatischen intrakraniellen Blutungen und Todesfällen, in direktem Zusammenhang mit der Intervention, sind ein Indikator für die hohe Sicherheit der beiden untersuchten SR und des TE-Verfahrens.

Mit der Entwicklung hochflexibler und großlumiger Aspirationskatheter kam es neben der Stent-Retriever-TE (SRTE) zum Einsatz einer weiteren Thrombektomie-Technik – der alleinigen Aspirationsthrombektomie (ATE) als Erstlinienversuch zur Revaskularisation der großen hirnversorgenden Arterien. Diese wurde unter dem Namen ADAPT (A Direct Aspiration First Pass Technique) bekannt. Dieses Verfahren verbreitete sich schnell, da die Vorteile in der Einfachheit und kurzen Interventionsdauer gesehen wurden. Allerdings wird diese Technik

kontrovers diskutiert, da der Verdacht besteht, dass es zu einem vermehrten Auftreten von Embolien durch Fragmentation und Abschwemmung von Thrombusbestandteilen kommen kann. Theoretisch könnte das Risiko einer Thrombusabschwemmung bei der ATE niedriger liegen, da der Thrombus nicht mit einem Katheter bzw. Stent-Retriever passiert werden muss, andererseits besteht das Risiko, dass die Sogwirkung des Aspirationskatheters ab einer bestimmten Thrombuslänge nicht ausreichend auf den distalen Thrombusanteil einwirkt und dieser fragmentiert oder sich vollständig ablöst Die Annahme einer höheren Rate neuer Embolien von Thrombusmaterial in zuvor nicht betroffene Gefäßterritorien bestätigte sich in dem eigenen Patientenkollektiv nach ATE bei Verschlüssen der A. cerebri media nicht. In der eigenen Arbeit stellte sich das alleinige Aspirationsverfahren zur SRTE als vergleichbar sicher und effektiv dar. Mit 85 Prozent zeigte sich eine hohe Rate an erfolgreichen Rekanalisationen, die mit den in der Literatur und den in den eigenen Studien erzielten Ergebnissen für die SRTE vergleichbar gut waren.
Ein Anhalt für ein im Vergleich zur SRTE häufigeres Vorkommen von angiographisch nicht sichtbaren Mikroembolien bei der ATE, die das klinische Outcome verschlechtern könnten, bestand nach den Ergebnissen im eigenen Patientenkollektiv nicht. Stattdessen zeigte sich in der vorliegenden Studie mit 56 Prozent eine hohe Rate an Patienten mit gutem klinischen Outcome (mRS 0–2), die mit der in dieser Arbeit zur SRTE vorgestellten Rate sowie der einer Metaanalyse der randomisierten fünf großen Stent-Retriever-Studien vergleichbar war (Goyal *et al.* 2016). Die Bedeutung der vorliegenden Studie zusammen mit den Ergebnissen anderer publizierter Studien zur ATE beziehungsweise ADAPT-Methode besteht darin, die zunehmende Evidenz für die Wirksamkeit dieser Technik aufzuzeigen (Wei *et al*. 2017; Turk *et al*. 2019).

Primäres Ziel der endovaskulären Schlaganfallbehandlung ist es, den Thrombus in kürzester Zeit mit möglichst nur einem Thrombektomiemanöver bei gleichzeitig minimaler Komplikationsrate vollständig zu entfernen. Daher stellt sich die Frage, welche TE-Technik am effektivsten eine Thrombusabschwemmung verhindern kann. Aktuell werden dazu verschiedene Techniken der SRTE evaluiert. Die in den eigenen Arbeiten verwendete lokale Aspiration mit vollständiger Retraktion des SR (Solumbra) in den Aspirationskatheter beziehungsweise als weitere Methode die Retraktion von Aspirationskatheter zusammen mit dem SR unter Einklemmung des Thrombus (SAVE) haben sich als effiziente und sichere Techniken herausgestellt. Letztendlich muss die entsprechende TE-Technik den jeweiligen anatomisch-technischen und morphologischen Gegebenheiten angepasst werden. Die SAVE-Technik scheint sich vor allem für sehr feste Thromben zu eignen. Diese sind zu wenig verformbar, um komplett aspiriert zu werden, sodass die Gefahr besteht, dass sie sich von der Katheterspitze abscheren, wenn der Katheter mit dem Thrombus um scharfe Kurven

manövriert wird. Zudem ist denkbar, dass vor allem langstreckige Thromben durch einen SR besser vollständig erfasst werden. In den Fällen, die in dieser Arbeit mit einer alleinigen ATE behandelt wurden, wurde weicher roter (erythrozytenreicher) Thrombus geborgen. Für weiche Thromben könnte die alleinige ATE ein gleichwertiges Verfahren sein, mit dem eine schnelle Thrombusentfernung erreicht wird, was zudem eine Erklärung für die hohe Rate an erfolgreicher Revaskularisation in der vorliegenden Arbeit zur alleinigen ATE wäre. Eine Situation, in dem die alleinige ATE bei bestimmten anatomischen Verhältnissen der SRTE gegenüber von Vorteil sein kann, ist ein Thrombus, der vor einer Gefäßaufteilung – zum Beispiel an der Aufteilung des M1- und der M2-Segmente oder im Basilariskopf – liegt, insbesondere wenn es sich um kleinkalibrige periphere Gefäße distal des Thrombus handelt. Mit der alleinigen ATE muss der Thrombus nicht vollständig mit dem Mikrodraht/-katheter passiert werden, sodass die potenziell höhere Gefahr einer SAB durch Gefäßperforation an den Aufteilungsstellen reduziert wird.

Ein in dieser Arbeit gezeigter weiterer Vorteil der alleinigen ATE liegt in der Behandlung von Stentthrombosen hirnversorgender und intrakranieller Gefäße, die als akute oder verzögerte Komplikation von neu eingebrachten endovaskulären Materialien, wie in dieser Arbeit am Beispiel der Flow-Diverter-Stent-Implantation zur Behandlung komplexer Hirnaneurysmen beschrieben, auftreten können. Eine Rekanalisation eines Stents durch eine TE mit Stent-Retrievern ist nahezu ausgeschlossen, da sich die Maschen des SR in denen des Stents verfangen und sich das Implantat verschiebt oder einfaltet. Dadurch kann es zu Gefäßwandverletzungen und im schlimmsten Fall zu einem bleibenden Verschluss des Hirngefäßes kommen, was in der Regel einen ausgedehnten Infarkt des zugehörigen Versorgungsgebietes zur Folge hat. Damit ein Stent fest in dem betreffenden Gefäß verankert und nicht mehr durch Manipulation verschiebbar ist, muss er von Gefäßwandendothel überwachsen sein. Insbesondere bei Thrombosen von Stents, die noch nicht vollständig eingewachsen sind, kann – wie in dieser Arbeit beschrieben – die alleinige ATE mit einem großlumigen, flexiblen Aspirationskatheter mit nur geringem Risiko der Implantatdislokation eingesetzt werden.

Diese Beobachtungen zeigen, dass die Wahl der TE-Technik von verschiedenen Faktoren abhängig ist, zu denen die Gefäßanatomie, Thrombusbeschaffenheit, Lokalisation des Thrombus sowie spezielle anatomisch-technische Gegebenheiten im Rahmen des Komplikationsmanagements gehören.

Insgesamt ist festzustellen, dass die unterschiedlichen TE-Techniken keine konkurrierenden, sondern sich ergänzende Verfahren darstellen.

Eine spezielle Situation liegt bei Schlaganfallpatienten mit Verschluss der großen Hirngefäße und geringerer Ausprägung der Symptome vor. Eine genaue Definition eines sogenannten ‚Minor-Stroke' existiert nicht. Auch bei einem niedrigen NIHSS-Wert können schwerwiegende

neurologische Symptome wie Aphasie, Hemianopsie oder eine Monoplegie vorliegen. Demgegenüber kann aber auch lediglich eine geringe Behinderung vorhanden sein, sodass sich bei diesen Patienten die Frage stellt, inwieweit eine TE mit in den meisten Fällen geringem, aber potenziell vorhandenem Komplikationsrisiko den klinischen Nutzen rechtfertigt. Seit 2016 wird in den deutschen Leitlinien keine NIHSS-Untergrenze für die TE mehr angegeben. Allerdings liegen noch wenig randomisiert-kontrollierte Daten zur TE bei Patienten mit milden Schlaganfällen vor.

In der Studie zur TE bei Patienten mit milden Schlaganfällen konnte dargelegt werden, dass auch Patienten mit niedrigem NIHSS bei Hauptstammverschlüssen der A. cerebri media (ACM) von einer TE profitieren können. Die Ergebnisse zeigten bereits im kurzfristigen postinterventionellen Verlauf eine signifikante neurologische Verbesserung ohne das Auftreten therapeutisch relevanter prozeduraler und postinterventioneller Komplikationen. Anhand des angiographisch weiterhin nachweisbaren Thrombus stellte sich bei denjenigen Patienten heraus, die eine präinterventionelle i. v. Lyse erhielten, dass diese einen unzureichenden Effekt hatte. Die geringe Symptomatik der Patienten mit M1-Verschlüssen ist durch die anfangs gute Kollateralisierung zu erklären. Jedoch besteht das hohe Risiko einer frühen progressiven Verschlechterung der Symptomatik durch Zusammenbruch einer ausreichenden Kollateralisierung, wie im Fall von zwei Patienten in dem untersuchten Kollektiv, bei denen es nach i. v. Thrombolyse und trotz in der CTA nachgewiesener guter Kollateralisierung zu einer progredienten neurologischen Verschlechterung nach mehreren Stunden kam. Zudem zeigten frühere Studien für Patienten mit geringen Schlaganfallsymptomen bei Verschluss der großen Hirngefäße, die keine akute Rekanalisation erhalten haben, ein schlechtes klinisches Outcome nach 90 Tagen (Smith *et al.* 2011; Mokin *et al.* 2014). Auch wenn potenzielle Gefahren der TE wie Reperfusionshämatome, Gefäßperforation und -dissektion mit symptomatischer Subarachnoidalblutung sowie Embolien in andere Gefäßterritorien mit einer Rate zwischen 0,5 und 4,9 Prozent bestehen, ist das Komplikationsrisiko einer TE im M1-Segment gegenüber der Wahrscheinlichkeit einer relevanten klinischen Verschlechterung bei fehlender Rekanalisation eines Hauptstammverschlusses der ACM als deutlich höher einzuschätzen. Des Weiteren kann auch bei einem geringen Wert auf der NIHSS-Punkteskala eine für den Patienten in individuellem Ausmaß lebenslange relevante neurologische Behinderung vorliegen, die durch den NIHSS nicht ausreichend abgebildet wird. Diesen Überlegungen zufolge scheint die frühzeitige TE bei Patienten mit gering symptomatischen M1-Verschlüssen nach sorgfältiger Einschätzung des Interventionsrisikos sinnvoll.

Zudem waren die guten Rekanalisationsraten verbunden mit einem guten klinischen Outcome trotz des kurzen medianen 9-Tagesverlaufes sowie die sehr geringe Komplikationsrate in

dieser Studie ein weiterer deutlicher Hinweis auf die Wirksamkeit der TE bei Patienten mit niedrigem NIHSS bei M1-Verschluss.

Im Zuge der kontinuierlichen Weiterentwicklung von immer kleineren und flexibleren Kathetern und SR weitet sich die Indikation zur Behandlung von proximalen Gefäßverschlüssen des Mediahauptstammes auch auf peripherere Verschlüsse des Mediastromgebietes aus, wobei die Evidenz für die distalen Mediaverschlüsse, die sogenannten M2-Verschlüsse, im Verhältnis zu den Mediahauptstammverschlüssen (M1-Segmentverschlüssen) gering ist. Hier stand zum einen die Frage im Vordergrund, inwieweit Patienten mit einem M2-Verschluss neurologisch von einer TE profitieren und zum anderen, ob es Hinweise darauf gibt, dass die TE im M2-Stromgebiet mit einem höheren prozeduralen Komplikationsrisiko beispielsweise durch Gefäßperforationen und Subarachnoidalblutungen assoziiert ist als bei M1-Verschlüssen, insbesondere in Abhängigkeit einer proximalen gegenüber einer distalen M2-Verschluss-Lokalisation. Proximale M2-Verschlüsse haben große Perfusionsausfälle zur Folge, die vergleichbar mit M1-Verschlüssen sind und dementsprechend zu schwereren neurologischen Ausfällen führen. Aber auch periphere M2-Verschlüsse können relevante funktionelle neurologische Symptome verursachen, vor allem wenn die dominante Hemisphäre mit dem Sprachzentrum betroffen ist, und können ebenfalls mit einem relevanten Infarktvolumen einhergehen (Sheth et al. 2016). In den eigenen Studien konnte gezeigt werden, dass es in einem Großteil der Fälle sowohl mit proximalen als auch mit distalen M2-Verschlüssen zu einer statistisch signifikanten neurologischen Verbesserung nach der TE gekommen ist. Im Gegensatz zu zahlreichen bisher publizierten Studien wurde in der eigenen Arbeit der Nutzen der M2-TE in Abhängigkeit bestimmter Gefäßterritorien mit der Fragestellung untersucht, ob bestimmte Territorien wie die Rekanalisation der Zentralregion zu einem höheren Grad der Verbesserung des neurologischen Outcomes als beispielsweise die Rekanalisation der parietalen oder temporalen Regionen führen könnten. Die Studie zeigte, dass sich unabhängig vom Verschluss eines bestimmten Territoriums eine signifikante Verbesserung des neurologischen Outcomes (mRS) und eine Rückbildung der Schwere des Schlaganfalls (NIHSS) ergaben. Zudem konnte kein signifikanter Unterschied zwischen einem proximal und peripher gelegenen Astverschluss hinsichtlich des postinterventionellen mRS, NIHSS und der Komplikationsraten festgestellt werden. Diese Beobachtungen sind insofern interessant, als sich daraus der Hinweis ergibt, dass auch die Rekanalisation distaler Verschlüsse immer noch eine relevante Verbesserung des klinischen Outcomes zur Folge haben kann, obwohl im Vergleich zu proximalen Verschlüssen kleinere Areale betroffen sind, die aber eine funktionell hohe Relevanz haben können. Darüber hinaus konnte im Vergleich der einzelnen Territorien kein relevanter Unterschied zu Komplikationen wie häufigere

postinterventionelle symptomatische intrakranielle Blutungen oder prozedurale Komplikationen festgestellt werden.

Die Ergebnisse der Arbeit zum direkten Vergleich zwischen M1- und M2-Thrombektomien zeigten ein vergleichbar niedriges Interventionsrisiko im M1- sowie im proximalen als auch distalen M2-Gefäßgebiet ohne das Auftreten behandlungsbedürftiger Komplikationen. Die Rate an symptomatischen intrazerebralen (Infarkt-)Blutungen im postinterventionellen Verlauf waren mit sieben Prozent für die M1-TE und fünf bis neun Prozent für die M2-TE insgesamt niedrig und wiesen keine statistisch signifikanten Unterschiede zwischen den einzelnen Gefäßsegmenten auf. Eine Erklärung hierfür wird in der Ähnlichkeit der Kaliberdurchmesser des M1- und der proximalen M2-Segmente gesehen. Auch bei den peripheren M2-Verschlüssen, die wegen der teils deutlich geringeren Gefäßkaliber und der kurvigen Gefäßverläufe technisch-anatomisch anspruchsvoller zu behandeln sind, stellte sich die TE peripherer M2-Äste verglichen mit M1- und proximalen M2-Verschlüssen hinsichtlich prozeduraler Komplikationen in den untersuchten Patientenkollektiven ebenfalls als sicher dar. Grund für die erreichte hohe Sicherheit des Verfahrens könnten neben der Erfahrung der Behandler die technischen Eigenschaften der verwendeten SR und Katheter sein. Die in den vorliegenden Studien verwendeten SR sind aus repetitiven funktionellen Segmenten aufgebaut (Abb. 2A), die eine Anpassung an die Gefäßanatomie ermöglichen, wodurch der Thrombus gerade bei schwieriger Gefäßanatomie in der Peripherie schonend entfernt werden soll. Die Erkenntnisse aus den vorliegenden Arbeiten sprechen dafür, Patienten mit gut erreichbarem Verschluss eines proximalen und auch distalen M2-Segmentes einer TE zuzuführen, wenn ein großes rettbares Areal betroffen ist oder ein relevantes neurologisches Defizit vorliegt. Auch wenn noch größere randomisierte Studien ausstehen, unterstützen die Ergebnisse dieser Arbeit die mittlerweile in den deutschen Leitlinien aufgenommene Empfehlung zur TE von M2-Verschlüssen (Ringleb *et al*. 2021).

Der Zeitraum, in dem eine TE mit Erfolg durchgeführt werden kann, wird nicht mehr wie vor einigen Jahren auf sechs Stunden begrenzt, sondern es wird bereits in den deutschen Leitlinien empfohlen, bei ausgewählten Patienten den Zeitraum für eine TE auf mehr als sechs Stunden zu erweitern (Ringleb *et al.* 2021). Hierbei spielt das Ausmaß der Kollateralisierung eine entscheidende Rolle, da eine gute Kollateralisierung mit einem besseren Behandlungsergebnis in Verbindung steht (Miteff *et al.* 2009): Bei guter Kollateralisierung kann das ischämische Hirngewebe auch noch nach längerer Zeit gerettet werden. Vor allem bei Patienten mit bereits teilweise infarziertem Parenchym ist eine erweiterte Bildgebung mit CTA, CTP oder MRA und DWI-Bildgebung unerlässlich, um über eine Mismatch-Bildgebung zu entscheiden, wie ausgedehnt der Anteil von ischämischem, aber noch rettbarem

Hirnparenchym ist. In der vorliegenden Arbeit korrelierte der Kollateralstatus, der anhand verschiedener Scores in der CTA erfasst wurde, gut mit der Kollateralisierung in der CTP. Durch diesen ließ sich das funktionelle klinische Outcome vorhersagen. So könnte es möglich sein, bereits auf Grundlage der CTA Patienten anhand eines Kollateralscores zu identifizieren, die auch in einem Zeitraum von deutlich mehr als sechs Stunden nach Symptombeginn noch von einer TE funktionell-neurologisch profitieren (Nogueira *et al.* 2017; Albers *et al.* 2018). Zudem korrelierte in der Studie zur Behandlung von Patienten mit mildem Schlaganfall und Verschluss des Hauptstammes der ACM (Kapitel 3.4.1) ein höherer präinterventioneller Kollateralstatus mit einer geringeren Verschlechterung zwischen prä- und postinterventionellem ASPECTS. Dabei war das anhand des ASPECTS gemessene Infarktausmaß unabhängig von der Zeit zwischen Beginn der Schlaganfallsymptome und Rekanalisation. Aus diesen Beobachtungen lässt sich ableiten, dass vor allem bei Patienten mit guter Kollateralisierung noch ausgedehnte Anteile von rettbarem Hirngewebe vorliegen, die durch eine Rekanalisierung erhalten werden können.
Die Ergebnisse aus den vorliegenden Arbeiten zeigen, dass der Erfolg einer Thrombektomie nicht allein von einem fest definierten Zeitraum nach Beginn der Symptome, in dem die Intervention durchgeführt wird, abhängt. Stattdessen ist der Grad der Kollateralisierung neben weiteren potenziell relevanten Faktoren wie individueller Ischämietoleranz, Ausmaß des bereits geschädigten Gewebes und systolischer Blutdruck entscheidend, in welchem Zeitrahmen eine TE zu einem guten klinischen Outcome führt.

In Zusammenhang mit der Kollateralisierung wurde in der vorliegenden Arbeit in einem Kollektiv von Patienten mit Hauptstammverschluss der A. cerebri media, bei denen die gesamten lentikulostriären Äste des M1-Segmentes durch den Thrombus überdeckt waren, die Beobachtung gemacht, dass die Basalganglien (BG) bei einem Großteil der Patienten nach erfolgreicher Revaskularisation nicht infarziert waren, obwohl die BG keine anatomisch bekannten Kollateralen aufweisen. Der in diesem Patientenkollektiv neben dem zerebralen Blutvolumen bestehende signifikante Zusammenhang zwischen gutem Kollateralstatus des vorderen Kreislaufs in der CTA und Überleben der BG lässt auf eine angiographisch nicht darstellbare Kollateralisierung der BG schließen, die deren Ischämiezeit verlängert. Aus der Bildgebung erworbenen Kenntnis über eine zu erwartende ausgedehnte Infarzierung der BG könnten sich Konsequenzen für das interventionelle Vorgehen und die postinterventionelle Behandlung ableiten lassen – so zum Beispiel eine Verlegung von Patienten in Zentren mit der Möglichkeit einer schnellen neurochirurgischen Dekompression bei zu erwartenden raumfordernden Reperfusionsschäden der BG. Ein weiteres Beispiel wäre die Anpassung des Gerinnungsmanagements mit Thrombozytenaggregationshemmern und Fibrinolytika sowie das Blutdruckmanagement bei ausgedehnten BG-Infarkten.

5. Schlussfolgerungen

Die Thrombektomie (TE) mit modernen Stent-Retrievern (SR) bildet zusammen mit der pharmakologischen Therapie die Grundlage der Schlaganfallbehandlung. In dieser Arbeit konnte gezeigt werden, dass die Thrombektomie (TE) mit modernen Stent-Retrievern (SR) in Kombination mit lokalen Aspirationstechniken ein effektives und sicheres Verfahren zur Behandlung eines thrombotischen Verschlusses der großen Hirngefäße der vorderen Zirkulation bei Patienten mit einem ischämischen Schlaganfall ist, durch das bei einer großen Anzahl von Patienten eine funktionelle neurologische Unabhängigkeit erreicht werden kann. Bei einem Teil der Patienten stellte die alleinige Aspirationsthrombektomie (ATE) eine Alternative zur TE mit SR dar. Die unterschiedlichen TE-Techniken oder deren Kombination sind sich ergänzende Verfahren, deren Einsatz von verschiedenen Faktoren wie Gefäßanatomie, Thrombusbeschaffenheit, Lokalisation des Thrombus sowie speziellen anatomisch-technischen Aspekten abhängt.

Eine spezielle Indikation der alleinigen ATE ist die Behandlung der Komplikation einer akuten Stentthrombose in intrakraniellen Gefäßen, bei der der Thrombus schonend aspiriert wird, was vor allem bei neuen, noch nicht eingewachsenen Implantaten von großer Bedeutung sein kann. Bei Patienten mit einem akuten Hauptstammverschluss der A. cerebri media (M1-Segment) und nur geringer Schwere des Schlaganfalls kann der Nutzen der TE in ausgewählten Fällen mit deutlicher Verbesserung des neurologischen Outcomes das insgesamt geringe Komplikationsrisiko des Eingriffs überwiegen. Bei der TE der distalen Mediaverschlüsse (M2-Segmente) war eine deutliche funktionelle neurologische Verbesserung ohne ein häufigeres Auftreten relevanter Komplikationen im Vergleich zur TE im M1-Segment festzustellen, sodass bei ausgewählten Patienten mit relevantem neurologischen Defizit eine TE bei sicher erreichbaren M2-Segment-Verschlüssen durchgeführt werden sollte, vor allem dann, wenn funktionell relevante Hirnareale betroffen sind.

Die Intaktheit der Basalganglien (BG) nach erfolgreicher TE trotz länger bestehendem Verschluss lentikulostriärer Äste sind Indizien für eine Kollateralisierung der BG. Als prädiktive Faktoren für ein Überleben der BG wurden ein hoher CTA-Kollateralscore und das zerebrale Blutvolumen vor TE identifiziert. Eine Einschätzung über den Zustand der BG könnte Therapieentscheidungen beeinflussen und Prognosen über das neurologische Outcome zulassen. Die Korrelation der CT-Angiographie-(CTA-)Kollateralscores mit dem funktionellen Outcome der Patienten nach TE weist darauf hin, dass die Kollateralen ein wesentlicher Indikator für das Überleben des Hirnparenchyms und des neurologischen Outcomes sind. Mit der Weiterentwicklung der Kollateralscores sollten diese als wesentlicher Baustein in der präinterventionellen Akut-Diagnostik etabliert werden, um eine bessere Selektion geeigneter

Patienten zu erreichen, die auch bei länger zurückliegendem Schlaganfallereignis von einer TE klinisch profitieren.

Das Ziel weiterer Forschung auf dem Gebiet der Thrombektomie beim ischämischen Schlaganfall sollte darin bestehen, die am besten geeigneten TE-Methoden für die jeweilige Situation zu finden sowie eine immer größere Anzahl derjenigen Patienten zu identifizieren, die von den jeweiligen TE-Methoden profitieren.

Literaturverzeichniss

Adams, H.P., Bendixen, B.H., Kappelle, L.J., Biller, J., Love, B.B., Gordon, D.L., Marsh, E.E. (1993) "Classification of Subtype of Acute Ischemic Stroke," *Stroke*, 23(1), 35–41.

Ahlhelm, F.J., Ludwieg, A., Ahlhelm, D., Roth, C., Papanagiotou, P., Reith, W. (2009) "Magnetresonanz- und computertomographische Befunde bei lakunären Hirninfarkten," *Radiologe*, 49(4), 305–311.

Albers, G.W., Marks, M.P., Kemp, S., Christensen, S., Tsai, J.P., Ortega-Gutierrez, S., McTaggart, R.A., Torbey, M.T., Kim-Tenser, M., Leslie-Mazwi, T., Sarraj, A., Kasner, S.E., Ansari, S.A., Yeatts, S.D., Hamilton, S., Mlynash, M., Heit, J.J., Zaharchuk, G., Kim, S., Carrozzella, J., Palesch, Y.Y., Demchuk, A.M., Bammer, R., Lavori, P.W., Broderick, J.P., Lansberg, M.G. (2018) "Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging," *New England Journal of Medicine*, 378(8), 708–718.

Almekhlafi, M.A., Mishra, S., Desai, J.A., Nambiar, V., Volny, O., Goel, A., Eesa, M., Demchuk, A.M., Menon, B.K., Goyal, M. (2014) "Not all 'successful' angiographic reperfusion patients are an equal validation of a modified TICI scoring system," *Interventional Neuroradiology*, 20(1), 21–27.

Amarenco, P., Bogousslavsky, J., Caplan, L.R., Donnan, G.A., Wolf, M.E., Hennerici, M.G. (2013) "The ASCOD phenotyping of ischemic stroke (Updated ASCO Phenotyping)," *Cerebrovascular Diseases*, 36(1), 1–5.

Asadi, H., Dowling, R., Yan, B., Wong, S., Mitchell, P. (2015) "Advances in endovascular treatment of acute ischaemic stroke," *Internal Medicine Journal*, 45(8), 798–805.

Barber, P.A. (2000) "Erratum: Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy (The Lancet (2000) 13 May (1670))," *Lancet*, 355(9221), 2170.

Berkhemer, O.A., Fransen, P.S.S., Beumer, D., van den Berg, L.A., Lingsma, H.F., Yoo, A.J., Schonewille, W.J., Vos, J.A., Nederkoorn, P.J., Wermer, M.J.H., van Walderveen, M.A.A., Staals, J., Hofmeijer, J., van Oostayen, J.A., Lycklama à Nijeholt, G.J., Boiten, J., Brouwer, P.A., Emmer, B.J., de Bruijn, S.F., van Dijk, L.C., Kappelle, L.J., Lo, R.H., van Dijk, E.J., de Vries, J., de Kort, P.L.M., van Rooij, W.J.J., van den Berg, J.S.P., van Hasselt, B.A.A.M., Aerden, L.A.M., Dallinga, R.J., Visser, M.C., Bot, J.C.J., Vroomen, P.C., Eshghi, O., Schreuder, T.H.C.M.L., Heijboer, R.J.J., Keizer, K., Tielbeek, A. V., den Hertog, H.M., Gerrits, D.G., van den Berg-Vos, R.M., Karas, G.B., Steyerberg, E.W., Flach, H.Z., Marquering, H.A., Sprengers, M.E.S., Jenniskens, S.F.M., Beenen, L.F.M., van den Berg, R., Koudstaal, P.J., van Zwam, W.H., Roos, Y.B.W.E.M., van der Lugt, A., van Oostenbrugge, R.J., Majoie, C.B.L.M., Dippel, D.W.J. (2015) "A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke," *New England Journal of Medicine*, 372(1), 11–20.

Boujan, T., Neuberger, U., Pfaff, J., Nagel, S., Herweh, C., Bendszus, M., Möhlenbruch, M.A. (2018) "Value of contrast-enhanced MRA versus time-of-flight MRA in acute ischemic stroke MRI," *American Journal of Neuroradiology*, 39(9), 1710–1716.

Broderick, J.P., Palesch, Y.Y., Demchuk, A.M., Yeatts, S.D., Khatri, P., Hill, M.D., Jauch, E.C., Jovin, T.G., Yan, B., Silver, F.L., von Kummer, R., Molina, C.A., Demaerschalk, B.M., Budzik, R., Clark, W.M., Zaidat, O.O., Malisch, T.W., Goyal, M., Schonewille, W.J., Mazighi, M., Engelter, S.T., Anderson, C., Spilker, J., Carrozzella, J., Ryckborst, K.J., Janis, L.S., Martin, R.H., Foster, L.D., Tomsick, T.A. (2013) "Endovascular Therapy after Intravenous t-PA versus t-PA Alone for Stroke," *New England Journal of Medicine*, 368(10), 893–903.

Brott, T., Adams, H.P., Olinger, C.P., Marle, J.R., Barsan, W.G., Biller, J., Spilker, J., Holleran, R., Eberle, R., Hertzberg, V., Rorick, M., Moomaw, C.J., Walker, M. (1989) "Measurements of acute cerebral infarction: A clinical examination scale," *Stroke*, 20(7), 864–870.

Busch, M.A., Schienkiewitz, A., Nowossadeck, E., Gößwald, A. (2013) "Prävalenz des Schlaganfalls bei Erwachsenen im Alter von 40 bis 79 Jahren in Deutschland: Ergebnisse der Studie zur Gesundheit Erwachsener in Deutschland (DEGS1),"

Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz, 56(5–6), 656–660.

Campbell, B.C.V., Hill, M.D., Rubiera, M., Menon, B.K., Demchuk, A., Donnan, G.A., Roy, D., Thornton, J., Dorado, L., Bonafe, A., Levy, E.I., Diener, H.-C., Hernández-Pérez, M., Pereira, V.M., Blasco, J., Quesada, H., Rempel, J., Jahan, R., Davis, S.M., Stouch, B.C., Mitchell, P.J., Jovin, T.G., Saver, J.L., Goyal, M. (2016) "Safety and Efficacy of Solitaire Stent Thrombectomy," *Stroke*, STROKEAHA.115.012360.

Campbell, B.C.V., Mitchell, P.J., Kleinig, T.J., Dewey, H.M., Churilov, L., Yassi, N., Yan, B., Dowling, R.J., Parsons, M.W., Oxley, T.J., Wu, T.Y., Brooks, M., Simpson, M.A., Miteff, F., Levi, C.R., Krause, M., Harrington, T.J., Faulder, K.C., Steinfort, B.S., Priglinger, M., Ang, T., Scroop, R., Barber, P.A., McGuinness, B., Wijeratne, T., Phan, T.G., Chong, W., Chandra, R. v., Bladin, C.F., Badve, M., Rice, H., de Villiers, L., Ma, H., Desmond, P.M., Donnan, G.A., Davis, S.M. (2015) "Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection," *New England Journal of Medicine*, 372(11), 1009–1018, available: http://www.nejm.org/doi/10.1056/NEJMoa1414792.

Ciccone, A., Valvassori, L., Nichelatti, M., Sgoifo, A., Ponzio, M., Sterzi, R., Boccardi, E. (2013) "Endovascular Treatment for Acute Ischemic Stroke," *New England Journal of Medicine*, 368(10), 904–913.

Emberson, J., Lees, K.R., Lyden, P., Blackwell, L., Albers, G., Bluhmki, E., Brott, T., Cohen, G., Davis, S., Donnan, G., Grotta, J., Howard, G., Kaste, M., Koga, M., Von Kummer, R., Lansberg, M., Lindley, R.I., Murray, G., Olivot, J.M., Parsons, M., Tilley, B., Toni, D., Toyoda, K., Wahlgren, N., Wardlaw, J., Whiteley, W., Del Zoppo, G.J., Baigent, C., Sandercock, P., Hacke, W. (2014) "Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: A meta-analysis of individual patient data from randomised trials," *The Lancet*, 384(9958), 1929–1935.

Fransen, P.S.S., Beumer, D., Berkhemer, O.A., van den Berg, L.A., Lingsma, H., van der Lugt, A., van Zwam, W.H., van Oostenbrugge, R.J., Roos, Y.B.W.E.M., Majoie, C.B., Dippel, D.W.J. (2014) "MR CLEAN, a multicenter randomized clinical trial of endovascular treatment for acute ischemic stroke in the Netherlands: Study protocol for a randomized controlled trial," *Trials*, 15(1).

Goyal, M., Demchuk, A.M., Menon, B.K., Eesa, M., Rempel, J.L., Thornton, J., Roy, D., Jovin, T.G., Willinsky, R.A., Sapkota, B.L., Dowlatshahi, D., Frei, D.F., Kamal, N.R., Montanera, W.J., Poppe, A.Y., Ryckborst, K.J., Silver, F.L., Shuaib, A., Tampieri, D., Williams, D., Bang, O.Y., Baxter, B.W., Burns, P.A., Choe, H., Heo, J.H., Holmstedt, C.A., Jankowitz, B., Kelly, M., Linares, G., Mandzia, J.L., Shankar, J., Sohn, S. il, Swartz, R.H., Barber, P.A., Coutts, S.B., Smith, E.E., Morrish, W.F., Weill, A., Subramaniam, S., Mitha, A.P., Wong, J.H., Lowerison, M.W., Sajobi, T.T., Hill, M.D. (2015) "Randomized assessment of rapid endovascular treatment of ischemic stroke," *New England Journal of Medicine*, 372(11), 1019–1030.

Goyal, M., Menon, B.K., Van Zwam, W.H., Dippel, D.W.J., Mitchell, P.J., Demchuk, A.M., Dávalos, A., Majoie, C.B.L.M., Van Der Lugt, A., De Miquel, M.A., Donnan, G.A., Roos, Y.B.W.E.M., Bonafe, A., Jahan, R., Diener, H.C., Van Den Berg, L.A., Levy, E.I., Berkhemer, O.A., Pereira, V.M., Rempel, J., Millán, M., Davis, S.M., Roy, D., Thornton, J., Román, L.S., Ribó, M., Beumer, D., Stouch, B., Brown, S., Campbell, B.C.V., Van Oostenbrugge, R.J., Saver, J.L., Hill, M.D., Jovin, T.G. (2016) "Endovascular thrombectomy after large-vessel ischaemic stroke: A meta-analysis of individual patient data from five randomised trials," *The Lancet*, 387(10029), 1723–1731.

Hacke W., Donnan G., Fieschi C., Kaste M., von Kummer R., Broderick J.P., Brott T., Frankel M., Grotta J.C., Haley E.C. Jr, Kwiatkowski T., Levine S.R., Lewandowski C., Lu M., Lyden P., Marler J.R., Patel S., Tilley B.C., Albers G., Bluhmki E., Wilhelm M., Hamilton S.; ATLANTIS Trials Investigators; ECASS Trials Investigators; NINDS rt-PA Study Group Investigators (2004) "Association of outcome with early stroke treatment: Pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials," *Lancet*, 363(9411), 768–774.

Hacke, W., Kaste, M., Bluhmki, E., Brozman, M., Dávalos, A., Guidetti, D., Larrue, V., Lees, K.R., Medeghri, Z., Machnig, T., Schneider, D., von Kummer, R., Wahlgren, N., Toni, D. (2008) “Thrombolysis with Alteplase 3 to 4.5 Hours after Acute Ischemic Stroke,” *New England Journal of Medicine*, 359(13), 1317–1329.

Hameed, A., Zafar, H., Mylotte, D., Sharif, F. (2017) “Recent Trends in Clot Retrieval Devices: A Review,” *Cardiology and Therapy*, 6(2), 193–202.

Hankey, G.J., Norrving, B., Hacke, W., Steiner, T. (2014) “Management of acute stroke in patients taking novel oral anticoagulants,” *International Journal of Stroke*, 9(5), 627–632.

Heuschmann, P., Busse, O., Wagner, M., Endres, M., Villringer, A., Röther, J., Kolominsky-Rabas, P., Berger, K. (2010) “Schlaganfallhäufigkeit und Versorgung von Schlaganfallpatienten in Deutschland,” *Aktuelle Neurologie*, 37(07), 333–340.

Higashida, R.T., Furlan, A.J. (2003) “Trial Design and Reporting Standards for Intra-Arterial Cerebral Thrombolysis for Acute Ischemic Stroke,” *Stroke*, 34(8).

van der Hoeven, E.J.R.J., Schonewille, W.J., Vos, J.A., Algra, A., Audebert, H.J., Berge, E., Ciccone, A., Mazighi, M., Michel, P., Muir, K.W., Obach, V., Puetz, V., Wijman, C.A.C., Zini, A., Kappelle, J.L. (2013) “The Basilar Artery International Cooperation Study (BASICS): Study protocol for a randomised controlled trial,” *Trials*, 14(1), 1–8.

Jovin, T.G., Chamorro, A., Cobo, E., de Miquel, M.A., Molina, C.A., Rovira, A., San Román, L., Serena, J., Abilleira, S., Ribó, M., Millán, M., Urra, X., Cardona, P., López-Cancio, E., Tomasello, A., Castaño, C., Blasco, J., Aja, L., Dorado, L., Quesada, H., Rubiera, M., Hernandez-Pérez, M., Goyal, M., Demchuk, A.M., von Kummer, R., Gallofré, M., Dávalos, A. (2015) “Thrombectomy within 8 Hours after Symptom Onset in Ischemic Stroke,” *New England Journal of Medicine*, 372(24), 2296–2306, available: http://www.nejm.org/doi/10.1056/NEJMoa1503780.

Kidwell, C.S., Jahan, R., Gornbein, J., Alger, J.R., Nenov, V., Ajani, Z., Feng, L., Meyer, B.C., Olson, S., Schwamm, L.H., Yoo, A.J., Marshall, R.S., Meyers, P.M., Yavagal, D.R., Wintermark, M., Guzy, J., Starkman, S., Saver, J.L. (2013) “A Trial of Imaging Selection and Endovascular Treatment for Ischemic Stroke,” *New England Journal of Medicine*, 368(10), 914–923.

Kumar, G., Shahripour, R.B., Alexandrov, A. v. (2015) “Recanalization of acute basilar artery occlusion improves outcomes: A meta-analysis,” *Journal of NeuroInterventional Surgery*, 7(12), 868–874.

Lapergue, B., Blanc, R., Gory, B., Labreuche, J., Duhamel, A., Marnat, G., Saleme, S., Costalat, V., Bracard, S., Desal, H., Mazighi, M., Consoli, A., Piotin, M. (2017) “Effect of endovascular contact aspiration vs stent retriever on revascularization in patients with acute ischemic stroke and large vessel occlusion: The ASTER randomized clinical trial,” *JAMA - Journal of the American Medical Association*, 318(5), 443–452.

Lees, K.R., Bluhmki, E., von Kummer, R., Brott, T.G., Toni, D., Grotta, J.C., Albers, G.W., Kaste, M., Marler, J.R., Hamilton, S.A., Tilley, B.C., Davis, S.M., Donnan, G.A., Hacke, W. (2010) “Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials,” *The Lancet*, 375(9727), 1695–1703.

Maegerlein, C., Mönch, S., Boeckh-Behrens, T., Lehm, M., Hedderich, D.M., Berndt, M.T., Wunderlich, S., Zimmer, C., Kaesmacher, J., Friedrich, B. (2018) “PROTECT: PRoximal balloon Occlusion TogEther with direCt Thrombus aspiration during stent retriever thrombectomy - evaluation of a double embolic protection approach in endovascular stroke treatment.,” *Journal of neurointerventional surgery*, 10(8), 751–755.

Mahoney, F.I., Barthel, D.W. (1965) “Baltimore City Medical Society Functional Evaluation : the Barthel Index,” *Maryland State Medical Journal*, 14, 56–61.

Maus, V., Behme, D., Kabbasch, C., Borggrefe, J., Tsogkas, I., Nikoubashman, O., Wiesmann, M., Knauth, M., Mpotsaris, A., Psychogios, M.N. (2017) “Maximizing First-Pass Complete Reperfusion with SAVE,” *Clinical Neuroradiology*, 1–12.

Meyer, B.C., Hemmen, T.M., Jackson, C.M., Lyden, P.D. (2002) “Modified National Institutes of Health Stroke Scale for use in stroke clinical trials: Prospective reliability and validity,” *Stroke*, 33(5), 1261–1266.

Mishra, N.K., Diener, H.C., Lyden, P.D., Bluhmki, E., Lees, K.R. (2010) “Influence of age on outcome from thrombolysis in acute stroke: A controlled comparison in patients from the virtual international stroke trials archive (VISTA),” *Stroke*, 41(12), 2840–2848.
Miteff, F., Levi, C.R., Bateman, G.A., Spratt, N., McElduff, P., Parsons, M.W. (2009) “The independent predictive utility of computed tomography angiographic collateral status in acute ischaemic stroke,” *Brain*, 132(8), 2231–2238.
Mokin, M., Masud, M.W., Dumont, T.M., Ahmad, G., Kass-Hout, T., Snyder, K. v., Hopkins, L.N., Siddiqui, A.H., Levy, E.I. (2014) “Outcomes in patients with acute ischemic stroke from proximal intracranial vessel occlusion and NIHSS score below 8,” *Journal of NeuroInterventional Surgery*, 6(6), 413–417.
Munich, S.A., Vakharia, K., Levy, E.I. (2019) “Overview of Mechanical Thrombectomy Techniques,” *Clinical Neurosurgery*, 85(1), S60–S67.
National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group (1995) “Recombinant tissue plasminogen activator for acute ischemic stroke,” *Cardiology Review*, 333(24), 1581–1587.
Nogueira, R.G. (2012) “Trevo2,” *Lancet*, 380(9849), 1231–1240.
Nogueira, R.G., Jadhav, A.P., Haussen, D.C., Bonafe, A., Budzik, R.F., Bhuva, P., Yavagal, D.R., Ribo, M., Cognard, C., Hanel, R.A., Sila, C.A., Hassan, A.E., Millan, M., Levy, E.I., Mitchell, P., Chen, M., English, J.D., Shah, Q.A., Silver, F.L., Pereira, V.M., Mehta, B.P., Baxter, B.W., Abraham, M.G., Cardona, P., Veznedaroglu, E., Hellinger, F.R., Feng, L., Kirmani, J.F., Lopes, D.K., Jankowitz, B.T., Frankel, M.R., Costalat, V., Vora, N.A., Yoo, A.J., Malik, A.M., Furlan, A.J., Rubiera, M., Aghaebrahim, A., Olivot, J.-M., Tekle, W.G., Shields, R., Graves, T., Lewis, R.J., Smith, W.S., Liebeskind, D.S., Saver, J.L., Jovin, T.G. (2017) “Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct,” *New England Journal of Medicine*, NEJMoa1706442.
Pérez, M.A., Miloslavski, E., Fischer, S., Bäzner, H., Henkes, H. (2012) “Intracranial thrombectomy using the Solitaire stent: A historical vignette,” *Journal of NeuroInterventional Surgery*, 4(6), 1–4.
Po Sit, S. (2009) “The penumbra pivotal stroke trial: Safety and effectiveness of a new generation of mechanical devices for clot removal in intracranial large vessel occlusive disease,” *Stroke*, 40(8), 2761–2768.
Rha, J.H., Saver, J.L. (2007) “The impact of recanalization on ischemic stroke outcome: A meta-analysis,” *Stroke*, 38(3), 967–973.
Ringleb P., Hamann G., Röther J., Jansen O., Groden C., Veltkamp R. (2015) “Deutsche Gesellschaft für Neurologie e.V. (DGN) (2015). S2k-Leitlinie ‘Akuttherapie des ischämischen Schlaganfalls, Ergänzung 2015 – Rekanalisierende Therapie’. AWMF: Reg.-Nr. 030 - 140.”
Ringleb P., Hametner C., Köhrmann M., Jansen O., Berlis A., Fischer U., Laufs U., Mordasini P., Schellinger P., Schubert G., Sonnberger M., Sykora M., Urbach H., Wachter R., Wagner M., Weiller C., Harloff A., Langguth P. (2021) “Akuttherapie des ischämischen Schlaganfalls, S2e-Leitlinie, 2021, in: Deutsche Gesellschaft für Neurologie (Hrsg.), Leitlinien für Diagnostik und Therapie in der Neurologie. Online: www.dgn.org/leitlinien.”
Röther, J., Schellinger, P.D., Gass, A., Siebler, M., Villringer, A., Fiebach, J.B., Fiehler, J., Jansen, O., Kucinski, T., Schoder, V., Szabo, K., Junge-Hülsing, G.J., Hennerici, M., Zeumer, H., Sartor, K., Weiller, C., Hacke, W. (2002) “Effect of intravenous thrombolysis on MRI parameters and functional outcome in acute stroke <6 hours,” *Stroke*, 33(10), 2438–2445.
Sandercock, P., Wardlaw, J.M., Lindley, R.I., Dennis, M., Cohen, G., Murray, G., Innes, K., Venables, G., Czlonkowska, A., Kobayashi, A., Ricci, S., Murray, V., Berge, E., Slot, K.B., Hankey, G.J., Correia, M., Peeters, A., Matz, K., Lyrer, P., Gubitz, G., Phillips, S.J., Arauz, A., Baigent, C., Chadwick, D., Tyrrell, P., Lowe, G., Collins, R., Bath, P., Van Gijn, J., Gray, R., Hart, R., Yusuf, S., Clark, A., Perry, D., Soosay, V., Buchanan, D., Grant, S., Sakka, E., Drever, J., Walker, P., Herath, I., Brown, A.L., Chmielnik, P., Armit, C., Walton, A., Hautvast, M., Lewis, S., Heron, G., Odusanya, S., Linksted, P., Kane, I., Whiteley, W., Sellar, R., White, P., Keston, P., Farrell, A., Morris, Z., Miranda, H., Blackwell, L. (2012) “The benefits and harms of intravenous thrombolysis with

recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): A randomised controlled trial," *The Lancet*, 379(9834), 2352–2363.
Santulli, G. (2012) "Thrombolysis outcomes in acute ischemic stroke patients with prior stroke and diabetes mellitus," *Neurology*, 78(11), 840.
Saver, J., Jahan, R., Levy, E., Jovin, T., Baxter, B., Nogueira, R., Clark, W., Budzik, R., Zaidat, O., SWIFT Trialists (2012) "Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial," *Lancet*, 380(9849), 1241–1249.
Saver, J.L., Goyal, M., Bonafe, A., Diener, H.-C., Levy, E.I., Pereira, V.M., Albers, G.W., Cognard, C., Cohen, D.J., Hacke, W., Jansen, O., Jovin, T.G., Mattle, H.P., Nogueira, R.G., Siddiqui, A.H., Yavagal, D.R., Baxter, B.W., Devlin, T.G., Lopes, D.K., Reddy, V.K., du Mesnil de Rochemont, R., Singer, O.C., Jahan, R. (2015) "Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke," *New England Journal of Medicine*, 372(24), 2285–2295, available: http://www.nejm.org/doi/10.1056/NEJMoa1415061.
Saver, J.L., Jahan, R., Levy, E.I., Jovin, T.G., Baxter, B., Nogueira, R., Clark, W., Budzik, R., Zaidat, O.O. (2014) "SOLITAIRE™ with the intention for thrombectomy (SWIFT) trial: Design of a randomized, controlled, multicenter study comparing the SOLITAIRE™ Flow Restoration device and the MERCI Retriever in acute ischaemic stroke," *International Journal of Stroke*, 9(5), 658–668.
Schellinger, P.D., Thomalla, G., Fiehler, J., Köhrmann, M., Molina, C.A., Neumann-Haefelin, T., Ribo, M., Singer, O.C., Zaro-Weber, O., Sobesky, J. (2007) "MRI-based and CT-based thrombolytic therapy in acute stroke within and beyond established time windows: An analysis of 1210 patients," *Stroke*, 38(10), 2640–2645.
Sheng, K., Tong, M. (2019) "Therapy for acute basilar artery occlusion: A systematic review and meta-analysis [version 1; peer review: 2 approved]," *F1000Research*, 8, 1–17.
Sheth SA, Yoo B, Saver JL, Starkmann S, Ali LK, Kim D, Gonzalez NR, Jahan R, Tateshima S, Duckwiler G, Vinuela F, Liebeskind DS (2016) "M2 occlusions as targets for endovascular therapy: comprehensive analysis of diffusion/perfusion MRI, angiography, and clinical outcomes," *J Neurointerv Surg. 2015 July ; 7(7): 478–483. doi:10.1136/neurintsurg-2014-011232.*, 176(1), 139–148.
Singer, O.C., Haring, H.P., Trenkler, J., Nolte, C.H., Bohner, G., Reich, A., Wiesmann, M., Bussmeyer, M., Mpotsaris, A., Neumann-Haefelin, T., Hohmann, C., Niederkorn, K., Deutschmann, H., Stoll, A., Bormann, A., Jander, S., Turowski, B., Brenck, J., Schlamann, M.U., Petzold, G.C., Urbach, H., Liebeskind, D.S., Berkefeld, J. (2013) "Age dependency of successful recanalization in anterior circulation stroke: The ENDOSTROKE study," *Cerebrovascular Diseases*.
Smith, E.E., Fonarow, G.C., Reeves, M.J., Cox, M., Olson, D.M., Hernandez, A.F., Schwamm, L.H. (2011) "Outcomes in mild or rapidly improving stroke not treated with intravenous recombinant tissue-type plasminogen activator: Findings from get with the guidelines-stroke," *Stroke*, 42(11), 3110–3115.
Smith, W.S., Sung, G., Saver, J., Budzik, R., Duckwiler, G., Liebeskind, D.S., Lutsep, H.L., Rymer, M.M., Higashida, R.T., Starkman, S., Gobin, Y.P. (2008) "Mechanical thrombectomy for acute ischemic stroke: Final results of the multi MERCI trial," *Stroke*, 39(4), 1205–1212.
Smith, W.S., Sung, G., Starkman, S., Saver, J.L., Kidwell, C.S., Gobin, Y.P., Lutsep, H.L., Nesbit, G.M., Grobelny, T., Rymer, M.M., Silverman, I.E., Higashida, R.T., Budzik, R.F., Marks, M.P. (2005) "Safety and efficacy of mechanical embolectomy in acute ischemic stroke: Results of the MERCI trial," *Stroke*, 36(7), 1432–1438.
Stahmeyer, J.T., Stubenrauch, S., Geyer, S., Weissenborn, K., Eberhard, S. (2019) "Häufigkeit und Zeitpunkt von Rezidiven nach inzidentem Schlaganfall," *Deutsches Arzteblatt International*, 116(42), 711–717.
Steiner, T., Böhm, M., Dichgans, M., Diener, H.C., Ell, C., Endres, M., Epple, C., Grond, M., Laufs, U., Nickenig, G., Riess, H., Röther, J., Schellinger, P.D., Spannagl, M., Veltkamp, R. (2013) "Recommendations for the emergency management of complications

associated with the new direct oral anticoagulants (DOACs), apixaban, dabigatran and rivaroxaban," *Clinical Research in Cardiology*, 102(6), 399–412.
van Swieten, J., Koudstaal, P., Visser, M., Schouten, H., J, van G. (1988) "Interobserver agreement for the assessment of handicap in stroke patients," *Stroke*, 49(4), 605–607.
Tan, I.Y.L., Demchuk, A.M., Hopyan, J., Zhang, L., Gladstone, D., Wong, K., Martin, M., Symons, S.P., Fox, A.J., Aviv, R.I. (2009) "CT angiography clot burden score and collateral score: Correlation with clinical and radiologic outcomes in acute middle cerebral artery infarct," *American Journal of Neuroradiology*, 30(3), 525–531.
Tirschwell, D. (2000) "Intra-arterial prourokinase for acute ischemic stroke.," *Journal of the American Medical Association*, 283(16).
Toni, D., Lorenzano, S., Agnelli, G., Guidetti, D., Orlandi, G., Semplicini, A., Toso, V., Caso, V., Malferrari, G., Fanucchi, S., Bartolomei, L., Prencipe, M. (2008) "Intravenous thrombolysis with rt-PA in acute ischemic stroke patients aged older than 80 years in Italy," *Cerebrovascular Diseases*, 25(1–2), 129–135.
Turk, A.S., Frei, D., Fiorella, D., Mocco, J., Baxter, B., Siddiqui, A., Spiotta, A., Mokin, M., Dewan, M., Quarfordt, S., Battenhouse, H., Turner, R., Chaudry, I. (2014) "ADAPT FAST study: A direct aspiration first pass technique for acute stroke thrombectomy," *Journal of NeuroInterventional Surgery*, 6(4), 260–264.
Turk, A.S., Siddiqui, A., Fifi, J.T., De Leacy, R.A., Fiorella, D.J., Gu, E., Levy, E.I., Snyder, K. V., Hanel, R.A., Aghaebrahim, A., Woodward, B.K., Hixson, H.R., Chaudry, M.I., Spiotta, A.M., Rai, A.T., Frei, D., Almandoz, J.E.D., Kelly, M., Arthur, A., Baxter, B., English, J., Linfante, I., Fargen, K.M., Mocco, J. (2019) "Aspiration thrombectomy versus stent retriever thrombectomy as first-line approach for large vessel occlusion (COMPASS): a multicentre, randomised, open label, blinded outcome, non-inferiority trial," *The Lancet*, 393(10175), 998–1008.
Wahlgren, N., Ahmed, N., Dávalos, A., Ford, G.A., Grond, M., Hacke, W., Hennerici, M.G., Kaste, M., Kuelkens, S., Larrue, V., Lees, K.R., Roine, R.O., Soinne, L., Toni, D., Vanhooren, G. (2007) "Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study," *Lancet*, 369(9558), 275–282.
Wahlgren, N., Ahmed, N., Dávalos, A., Hacke, W., Millán, M., Muir, K., Roine, R.O., Toni, D., Lees, K.R. (2008) "Thrombolysis with alteplase 3-4·5 h after acute ischaemic stroke (SITS-ISTR): an observational study," *The Lancet*, 372(9646), 1303–1309, available: http://dx.doi.org/10.1016/S0140-6736(08)61339-2.
Wei, D., Mascitelli, J.R., Nistal, D.A., Kellner, C.P., Fifi, J.T., Mocco, J.D., De Leacy, R.A. (2017) "The Use and Utility of Aspiration Thrombectomy in Acute Ischemic Stroke: A Systematic Review and Meta-Analysis," *American Journal of Neuroradiology*, 38(10), 1978–1983.
Winter, R., Hacke, W. (1998) "Ischämischer Schlaganfall," *Internist (Berl.)*, 39(6), 623–643.
Wolfe, C.D.A. (2009) "Incidence of stroke in Europe at the beginning of the 21st century," *Stroke*, 40(5), 1557–1563.
Zaidat, O.O., Castonguay, A.C., Nogueira, R.G., Haussen, D.C., English, J.D., Satti, S.R., Chen, J., Farid, H., Borders, C., Veznedaroglu, E., Binning, M.J., Puri, A., Vora, N.A., Budzik, R.F., Dabus, G., Linfante, I., Janardhan, V., Alshekhlee, A., Abraham, M.G., Edgell, R., Taqi, M.A., Khoury, R. el, Mokin, M., Majjhoo, A.Q., Kabbani, M.R., Froehler, M.T., Finch, I., Ansari, S.A., Novakovic, R., Nguyen, T.N. (2017) "TREVO stent-retriever mechanical thrombectomy for acute ischemic stroke secondary to large vessel occlusion registry," *Journal of NeuroInterventional Surgery*, (September), neurintsurg-2017-013328, available: http://jnis.bmj.com/lookup/doi/10.1136/neurintsurg-2017-013328.
Zaidat, O.O., Yoo, A.J., Khatri, P., Tomsick, T.A., von Kummer, R., Saver, J.L., Marks, M.P., Prabhakaran, S., Kallmes, D.F., Fitzsimmons, B.F.M., Mocco, J., Wardlaw, J.M., Barnwell, S.L., Jovin, T.G., Linfante, I., Siddiqui, A.H., Alexander, M.J., Hirsch, J.A., Wintermark, M., Albers, G., Woo, H.H., Heck, D. v., Lev, M., Aviv, R., Hacke, W., Warach, S., Broderick, J., Derdeyn, C.P., Furlan, A., Nogueira, R.G., Yavagal, D.R., Goyal, M., Demchuk, A.M., Bendszus, M., Liebeskind, D.S. (2013) "Recommendations

on angiographic revascularization grading standards for acute ischemic stroke: A consensus statement," *Stroke*, 44(9), 2650–2663.

Originalarbeiten

Die folgenden Originalarbeiten wurden in dieser kumulativen Habilitationsschrift zusammengefasst und im Rahmen der Autorenrechte abgedruckt:

1. **Marius Georg Kaschner**, Daniel Weiss, Christian Rubbert, John-Ih Lee, Michael Gliem, Sebastian Jander, Vivien Ivan, Bastian Kraus, Bernd Turowski, Julian Caspers (2019). *One-year single-center experience with the Aperio thrombectomy device in large vessel occlusion in the anterior circulation: safety, efficacy, and clinical outcome.* Neurol Sci 40:1443–1451.

2. **Marius Kaschner**, Thorsten Lichtenstein, Daniel Weiss, Bernd Turowski, Lukas Goertz, Claudia Kluner, Marc Schlamann, Christian Mathys, Christoph Kabbasch (2020). *The New Fully Radiopaque Aperio Hybrid Stent-Retriever: Efficient and Safe? An Early Multicenter Experience.* World Neurosurg 141:e278–e288.

3. **Marius G. Kaschner,** Christian Rubbert, Julian Caspers, Jennifer Karsten, Bastian Kraus, John-Ih Lee, Michael Gliem, Sebastian Jander, Bernd Turowski (2017). *A Retrospective Single-Center Case Series of Direct Aspiration Thrombectomy as First-Line Approach in Ischemic Stroke and Review of the Literature.* J Stroke Cerebrovasc Dis 28:640–648.

4. **Marius Georg Kaschner**, Julian Caspers, Christian Rubbert, Raul Lande, Bastian Kraus, John-Ih Lee, Michael Gliem, Sebastian Jander, Bernd Turowski (2018). *Mechanical thrombenctomy in MCA-mainstem occlusion in patients with low NIHSS scores.* Interv Neuroradiol 24:398–404.

5. Vivien Lorena Ivan, Christian Rubbert, Julian Caspers, John-Ih Lee, Michael Gliem, Sebastian Jander, Bernd Turowski, **Marius Kaschner** (2020). *Mechanical thrombectomy in acute middle cerebral artery M2 segment occlusion with regard to vessel involvement.* Neurol Sci 41:3165–3173.

6. Daniel Weiss, Christian Rubbert, Julian Caspers, Sebastian Jander, Michael Gliem, John-Ih Lee, Vivien Lorena Ivan, Bernd Turowski, **Marius Kaschner** (2022). *Thrombectomy in stroke patients with acute occlusion of the M1 compared to the M2-segment: safety, efficacy, and clinical outcome.* Neuroradiol J 35:600–606.

7. **Marius G. Kaschner**, Athanasios Petridis, Bernd Turowski (2020). *Single-center experience with the new-generation Derivo embolization device for ruptured and unruptured intracranial aneurysms.* J Neurosurg Sci 64:353–363.

8. Daniel Weiss, Bastian Kraus, Christian Rubbert, **Marius Kaschner**, Sebastian Jander, Michael Gliem, John-Ih Lee, Carl-Albrecht Haensch, Bernd Turowski, Julian Caspers (2019). *Systematic evaluation of computed tomography angiography collateral scores for estimation of long-term outcome after mechanical thrombectomy in acute ischaemic stroke.* Neuroradiol J 32:277–286.

9. **Marius Georg Kaschner**, Raul Lande, Christian Rubbert, Julian Caspers, John-Ih Lee, Michael Gliem, Sebastian Jander, Bernd Turowski (2019). *Predictors for basal ganglia viability after mechanical thrombectomy in proximal middle cerebral artery occlusion.* Clin Imaging 57:1–6.

Neurological Sciences
https://doi.org/10.1007/s10072-019-03861-z

ORIGINAL ARTICLE

One-year single-center experience with the Aperio thrombectomy device in large vessel occlusion in the anterior circulation: safety, efficacy, and clinical outcome

Marius Georg Kaschner[1] · Daniel Weiss[1] · Christian Rubbert[1] · John-Ih Lee[2] · Michael Gliem[2] · Sebastian Jander[2] · Vivien Ivan[1] · Bastian Kraus[1] · Bernd Turowski[1] · Julian Caspers[1]

Received: 9 October 2018 / Accepted: 20 March 2019

Abstract

Background and purpose The Aperio thrombectomy device (Aperio) is a stent retriever designed to achieve rapid and substantial flow restoration in acute ischemic stroke due to large-vessel occlusions (LVOs). We evaluated the safety and efficacy of the Aperio device and compared it with published data of established stent retrievers.

Methods We retrospectively analyzed institutional data of consecutive stroke procedures in patients with LVO in the anterior circulation that were treated between January 2017 and December 2017 with the Aperio. Reperfusion rate regarding to the extended thrombolysis in cerebral infarction scale (eTICI), procedural times, early clinical outcome, and complications were documented.

Results Eighty-two patients were treated by using the Aperio in LVO in the anterior circulation. Median age was 77 (± 12) years (w = 59.8%). Median Baseline National Institutes of Health Stroke Scale (NIHSS) score was 14. Fifty-three (64.6%) patients received intravenous thrombolysis. Successful recanalization (eTICI≥2b) was achieved in 85.3%. Mean time from groin puncture to final recanalization was 52.3 ± 34.8 min. Embolization to new territories occurred in one case. Symptomatic intracranial hemorrhage within 24 h was observed in six patients (7.3%). Twenty-eight (41.2%) out of 68 patients available for assessment of functional outcome at 3 months achieved favorable outcome (mRS 0–2).

Conclusion The Aperio stent retriever mechanical thrombectomy device demonstrated high rates of successful reperfusion and a good safety profile in patients with acute ischemic stroke due to LVO in the anterior circulation.

Keywords Ischemic stroke · M1 segment occlusion · Aperio thrombectomy device · Thrombectomy · Clinical outcome

Introduction

Major acute ischemic stroke trials have demonstrated the clinical benefit and superior reperfusion efficacy of endovascular therapy using stent retriever thrombectomy devices compared to medical treatment [1–4]. Presently, stent retrievers are considered as the standard of care for treatment of acute ischemic stroke secondary to large-vessel occlusion [5]. The first-generation devices for thrombectomy (TE) included the Merci Retriever system (Stryker, Kalamazoo, MI, USA) and the Penumbra aspiration system (Penumbra Inc., Alameda, CA, USA). Second-generation treatment devices included modern endovascular stent retrieval devices, such as the Solitaire (ev3/Covidien, Irvine, CA, USA) and the Trevo (Stryker), which demonstrated high rates of successful recanalization and good neurological outcome. The purpose of this single-center case series was to evaluate the technical effectiveness of the Aperio device in achieving revascularization of anterior circulation large-vessel occlusions (LVOs) in comparison with the results of the major stent retriever trials.

✉ Daniel Weiss
DanielArvid.Weiss@med.uni-duesseldorf.de

[1] Medical Faculty, Department of Diagnostic and Interventional Radiology, University Duesseldorf, Moorenstr.5, 40225 Duesseldorf, Germany

[2] Medical Faculty, Department of Neurology, University Duesseldorf, Moorenstr. 5, 40225 Duesseldorf, Germany

Published online: 04 April 2019

Material and methods

Our study was approved by our hospital's institutional review board. We retrospectively analyzed our institutional neurointerventional database to examine the radiological and clinical outcomes in all consecutive patients with LVO in the anterior circulation who were treated with TE using the Aperio stent retriever between January 2017 and December 2017. Patients were informed about the approach, benefits, and risks of the planned procedure in the emergency setting, and the informed consent was obtained prior to intervention. The current cohort is part of a larger study group in which written informed consent for retrospective data analysis was obtained from all patients or their next of kin. When patients passed away during hospitalization, the requirement for written informed consent was waived.

Inclusion criteria

The study enrolled adults with occlusion of the M1 segment of the middle cerebral artery (MCA), tandem occlusion (internal carotid artery (ICA) and carotid-T or ICA and M1/M2 occlusion), proximal M2 segment occlusion, carotid T-occlusion, and intracranial ICA occlusion receiving stent retriever thrombectomy as first-line endovascular treatment; no age limit, no baseline National Institutes of Health Stroke Scale (NIHSS) score limit at admission, and no time limit from symptom onset to treatment were applied to restrict study inclusion. Standardized stroke imaging at our institution included non-contrast-enhanced cranial computed tomography (NECCT), CT perfusion (CTP), and CT angiography (CTA). If the time from symptom onset to admission was uncertain, patients were scanned with magnetic resonance imaging (MRI), applying diffusion-weighted imaging (DWI), MR perfusion scanning, and fluid-attenuated inversion recovery (FLAIR) image to discern between salvageable and terminally infarcted tissue. Patients received intravenous thrombolysis (IVT), if eligible, according to the guidelines of the German Society of Neurology. Extensive early ischemic signs or hemorrhage were excluded in pre-interventional imaging by CT or MRI on a case-by-case basis. Treatment of patients was not restricted in regard to ASPECTS. Eligibility for thrombectomy, as established in CTA or TOF-MRA, was determined individually for each patient in consensus between neurologists and neurointerventionalists. The decision is primarily based on the infarct-core/penumbra mismatch, stroke severity, estimated procedural risk, probability of recanalization by IVT, contraindication for IVT, comorbidities, and social and medical pre-stroke conditions. Exclusion criteria were intracranial hemorrhage.

Interventional procedure

The interventional procedures were performed under analgesia (1–2 g novaminsulfone as short infusion) and local anesthesia of the groin. General anesthesia was performed in patients with Glasgow coma scale < 8 or in case of extreme agitation. After local anesthesia of the groin, access was performed using a long 8F sheath or additional guiding catheter positioned in the distal ICA. Stent retriever thrombectomy (Aperio 4.5 × 40 mm, 4.5 × 30 mm, or 3.5 × 28 mm) combined with local thromboaspiration via 5F or 6F intracranial intermediate catheter (SOFIA®, MicroVention, Düsseldorf, Germany) at the proximal occlusion site was performed. After passing the clot with a 0.014 microwire, a microcatheter was advanced beyond the distal end of the clot and the position was verified by angiographic control run via the microcatheter. The Aperio was advanced through the microcatheter until its distal markers were lined up beyond the occlusion. The aim was an overlap of the stent retriever and the clot to catch the lost embolic fragments. The Aperio was deployed by withdrawing the microcatheter by gently pushing the stent retriever to improve expansion into the clot. Subsequently, the stent retriever was removed into the intracranial intermediate catheter under manual local aspiration via a 20-ml syringe (termed the Solumbra technique) [6]. A resistance during retraction of the stent retriever into the intermediate catheter (IMC) indicated a mismatch between clot size and lumen of the IMC. In these cases, the entire assembly (IMC and stent retriever with the trapped clot as one unit) was locked and carefully withdrawn under continuous distal and proximal manual aspiration into the long 8F sheath or guiding catheter referring to the currently described SAVE technique [7]. Biplane follow-up angiograms were performed to document final revascularization results. In case of persistent thrombus, the procedure was repeated. Arterial puncture sites were closed by vascular closure devices (Angio-Seal™, Terumo, Tokyo, Japan).

The time from symptom onset to stroke imaging, to groin puncture, and to recanalization was captured. Devices and medication used during the interventional procedures, the duration, and intraprocedural complications were evaluated from the treatment protocols. After the intervention, patients were admitted to the stroke unit of our hospital and treated according to in-house standard operating procedures.

Device description

The Aperio thrombectomy device (Aperio; Acandis, Pforzheim, Germany) is a further innovative self-expanding thrombectomy device with a hybrid cell design aiming to facilitate a good vessel wall apposition, clot interaction, and efficient clot retention. The repeating functional segments allow adapting the working length to the thrombus length with retained functionality also in tortuous vessels (Fig. 1). The

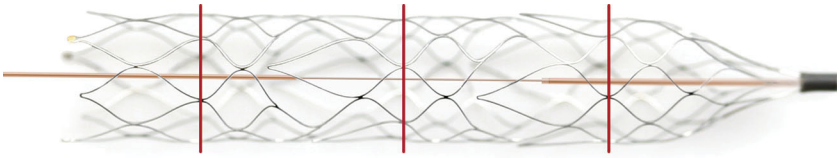


Fig. 1 The Aperio device. Photograph (with kind permission of Acandis). Functional segment (between red lines): small closed cells, large open cells; repeating functional segments allowing adaption of working length to thrombus length

device has two wire markers to support the positioning of the device and three distal device markers to indicate the distal device end and the grade of expansion under fluoroscopy (Fig. 2).

Imaging data

The location of the occlusion was assessed on CT or MR angiographic images. Collateral supply of the occluded MCA territory from pre-interventional CTA scans was scored based on collateral grading system of Tan et al. on a scale of 0–3 [8]. Pretreatment cerebral infarction, according to the Alberta Stroke Program Early CT score (ASPECTS), was assessed by CCT or according to the DWI-ASPECTS by MRI. Posttreatment ASPECTS and intracerebral hemorrhage (ICH), according to the European Cooperative Acute Stroke Study classification (ECASS: not space occupying hemorrhagic infarction (HI1, HI2), space occupying parenchymal hematoma (PH1, PH2)) [9], were assessed by follow-up imaging CCT that was routinely performed 6–24 h after treatment.

Clinical and angiographic assessment, complications

For each patient, a neurological examination was performed at admission by the attending neurologist in the emergency department, including detailed assessment of NIHSS, modified Rankin Scale (mRS) scores. Postinterventional NIHSS and mRS were assessed by the treating neurologist at discharge. mRS at 3-month follow-up was assessed by a standardized telephone interview by one investigator (D.W.). The time from symptom onset to start of angiography (groin puncture) and the time to final recanalization (TTFR) were captured. Angiographic outcome was graded by the extended thrombolysis in cerebral infarction scale (eTICI, in the following abbreviated as TICI) that includes TICI 2c grade referring to near complete perfusion except for slow flow in a few distal cortical vessels, or presence of small distal cortical emboli [10, 11]. Revascularization success was evaluated independently by two experienced neuroradiologists (MGK and JC) in a blinded imaging reading. In case of differing results, consensus reading was performed. Number of device passes to successful recanalization (TICI≥2b) and grade of revascularization TICI 2b, TICI 2c, and TICI 3 after first device pass (FP) were obtained. Complications such as embolization in a previously uninvolved territory on angiogram (embolization to new territories (ENT)), symptomatic intracranial hemorrhage (sICH), and procedure-related mortality rate were assessed.

Results

In 97 stroke patients with the predefined occlusion patterns of the anterior circulation a mechanical TE was performed between January 2017 and December 2017 with ICA occlusion in 3 (3.1%), carotid-T in 2 (2.1%), M1 in 63 (64.9%), tandem occlusion in 14 (14.4%), and proximal M2 segment occlusion in 15 (15.5%). Of 97 patients, 82 (85.6%) underwent TE using the Aperio stent retriever. Detailed occlusion patterns of patients that were treated with the Aperio are given in Table 1. First-line intention to treat (ITT) with the Aperio stent retriever was in 88 patients. There were 6 cases of first-line ITT with the Aperio in that the device was not deployed. In one patient, after extracranial carotid stent deployment, intracranial occlusion of

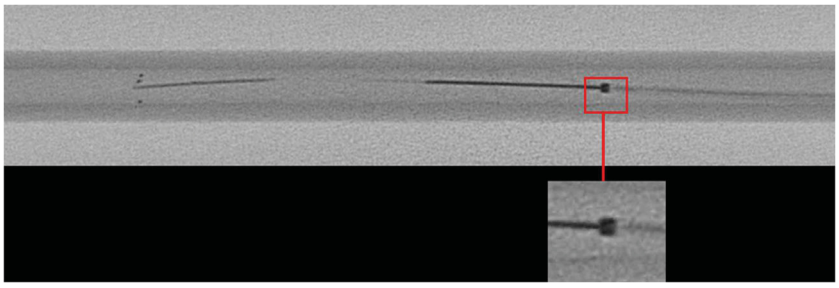


Fig. 2 Fluoroscopy image of the complete released Aperio device (with kind permission of Acandis). Visible parts from proximal to distal are (1) tip of the microcatheter (red frame); (2) + (3) proximal and distal transport wire marker makes total length visible; (4) three distal device markers indicating complete expansion

Table 1 Baseline data, angiographic results, clinical outcome, and complications

	Overall patients treated with Aperio	Patients with follow-up	Patients without follow-up	Patients with failed intention to treat with Aperio
Sample size	*n* = 82 patients	*n* = 68 patients	*n* = 14 patients	*n* = 6 patients
Age (mean ± SD)	77 ± 12	76 ± 12	78 ± 14	75 ± 12
Sex (*n*)	w = 49, m = 33	w = 43, m = 25	w = 6, m = 8	w = 3, m = 3
Medical history, *n* (%)				
Hypertension	66 (80.5)	54 (79.4)	12 (85.7)	5 (83.3)
Diabetes mellitus	22 (26.8)	19 (27.9)	3 (21.4)	0 (0)
Atrial fibrillation	49 (59.8)	40 (58.8)	9 (64.3)	1 (16.7)
Dyslipidemia	37 (45.1)	30 (44.1)	7 (50)	4 (66.7)
Smoking	17 (20.7)	15 (22.1)	2 (14.3)	1 (16.7)
Previous ischemic stroke/transient ischemic attack	14 (17.1)	11 (16.2)	3 (21.4)	0 (0)
IVT	53 (64.6)	42 (61.8)	11 (78.6)	6 (100)
NIHSS pre, median	14	14	14	7
mRS pre, median	5	5	5	5
Prestroke imaging				
CTA-collateral score (0–3), median	1	1	1	2
ICA occlusion, *n* (%), right/left	0 (0)/1 (1.2)	0 (0)/1 (1.5)	0 (0)/0 (0)	0 (0)/1 (16.7)
Carotid T-occlusion n(%), right/left	1 (1.2)/1 (1.2)	1 (1.5)/1 (1.5)	0 (0)/0 (0)	0 (0)/0 (0)
M1-occlusion, *n* (%), right/left	29 (35.4)/33 (40.2)	27 (39.7)/26 (38.2)	2 (14.3)/7 (50)	0 (0)/0 (0)
Tandem (ICA + carotid-T/M1/M2) occlusion, *n* (%), right/left	5 (6.1)/4 (4.9)	5 (7.4)/4 (5.9)	0 (0)/0 (0)	4 (66.7)/0 (0)
Proximal M2 occlusion, *n* (%), right/left	3 (4.7)/5 (6.1)	0 (0)/3 (4.4)	3 (21.4)/2 (14.3)	0 (0)/1 (16.7)
ASPECTS, median	10 (range 6–10)	10 (range 6–10)	10 (range 7–10)	10 (range 10–10)
Procedural data				
Onset to groin puncture (min), mean ± SD	204.9 ± 94.3	211.9 ± 105.3	190 ± 68.7	111.0 ± 45.5
Time from groin puncture to final recanalization (min), mean ± SD	52.3 ± 34.8	47.9 ± 35.5	65.6 ± 32.8	47.3 ± 16.3
Number of passes, mean ± SD	2.6 ± 1.7	2.6 ± 1.7	2.8 ± 1.4	NA
Number of device passes to TICI 2b-3 recanalization, median (range)	2 (1–6)	2 (1–6)	2 (1–4)	NA
Rate of recanalization after stent retriever first pass:				
TICI 2b, *n* (%)	22 (26.8)	18 (26.5)	5 (35.7)	NA
TICI 2c, *n* (%)	4 (4.9)	4 (5.9)	0 (0)	NA
TICI 3, *n* (%)	10 (12.2)	8 (11.8)	2 (14.3)	NA
IA tPA, *n* (%)	25 (30.5)	22 (32.4)	3 (21.4)	2 (33.3)
Final angiographic and postprocedural imaging outcomes				
TICI 0, *n* (%)	3 (3.7)	2 (2.9)	1 (7.1)	2 (33.3)
TICI 2a, *n* (%)	9 (11)	8 (11.8)	1 (7.1)	1 (16.7)
TICI 2b, *n* (%)	25 (30.5)	21 (30.9)	4 (28.6)	2 (33.3)
TICI 2c, *n* (%)	18 (21.9)	19 (27.9)	0 (0)	0 (0)
TICI 3, *n* (%)	27 (32.9)	18 (26.5)	8 (57.1)	1 (16.7)
ASPECTS, median	6	6	6	8
Clinical outcome				
Mortality (30 days), *n* (%)	14 (17.1)	14 (20.5)	NA	2 (33.3)
3-month mRS (median)	3	3	NA	6 (*n* = 5 patients available for follow-up)
n of patients (%) of mRS $\leq$ 2 (at 3-month follow-up)	28 (34.1)	28 (41.2)	NA	2 (40.0)
n (%) mRS 0	11 (13.4)	11 (16.2)	NA	1 (20.0)
n (%) mRS 1	9 (11.0)	9 (13.2)	NA	1 (20.0)

Table 1 (continued)

	Overall patients treated with Aperio	Patients with follow-up	Patients without follow-up	Patients with failed intention to treat with Aperio
n (%) mRS 2	8 (9.8)	8 (11.8)	NA	0 (0)
n (%) mRS 3	6 (7.3)	6 (8.9)	NA	0 (0)
n (%) mRS 4	13 (15.9)	13 (19.1)	NA	0 (0)
n (%) mRS 5	6 (7.3)	6 (8.8)	NA	0 (0)
Mortality (3-month), *n* (%) mRS 6	15 (18.3)	15 (22.1)	NA	3 (60.0)
Complications				
Emboli to new territories (ENT), *n* (%)	1 (1.2)	1(1.5)	0 (0)	0 (0)
sICH within 24 h, *n* (%)	6 (7.3) (PH Typ2)	4(5.9) (PH Typ2)	1 (7.1) (PH Typ2)	0 (0)
Serious adverse device events, *n* (%)	0 (0)	0(0)	0 (0)	NA
Procedure-related serious adverse events, *n* (%)	0 (0)	0(0)	0 (0)	NA

NA not available

M1 was already recanalized; in two patients with tandem occlusion, ICA was occluded over a long distance and aspiration TE was performed as FP, resulting in full recanalization of ICA and M1 segment occlusion; and in two patients (one ICA occlusion, one M2 occlusion), TE had to be terminated because supra-aortal access failed due to anatomic and technically reasons. In one patient, Aperio was not deployable because of kinking of the M2 segment with small diameter. In one case, a solitaire stent retriever was used for FP and in another case, an ERIC stent retriever for FP of M1 segment occlusions; in both cases, choice of the device used was at the discretion of the operator.

In seven patients, sole aspiration was intended and performed as FP, in one patient due to a long-segment extra- and intracranial ICA occlusion without M1 occlusion, and in six patients with M2 occlusions due to the curved vessel anatomy with small vessel diameter.

Fifty-three patients (64.6%) of the stent retriever group received intravenous tissue plasminogen activator (IVT) prior to endovascular procedure. Mean age of the patients was 77 years (SD ± 12); 59.8% were women. Median baseline NIHSS was 14, and median pretreatment mRS was 5. Baseline median ASPECTS was 10, and median collateral score was 1. The mean time from symptom onset to groin puncture was 204.9 ± 94.3 min (Table 1).

There were no noticeable differences in the baseline data of the medical history between patients with 3-month follow-up (FU) compared to patients without FU with exception of a higher IVT rate in patients without FU (78.6% vs. 61.8%). Prestroke imaging revealed higher M1 occlusion rates in patients in the FU group than in patients without FU (77.9% vs. 64.3%), but proximal M2 occlusion was markedly higher in patients without FU (35.7% vs. 4.4%). Overall baseline median collateral score was 1.

Technical success

Major revascularization (TICI≥2b) was achieved in 85.3%. Detailed final and FP TICI recanalization grade is summarized in Table 1. Cohen's kappa demonstrated a high interrater reliability for TICI scoring (kappa 0.9422). Overall mean time to final recanalization (TTFR) proceeding from femoral access to final revascularization was 52.3 ± 34.8 min. Median ASPECTS after treatment was 6. Mean of stent retriever passes was 2.6. FP final recanalization (TICI2b-3) was achieved in 43.9% (36/82). In all cases, the Aperio was the first-line stent retriever device without using more than one stent retriever device. Aperio devices with a size of 4.5 × 40 mm were used in 42 patients, 4.5 × 30 mm in 37 patients, and of 3.5 × 28 mm in 3 patients.

Median of device passes to TICI 2b/3 revascularization was 2. IA tPA rate was higher in patients with follow-up examination compared to those without (32.4% vs. 21.4%). Final TICI≥2b rate was comparable in patients with and without available FU (85.3% vs. 85.7%), but patients without FU demonstrate a markedly higher rate of TICI 3 revascularization (57.1% vs. 26.5%). Final TICI≥2c was achieved in 54.9%. The posttreatment median ASPECTS was 6 (Table 1).

Clinical outcome and complications

Out of 82 patients, 68 (82.9%) were available for a follow-up after 3 months. A favorable clinical outcome according to the mRS scale (mRS 0–2) was achieved in 41.2% (28/68) patients (Table 1). Overall early mortality was 17% (14/82). Overall mortality after 3 months was 22.1% (15/68). There was no procedure-related death. Postprocedure sICH due to hemorrhagic infarction occurred in six patients (7.3%). Asymptomatic hemorrhagic transformation or parenchymal hematoma (HI1, HI2, PH1) was observed in 15 patients

(18.3%) and asymptomatic SAH in 6 patients (7.3%). Embolization of previously unaffected territories by fragmented or lost clots was observed in one case (1.2%). In one patient, bleeding due to perforation of the right femoral communicating artery after groin puncture occurred. Temporary balloon occlusion resulted in a successful hemostasis without occurrence of clinical complications. The overall rate of sICH was 7.3%. Patients with failed ITT had a high rate of good clinical outcome (66.6%, [2/6]) despite a low rate of favorable recanalization rates (TICI≥2b = 50%) due to bias from the small sample size.

Discussion

The aim of this single-center trial was to evaluate efficacy, safety, and clinical outcome of treatment with the Aperio thrombectomy device in stroke patients with LVO in the anterior circulation. In this retrospective, single-center trial, the Aperio achieved high rates of reperfusion among patients with LVO in the anterior circulation, with substantial reperfusion (85% TICI2≥b) that is remarkably higher as compared with the HERMES (71% TICI2≥b) and SEER (77% TICI2≥2b) individual patient data pooled analyses and in line with results of the current ASTER stent retriever arm (83% TICI2≥2b) [12–14]. The DAWN trial, and TRACK Registry in which Trevo devices were used, reported TICI≥2b recanalization in 84% and 80% of patients, respectively (Table 2) [15, 16]. In a recent retrospective single-center study, Yi et al. compared the Trevo stent retriever and the Solitaire stent retriever in 200 patients receiving neurothrombectomy. Rates of successful recanalization (TICI2≥2b) in the Solitaire group were 82.3% vs. 89.7 in the Trevo group [17]. Rates of successful recanalization in our study were also comparable with the reported rates (84.6%) of a recent core laboratory-audited single-center experience evaluating the performance of the EmboTrap [18].

The rate of excellent final reperfusion (TICI≥2c) achieved in 54.8% of the cases in the present study is superior to the outcome data of excellent reperfusion (TICI3) in the Trevo2 [19] trial (14%), and Trevo and Solitaire device retrospective registries (TRACK [16], 45%, and SEER [13], 36%, respectively) and is comparable with the stent retriever arm of the ASTER trial (56.6% achieving final TICI≥2c) [14]. First-pass complete recanalization rates of the EmboTrap in the recently published ARISEII trial (51.5% TICI≥2b, 40.1% TICI≥2c) were higher than in our study [20]. Use of a balloon guiding catheter (BGC) was reported with a rate of 47.3% in the TRACK registry [16]. However, compared to TRACK, we achieved a higher rate of near complete to TICI3 revascularization (54.9%) using a local lesional aspiration technique omitting a BGC. Mean number of passes was 2.6 and in line with results from nonrandomized trials for Trevo (mean 2.1, IQR 1–6) and Solitaire (mean 2.9, IQR 1–8) [17]. In no case more than one Aperio device was used due to lack of success with the initial one. Rescue maneuvers were not required.

There is only one non-trial case series available that evaluated the Aperio device in a clinical setting. One hundred nineteen patients from nine centers, where 42% had the occlusion site in the M1 segment, were treated. Rates of TICI2b-3 of 71% were slightly inferior to the present study, but rates of

Table 2 Clinical and angiographic outcome of selected randomized major stent retriever trials

Study	Endovascular treatment (*n*)	Device	Baseline NIHSS (Median)	TICI2b-3 (%)	%mRS ≤ 2	Mortality (%)	sICH (%)
MR Clean [1]	233	Various	17	59	33	19	8
ESCAPE [12]	165	Solitaire	17	76	52	10	4
REVASCAT [12]	103	Solitaire	17	66	44	18	2
SWIFT Prime [12]	98	Solitaire	17	88	60	12	0
EXTEND-IA [12]	35	Solitaire	15	86	71	7	0
HERMES [12]	634	Various	17	71	46	15	4
ENDOSTROKE [22]*	309	Various	16	77	41	27	15
NASA [23]	354	Solitaire	18.1#	72.5	42	30.2	9.9
TREVOII [19]	88	Trevo	19	68	40	29	4
ASTER [14] (stent retriever arm)	189	Various	16.1#	83	50	33	7
DAWN [15]	107	Trevo	17	84	49	19	6
Current study	82	Aperio	14	85.3	41.2	22.1	7.3

*Number of patients for whom TICI scoring was available

Mean value

TICI3 recanalization were achieved in 53% of patients and favorable comparable to our cohort. The reported rate of stent retriever passes (median 2, range 1–6) was similar to the present study [21]. The rate of 3-month favorable clinical outcome (mRS 0–2) achieved in 41.2% of our patient sample was comparable to Endostroke Registry [22] (41%), NASA Registry [23] (42%), Trevo2 [19] (40%), and HERMES [12] (46%). The rate of favorable outcome was also comparable to the reported results of the Solitaire group (mRS 0–2, 42.1%) in a current published non-trial stent retriever case series [17]. Higher rates of 3-month favorable outcome for the anterior circulation are reported in the TRACK [16] Registry for the Trevo devices with a rate of 51.4%. The SEER [13] meta-analysis for Solitaire devices (54%) and a recent non-trial study for the EmboTrap device reported 3-month mRS rates of 54% and 52.8%, respectively [18]. The safety of the Aperio device in the current study was within the range of recent stent retriever trials. The rate of 7.3% for sICH was slightly higher compared to 4% in the HERMES [12] data, 5% in the ARISE II trial [20], and 2% and 4% sICH rates in SWIFT [24] and Trevo2 [19], respectively. The risk of clot fragment embolization to previously unaffected territories appears low as reported in the literature and occurred in one patient in our study [1]. The all-cause mortality rate at 90 days was 22.1%, which is comparable with the HERMES data [12], the ASTER (19%) [14], and DAWN (19%) [15] trials and was lower compared to Endostroke (27%), NASA [23], and Trevo2 [19] at 30.2% and 29%, respectively. These safety results support an acceptable benefit–risk profile for the device. The major limitations of this study are the non-randomized retrospective nature, a missing reference group, and the relatively small sample. A further limitation is the lost to FU rate of 17.1%, which harbors a potential bias. To attain homogeneity in the procedure, (i) we only used Aperio stent retrievers and (ii) thrombectomies were performed by five neurointerventionalists. Three interventionalists had an experience of 4 years. Two interventionalists had an experience of 1 year each and performed thrombectomies under the supervision of a neurointerventionalist with more than 15 years of experience; (iii) the same local aspiration techniques for clot retrieval described above were used.

The hybrid design of the Aperio with small closed cells to attain a good vessel wall apposition and improve expansion into the clot, and large open cells with integrated anchoring elements to assure efficient clot retention are the features of the device that are supposed to result in favorable recanalization rates. In the present study, a local aspiration technique with stent-retriever retrieval was used; however, a combination also of BGC or aspiration have been shown to facilitate stent-retriever retrieval in addition to "only" BGC or "only" distal aspiration [25, 26]. It is conceivable that the additional use of the Aperio with BGC combined with lesional local aspiration techniques might increase the rate of excellent reperfusion after first device pass [27]. This again might result in an increased rate of good functional outcome and needs to be proven in further studies.

Conclusion

This single-center experience demonstrated that the Aperio device achieved high rates of successful reperfusion in LVO in the anterior circulation with local aspiration techniques in the setting of acute stroke. Absence of device-related procedural complications demonstrated an adequate safety profile. These promising results should be confirmed by further randomized trials.

Contributors All authors contributed to the conception of the work and the acquisition, analysis, and interpretation of data. They edited, revised, and finally approved the manuscript version to be published. They agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. BT received personal fees from Acandis outside the submitted work.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Patients were informed about the approach, benefit, and risks of the planned procedure in the emergency setting, and informed consent was obtained prior to intervention. Consent for retrospective data analysis was waived.

Ethics approval The study was approved by the local ethics committees.

Provenance and peer review Not commissioned; externally peer reviewed.

References

1. Berkhemer OA, Fransen PSS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, Schonewille WJ, Vos JA, Nederkoorn PJ, Wermer MJH, van Walderveen MAA, Staals J, Hofmeijer J, van Oostayen JA, Lycklama à Nijeholt GJ, Boiten J, Brouwer PA, Emmer BJ, de Bruijn SF, van Dijk LC, Kappelle LJ, Lo RH, van Dijk EJ, de Vries J, de Kort PLM, van Rooij WJJ, van den Berg JSP, van Hasselt BAAM, Aerden LAM, Dallinga RJ, Visser MC, Bot JCJ, Vroomen PC, Eshghi O, Schreuder THCML, Heijboer RJJ, Keizer K, Tielbeek AV, den Hertog HM, Gerrits DG, van den Berg-Vos RM, Karas GB, Steyerberg EW, Flach HZ, Marquering HA, Sprengers MES, Jenniskens SFM, Beenen LFM, van den Berg R, Koudstaal PJ, van Zwam WH, Roos YBWEM, van der Lugt A, van

Oostenbrugge RJ, Majoie CBLM, Dippel DWJ (2015) A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 372(1):11–20
2. Campbell BCV, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, Yan B, Dowling RJ, Parsons MW, Oxley TJ, Wu TY, Brooks M, Simpson MA, Miteff F, Levi CR, Krause M, Harrington TJ, Faulder KC, Steinfort BS, Priglinger M, Ang T, Scroop R, Barber PA, McGuinness B, Wijeratne T, Phan TG, Chong W, Chandra RV, Bladin CF, Badve M, Rice H, de Villiers L, Ma H, Desmond PM, Donnan GA, Davis SM (2015) Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 372(11):1009–1018
3. Saver JL, Goyal M, Bonafe A, Diener H-C, Levy EI, Pereira VM, Albers GW, Cognard C, Cohen DJ, Hacke W, Jansen O, Jovin TG, Mattle HP, Nogueira RG, Siddiqui AH, Yavagal DR, Baxter BW, Devlin TG, Lopes DK, Reddy VK, du Mesnil de Rochemont R, Singer OC, Jahan R (2015) Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med 372(24): 2285–2295
4. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, San Román L, Serena J, Abilleira S, Ribó M, Millán M, Urra X, Cardona P, López-Cancio E, Tomasello A, Castaño C, Blasco J, Aja L, Dorado L, Quesada H, Rubiera M, Hernandez-Pérez M, Goyal M, Demchuk AM, von Kummer R, Gallofré M, Dávalos A (2015) Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 372(24):2296–2306
5. Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC, Johnston KC, Johnston SC, Khalessi AA, Kidwell CS, Meschia JF, Ovbiagele B, Yavagal DR (2015) American Heart Association Stroke Council. 2015 American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment. Stroke. 46(10):3020–3035
6. Humphries W, Hoit D, Doss VT, Elijovich L, Frei D, Loy D, Dooley G, Turk AS, Chaudry I, Turner R, Mocco J, Morone P, Fiorella D, Siddiqui A, Mokin M, Arthur AS (2015) Distal aspiration with retrievable stent assisted thrombectomy for the treatment of acute ischemic stroke. J Neurointerv Surg. 7(2):90–94
7. Maus V, Behme D, Kabbasch C, Borggrefe J, Tsogkas I, Nikoubashman O, Wiesmann M, Knauth M, Mpotsaris A, Psychogios MN (2017) Maximizing first-pass complete reperfusion with SAVE. Clin Neuroradiol:1–12
8. Tan IYL, Demchuk AM, Hopyan J, Zhang L, Gladstone D, Wong K, Martin M, Symons SP, Fox AJ, Aviv RI (2009) CT angiography clot burden score and collateral score: correlation with clinical and radiologic outcomes in acute middle cerebral artery infarct. Am J Neuroradiol 30(3):525–531
9. Fiorelli M, Bastianello S, von Kummer R, del Zoppo GJ, Larrue V, Lesaffre E, Ringleb AP, Lorenzano S, Manelfe C, Bozzao L (1999) Hemorrhagic transformation within 36 hours of a cerebral infarct: relationships with early clinical deterioration and 3-month outcome in the European Cooperative Acute Stroke Study I (ECASS I) cohort. Stroke 30(11):2280–2284
10. Kaesmacher J, Dobrocky T, Heldner MR, Bellwald S, Mosimann PJ, Mordasini P, Bigi S, Arnold M, Gralla J, Fischer U (2018) Systematic review and meta-analysis on outcome differences among patients with TICI2b versus TICI3 reperfusions: success revisited. J Neurol Neurosurg Psychiatry 89(9):910–917
11. Rizvi A, Seyedsaadat SM, Murad MH, Brinjikji W, Fitzgerald ST, Kadirvel R, Rabinstein AA, Kallmes DF (2019) Redefining 'success': a systematic review and meta-analysis comparing outcomes between incomplete and complete revascularization. J Neurointerv Surg 11(1):9–13
12. Goyal M, Menon BK, Van Zwam WH, Dippel DWJ, Mitchell PJ, Demchuk AM, Dávalos A, Majoie CBLM, Van Der Lugt A, De Miquel MA, Donnan GA, Roos YBWEM, Bonafe A, Jahan R, Diener HC, Van Den Berg LA, Levy EI, Berkhemer OA, Pereira VM, Rempel J, Millán M, Davis SM, Roy D, Thornton J, Román LS, Ribó M, Beumer D, Stouch B, Brown S, Campbell BCV, Van Oostenbrugge RJ, Saver JL, Hill MD, Jovin TG (2016) Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet. 387(10029):1723–1731
13. Campbell BCV, Hill MD, Rubiera M, Menon BK, Demchuk A, Donnan GA, Roy D, Thornton J, Dorado L, Bonafe A, Levy EI, Diener H-C, Hernández-Pérez M, Pereira VM, Blasco J, Quesada H, Rempel J, Jahan R, Davis SM, Stouch BC, Mitchell PJ, Jovin TG, Saver JL, Goyal M (2016) Safety and efficacy of solitaire stent thrombectomy. Stroke. https://doi.org/10.1161/STROKEAHA.115.012360
14. Lapergue B, Blanc R, Gory B, Labreuche J, Duhamel A, Marnat G, Saleme S, Costalat V, Bracard S, Desal H, Mazighi M, Consoli A, Piotin M (2017) Effect of endovascular contact aspiration vs stent retriever on revascularization in patients with acute ischemic stroke and large vessel occlusion: the ASTER randomized clinical trial. JAMA J Am Med Assoc 318(5):443–452
15. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, Yavagal DR, Ribo M, Cognard C, Hanel RA, Sila CA, Hassan AE, Millan M, Levy EI, Mitchell P, Chen M, English JD, Shah QA, Silver FL, Pereira VM, Mehta BP, Baxter BW, Abraham MG, Cardona P, Veznedaroglu E, Hellinger FR, Feng L, Kirmani JF, Lopes DK, Jankowitz BT, Frankel MR, Costalat V, Vora NA, Yoo AJ, Malik AM, Furlan AJ, Rubiera M, Aghaebrahim A, Olivot J-M, Tekle WG, Shields R, Graves T, Lewis RJ, Smith WS, Liebeskind DS, Saver JL, Jovin TG (2017) Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl J Med NEJMoa1706442
16. Zaidat OO, Castonguay AC, Nogueira RG, Haussen DC, English JD, Satti SR, Chen J, Farid H, Borders C, Veznedaroglu E, Binning MJ, Puri A, Vora NA, Budzik RF, Dabus G, Linfante I, Janardhan V, Alshekhlee A, Abraham MG, Edgell R, Taqi MA, Khoury RE, Mokin M, Majjhoo AQ, Kabbani MR, Froehler MT, Finch I, Ansari SA, Novakovic R, Nguyen TN (2017) TREVO stent-retriever mechanical thrombectomy for acute ischemic stroke secondary to large vessel occlusion registry. J Neurointerv Surg (September) neurintsurg-2017-013328
17. Yi HJ, Lee DH, Kim SU (2018) Effectiveness of Trevo stent retriever in acute ischemic stroke: comparison with solitaire stent. Medicine (Baltimore) 97(20):2–8
18. Brouwer PA, Yeo LLL, Holmberg A, Andersson T, Kolloch J, Kuntzesöderqvist Å, Ohlsson M, Holmin S, Anastasios M, Gontu VK, Bhogal P, Söderman M (2018) Thrombectomy using the EmboTrap device: Core laboratory-assessed results in 201 consecutive patients in a real-world setting. J Neurointerv Surg:1–6
19. Nogueira RG (2012) Trevo2. Lancet. 380(9849):1231–1240
20. Zaidat OO, Bozorgchami H, Ribó M, Saver JL, Mattle HP, Chapot R, Narata AP, Francois O, Jadhav AP, Grossberg JA, Riedel CH, Tomasello A, Clark WM, Nordmeyer H, Lin E, Nogueira RG, Yoo AJ, Jovin TG, Siddiqui AH, Bernard T, Claffey M, Andersson T (2018) Primary results of the multicenter ARISE II study (analysis of revascularization in ischemic stroke with EmboTrap). Stroke. https://doi.org/10.1161/STROKEAHA.117.020125
21. Kallenberg K, Solymosi L, Taschner CA, Berkefeld J, Schlamann M, Jansen O, Arnold S, Tomandl B, Knauth M, Turowski B (2016) Endovascular stroke therapy with the Aperio thrombectomy device. J Neurointerv Surg. 8(8):834–839
22. Singer OC, Haring HP, Trenkler J, Nolte CH, Bohner G, Reich A, Wiesmann M, Bussmeyer M, Mpotsaris A, Neumann-Haefelin T, Hohmann C, Niederkorn K, Deutschmann H, Stoll A, Bormann A, Jander S, Turowski B, Brenck J, Schlamann MU, Petzold GC, Urbach H, Liebeskind DS, Berkefeld J (2013) Age dependency of

successful recanalization in anterior circulation stroke: the ENDOSTROKE study. Cerebrovasc Dis 36:437–445

23. Zaidat OO, Castonguay AC, Gupta R, Sun C-HJ, Martin C, Holloway WE, Mueller-Kronast N, English JD, Linfante I, Dabus G, Malisch TW, Marden FA, Bozorgchami H, Xavier A, Rai AT, Froehler MT, Badruddin A, Nguyen TN, Taqi MA, Abraham MG, Janardhan V, Shaltoni H, Novakovic R, Yoo AJ, Abou-Chebl A, Chen PR, Britz GW, Kaushal R, Nanda A, Issa MA, Nogueira RG (2014) North American solitaire stent retriever acute stroke registry: post-marketing revascularization and clinical outcome results. J Neurointerv Surg. 6(8):584–588
24. Saver JL, Jahan R, Levy EI, Jovin TG, Baxter B, Nogueira R, Clark W, Budzik R, Zaidat OO (2014) SWIFT Trialists. SOLITAIRE™ with the intention for thrombectomy (SWIFT) trial: design of a randomized, controlled, multicenter study comparing the SOLITAIRE™ flow restoration device and the MERCI retriever in acute ischaemic stroke. Int J Stroke 9(5):658–668
25. Stampfl S, Pfaff J, Herweh C, Pham M, Schieber S, Ringleb PA, Bendszus M, Möhlenbruch MA (2017) Combined proximal balloon occlusion and distal aspiration: a new approach to prevent distal embolization during neurothrombectomy. J Neurointerv Surg. 9(4):346–351
26. Maegerlein C, Mönch S, Boeckh-Behrens T, Lehm M, Hedderich DM, Berndt MT, Wunderlich S, Zimmer C, Kaesmacher J, Friedrich B (2018) PROTECT: PRoximal balloon Occlusion TogEther with direCt Thrombus aspiration during stent retriever thrombectomy—evaluation of a double embolic protection approach in endovascular stroke treatment. J Neurointerv Surg 10(8):751–755
27. Zaidat OO, Castonguay AC, Linfante I, Gupta R, Martin CO, Holloway WE, Mueller-Kronast N, English JD, Dabus G, Malisch TW, Marden FA, Bozorgchami H, Xavier A, Rai AT, Froehler MT, Badruddin A, Nguyen TN, Asif Taqi M, Abraham MG, Yoo AJ, Janardhan V, Shaltoni H, Novakovic R, Abou-Chebl A, Chen PR, Britz GW, Sun CHJ, Bansal V, Kaushal R, Nanda A, Nogueira RG (2018) First pass effect: a new measure for stroke thrombectomy devices. Stroke. 49(3):660–666

The New Fully Radiopaque Aperio Hybrid Stent Retriever: Efficient and Safe? An Early Multicenter Experience

Marius Kaschner[1], Thorsten Lichtenstein[2], Daniel Weiss[1], Bernd Turowski[1], Lukas Goertz[2,3], Claudia Kluner[4], Marc Schlamann[2], Christian Mathys[1,4,5], Christoph Kabbasch[2]

■ OBJECTIVE: **To investigate the visibility, safety, and efficacy of the full-length radiopaque Aperio Hybrid stent retriever (APH) in mechanical thrombectomy of large vessel occlusions.**

■ METHODS: **Multicentric retrospective analysis of patients with stroke, treated with the APH due to an acute ischemic stroke by large vessel occlusions in the anterior or posterior circulation, was performed. We focused on technical and angiographic parameters including device visibility, perfusion results (modified thrombolysis in cerebral infarction scale [mTICI]), procedural times, periprocedural complications, and favorable clinical outcome (modified Rankin Scale, 0–2) at discharge and after 90 days.**

■ RESULTS: **A total of 48 patients (male: n = 22, 45.8%, mean age 73 years [standard deviation (SD), ±15], median baseline National Institutes of Health Stroke Scale: 15 [2–36], n = 25, 52.1% received additional intravenous thrombolytics) were treated with the APH with a mean number of 2 device passes (SD, +3) in APH-only cases (n = 41). The median time from groin puncture to the final mTICI was 54 minutes (SD, +33). In 46 patients (95.8%), mTICI 2b–3 was achieved (mTICI 2c, 12.5%; mTICI 3, 47.9%). Favorable outcome (modified Rankin Scale <2) was achieved in 15 (32.6%) patients at discharge and in 11 of the 30 (36.7%) patients available for 90-day follow-up. Symptomatic intracranial hemorrhage was recorded in 3 of 48 cases (6.3%). Difficulties during device delivery and/or deployment occurred in 6.3% (3 of 48). APH-related adverse events did not occur. APH radiopacity was rated as good and very good in 97.9% (47 of 48).**

■ CONCLUSIONS: **Mechanical thrombectomy with the APH appeared feasible, efficient, and safe. Full-length device radiopacity may facilitate thrombectomy or support to adapt the course of action during retrieval, if required.**

INTRODUCTION

Mechanical thrombectomy (MT) in acute ischemic stroke treatment caused by large vascular occlusions (LVO) has evolved into the gold standard of care.[1,2] Mechanical retrieval of the vessel occluding clot may lead to reliable and fast vessel recanalization. The superiority of stent-retriever–based thrombectomy over intravenous thrombolysis (IVT) alone was demonstrated in numerous large, randomized,

Key words
- Aperio Hybrid
- Ischemic stroke
- Mechanical thrombectomy
- Recanalization
- Stent retriever

Abbreviations and Acronyms
APH: Aperio Hybrid stent retriever
ARISE II: Analysis of Revascularization in Ischemic Stroke with EmboTrap
ASPECTS: Alberta Stroke Program Early CT Score
CT: Computed tomography
DFT: Drawn filled tubing
IVT: Intravenous thrombolysis
LVO: Large vascular occlusions
mRS: Modified Rankin Scale
MT: Mechanical thrombectomy
mTICI: Modified thrombolysis in cerebral infarction
NIHSS: National Institutes of Health Stroke Scale
RCT: Randomized controlled trial
SAH: Subarachnoid hemorrhage
sICH: Symptomatic intracranial hemorrhage

From the [1]Medical Faculty, Department of Diagnostic and Interventional Radiology, University Duesseldorf, Duesseldorf; [2]Institute for Diagnostic and Interventional Radiology, and [3]Center for Neurosurgery, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne; [4]Institute of Radiology and Neuroradiology, Evangelisches Krankenhaus, University of Oldenburg; and [5]Research Center Neurosensory Science, Carl von Ossietzky Universität Oldenburg, Oldenburg, Germany

To whom correspondence should be addressed: Christoph Kabbasch, M.D. [E-mail: christoph.kabbasch@uk-koeln.de]

All listed authors contributed to the work. M. Kaschner and T. Lichtenstein contributed equally and share first authorship. C. Mathys and C. Kabbasch contributed equally and share the last authorship.

Citation: World Neurosurg. (2020). https://doi.org/10.1016/j.wneu.2020.05.104

*Journal homepage: **www.journals.elsevier.com/world-neurosurgery***

*Available online: **www.sciencedirect.com***

multicenter studies,[3-7] in particular when a certain clot length is exceeded.[8] Furthermore, recent studies have shown that, in specific circumstances, even in an extended time window of up to 16 or 24 hours after symptom onset, mechanical recanalization may lead to an improved outcome compared with sole conservative care.[9,10]

In addition, stent retrievers with enhanced radiopacity characteristics as the Trevo ProVue (Stryker Neurovascular, Fremont, California, USA) and the Solitaire Platinum (Medtronic, Minneapolis, Minnesota, USA) could demonstrate a positive influence on the intervention procedure.[11,12]

The first-generation Aperio stent retriever (Acandis, Pforzheim, Germany) has been available since 2011 and proved to be efficient and safe.[13] A successor version, the Aperio Hybrid stent retriever (APH), recently obtained European CE mark approval. The APH offers full-length visibility through embedded radiopaque drawn filled tubing (DFT) wires that aim to achieve better assessment of stent-retriever positioning and interaction with the clot and vessel wall under fluoroscopy.

In this multicenter study, we report on our early experience with the full-length radiopaque APH and focus on its safety and efficacy.

MATERIALS AND METHODS

In this observational study, the data of the first 48 consecutive patients with stroke from 3 university neurovascular centers treated with the APH due to an acute stroke by LVO in the anterior (carotid-T, M1, M2) or posterior circulation (basilar artery) were evaluated. Anonymized data were retrospectively evaluated; patient files and radiological imaging from the acute phase until hospital discharge were analyzed.

Primary endpoints were first-pass excellent and first-pass favorable recanalization rate, defined as the modified thrombolysis in cerebral infarction (mTICI) scale score of $\geq$2c and $\geq$2b, respectively. The secondary outcome parameters contained final excellent and favorable reperfusion rate, favorable clinical outcome (modified Rankin Scale [mRS], 0–2) at discharge and at 90 days, symptomatic intracranial hemorrhage (sICH) with neurological deterioration (National Institutes of Health Stroke Scale [NIHSS] worsening >4) within 24 hours after intervention, periprocedural subarachnoid hemorrhage (SAH), embolisms into new territories, dissections, and material defects as well as evaluation of technical practicability, for example, pushability and deployment.

Aperio Hybrid Stent Retriever

The APH is a further development of its predecessor, the Aperio stent retriever. Like its predecessor, the APH is self-expanding and made of nitinol. Furthermore, it exhibits a hybrid cell design that should allow effective interaction with the clot, reliable clot recovery, and good vessel wall apposition (Figure 1). The APH is designed in repetitive functional segments, to enable adaptation of the working length to the thrombus length even in tortuous vessels, while maintaining the functionality. In addition, the APH offers improved full-length visibility under fluoroscopy due to embedded radiopaque DFT made of a nitinol tube and a highly radiopaque platinum core. The APH is delivered through a 0.021″ microcatheter and is available in working lengths from 30 to 50 mm and diameters from 3.5 to 6 mm.

Competing stent retrievers have also been developed with the intention to improve radiopaque visibility. By integration of

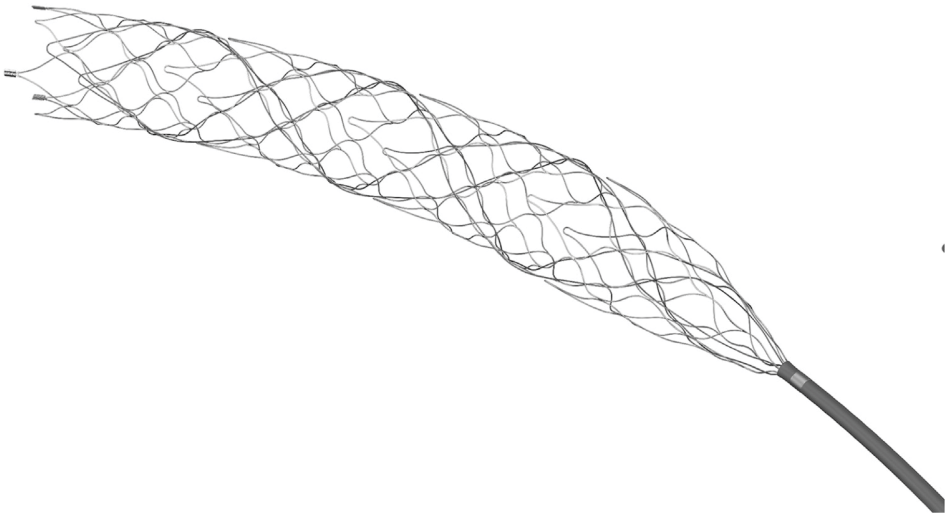


Figure 1. The Aperio Hybrid device (photograph provided by Acandis). Functional segment: small closed cells, large open cells; repeating functional segments allowing adaption of working length to thrombus length. (The small closed cells may attain a good vessel wall apposition and expansion into the clot, and large open cells with integrated anchoring elements aim to assure efficient clot retention and are supposed to result in favorable recanalization rates.)

platinum wires into the existing nitinol stent struts, the Trevo ProVue aims to visualize the complete working length, whereas the Solitaire Platinum only exhibits evenly spaced single platinum markers added every 10 mm (Figure 2).

Procedure Description

Thrombectomies were performed either under general anesthesia or conscious sedation at the discretion of the neurointerventionalist operator. As standard, a triaxial system was used via a femoral access. At first, a short 8F sheath was inserted to place an 8F guide catheter (e.g., Vista brite tip; Johnson & Johnson, New Brunswick, New Jersey, USA) into the internal carotid artery or a short 6F sheath to navigate a 6F catheter (e.g., Envoy MPC; Codman Neurovascular, Raynham, Massachusetts, USA) into the vertebral artery, respectively. Afterward, the occluded intracranial artery was visualized by contrast injection. The large majority of procedures were performed on a biplanar angiography suite using the "Solumbra technique," in which the stent retriever is usually retracted into an aspiration catheter placed proximal to the clot.[14] Under the guidance of a standard 0.014″ microguidewire, a microcatheter (Neuroslider 21, Acandis [n = 33]; Rebar 18, Medtronic [n = 15]) was placed distal to the clot and a large bore aspiration catheter (e.g., 6F Sofia Plus aspiration catheter in the anterior, or Sofia 5F in the posterior circulation; Microvention, Tustin, California, USA) was placed as proximal as possible to the thrombus. Afterward, the microguidewire was replaced by the APH. The size of the APH was determined considering the length and the cross-section of the thrombus and vessel, respectively. After deployment of the APH, the microcatheter was removed to maximize suction lumen inside the aspiration catheter. Correct deployment was confirmed under fluoroscopy until the APH was fully expanded. A 60 mL vacuum pressure syringe (VacLok; Merit Medical, South Jordan, Utah, USA) was attached to the aspiration catheter. Under continuous fluoroscopy and manual suction, the APH and thrombus were withdrawn into the large bore catheter. An example case is shown in Figure 3. Afterward, a control angiography was performed, and if necessary, the thrombectomy maneuver was repeated. If the recanalization attempts remained insufficient (<mTICI2b), a rescue device was used at the discretion of the treating physician.

Patient Selection

An ethical approval and patient consent were waived by the local ethics committees of the respective Faculties of Medicine for this retrospective observational study.

Inclusion criteria were as follows: the APH as the first-line device, LVO, and no evidence of intracranial bleeding in the initial magnetic resonance imaging or computed tomography (CT) examination. Furthermore, only patients with an Alberta Stroke Program Early CT Score (ASPECTS) ≥5 and an NIHSS ≥5 (unless they suffered from aphasia) were included. There was no age limit and no upper time limit between onset and expected groin puncture as long as the above criteria were met. No other

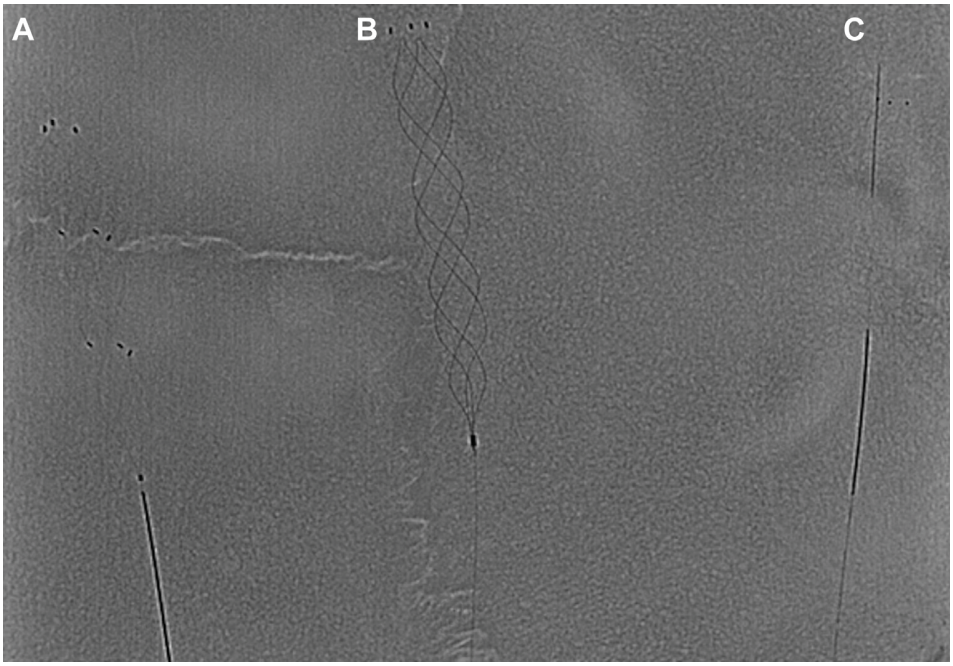


Figure 2. Image (provided by Acandis) demonstrating enhanced visibility of the Aperio Hybrid stent retriever (**B**) under fluoroscopy compared with the precursor device Aperio (**C**) and the Solitaire Platinum (**A**) stent retriever.

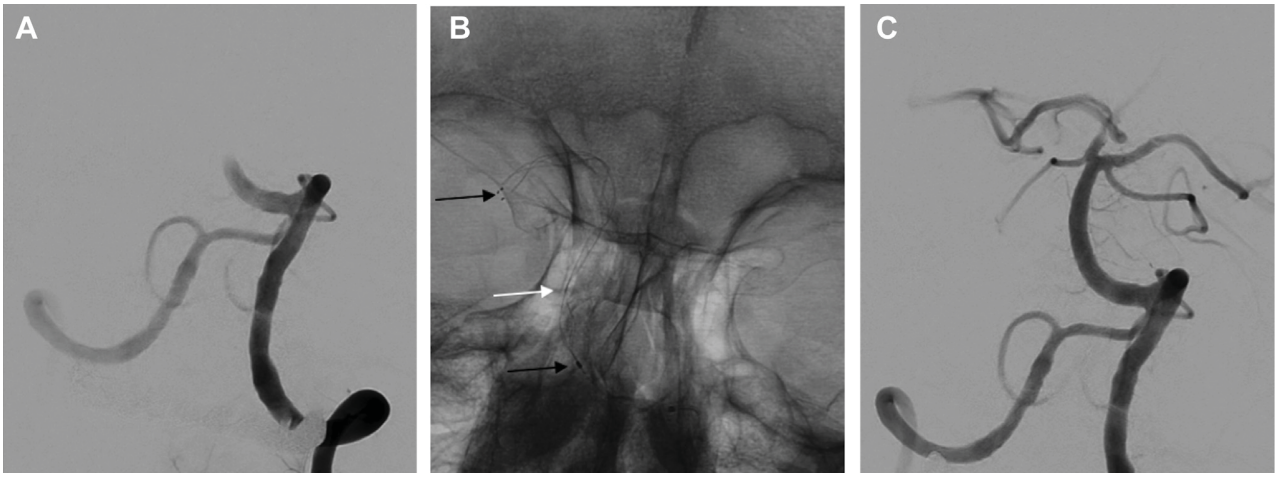


Figure 3. Images illustrate the case of a patient with a basilar artery occlusion. (**A**) Digital subtraction angiography shows the initial finding of a proximal basilar artery occlusion (mTICI 0). CTA (not shown) reveals long-sectioned thrombus load within the BA. (**B**) A nonsubtracted angiography shows the completely released 4.5 × 50 mm Aperio Hybrid stent retriever from the right posterior cerebral artery to the basilar artery origin. The Aperio Hybrid exhibits superior radiopacity; visibility is ensured not only at the proximal tip of the retriever and the 3 distal device markers (*black arrows*), but also within full length of the device due to integrated radiopaque drawn filled tubing wires. The tapering of the stent retriever at the level of the thrombus is clearly visible (*white arrow*). (**C**) Complete recanalization of the occlusion after first pass (mTICI 3). BA, basilar artery; CTA, computed tomography angiography; mTICI, modified thrombolysis in cerebral infarction.

exclusion criteria existed. IVT was administered according to the guidelines of the German Neurological Society.

Clinical and Radiological Data

Basic demographics (age and sex) and pre-existing conditions (e.g., previous strokes, high blood pressure, atrial fibrillation, diabetes) as well as premedications were derived from the routinely collected patient data. In addition, specific data on the acute stroke event itself were extracted: NIHSS and mRS at admission and discharge, 90-day mRS (which was available for 2 of the 3 participating centers), time of stroke or in case of unknown onset, the time when the patient was last well seen, the time of admission to hospital, and the time of initial imaging. In addition, it was documented if and when IVT was administered. Clinical data and scores were evaluated by a consultant neurologist.

From the radiological image documentation, the affected side, the affected vessel, the ASPECTS before and after intervention, the diameter of the affected vessel, the time of the inguinal puncture, the first and last attempt of recanalization, the number of thrombectomy maneuvers, and final perfusion result (mTICI) were evaluated. It was documented whether a rescue stent retriever was used, if supplementary intra-arterial lysis was administered and if any complications occurred during angiography or further clinical course. In particular, the number and severity of subarachnoid and intraparenchymal hemorrhages, and the number of embolisms into new territories, of periprocedural dissections, and of material defects (e.g., stent retriever fails to open, breaks, tears) were evaluated. The type (diameter and length) of the APH used was also documented. All image-based outcome was collected by blinded review of images by board-certified neuroradiologists at each site.

Questionnaire

A questionnaire about the technical performance of the APH, which was routinely issued by the manufacturer as part of the product launch, was completed by the operators for all cases. The following aspects were evaluated: transfer of the APH into the microcatheter, pushability into the microcatheter, positioning, device deployment, resheathing into the microcatheter and introducer, and visibility of the markers and the device itself. Therefore, a 5-point Likert scale from − (poor) to ++ (very good) was used. In addition, the operators had the opportunity to make individual comments. In particular, they were asked to comment if they had replaced the stent retriever due to the improved visibility, whether the improved visibility helped to evaluate the interaction of the device with the clot, and whether they could observe a deformation of the stent during the retraction of the stent retriever. Devices were compared with the ones routinely used at each institution (Solitaire Platinum and Aperio, respectively). The MT procedures were conducted by board-certified neuroradiologists with an experience ranging between 2 and 15 years in endovascular stroke treatment.

RESULTS

Patients

A total of 48 patients with acute stroke (26 women, 22 men, mean age: 73 ± 2 years) were treated by MT in 3 university neurovascular centers, between May 2019 and July 2019 with the following occlusion patterns: carotid-T in 8 (16.7%), M1-segment in 31 (64.6%), M2-segment in 4 (8.3%), and basilar artery in 5 (10.4%) cases. The incidence of carotid-T occlusion was significantly higher ($P = 0.03$) in the rescue group (3 of 7; 42.9%)

compared with the APH-only group (5 of 41; 12.2%) (Table 1). The mean diameter of the occluded vessels was 2.8 ± 0.1 mm. Before thrombectomy, 25 of 48 patients (52.1%) received IVT according to the guidelines of the German Neurological Society (Table 1).

Operator Evaluation of Aperio Hybrid Performance

In an ordinal rating scale, the device was rated "good" and "very good" in terms of transfer into a required 0.021″ microcatheter in all cases (100%), pushability in a microcatheter (93.8%), positioning of a stent retriever (98.0%), device deployment (97.9%), marker visibility (100%), and device contour visibility (97.9%). If necessarily performed, all procedures of resheathing into the microcatheter as well as resheathing into the introducer sheath were effortless and rated as good or very good.

In 2 of 48 (4.2%) cases, pushability of the device was rated as "poor" or "very poor" and positioning of the APH was rated "poor" in 1 of 48 cases (2.1%) due to increased force to advance the device within the microcatheter.

Technical Success

Overall favorable revascularization (mTICI ≥ 2b) was achieved in 95.8% (46 of 48) including a first-pass recanalization rate (mTICI > 2b) of 60.4% (29 of 48). Final mTICI ≥ 2c was achieved in 29 of 48 procedures (60.4%). Regarding the total number of 48 procedures, a recanalization rate of mTICI ≥ 2b was achieved in 83.4% (40 of 48), final mTICI ≥ 2c in 52.1% (25 of 48), first-pass recanalization mTICI ≥ 2b in 52.1% (25 of 48), and first-pass mTICI ≥ 2c in 31.3% (15 of 48) when the APH was used as an exclusive device (Table 1). The overall mean number of stent-retriever passes was 3 ± 3. The mean number of passages for additional devices was 1 ± 0 after a mean of 3 ± 1 passes with the APH before switching. Whenever the APH was used exclusively, the mean number of maneuvers accounted to 2 ± 3.

The overall mean time to final recanalization from femoral access to final revascularization was 54 ± 5 minutes. Intra-arterial recombinant tissue plasminogen activator was administered in a single case (2.1%). The post-treatment median ASPECTS in follow-up CT after 16–24 hours was 6 (0–10) (Table 1).

In all 48 cases, the APH was the first-line stent-retriever device using sizes of 4.5 × 50 mm in 7 patients, 4.5 × 40 mm in 32 patients, and 4.5 × 30 mm in 9 patients. In 7 procedures (14.6%), a rescue stent retriever was used at the discretion of the individual neurointerventionalist due to primary insufficient results with the APH. In 5 cases, stent retrievers from other manufacturers (NeVa Mi 4 × 30 mm [n = 1], Vesalio, Lake Forest, California, USA; pREset LITE 3 × 20 mm [n = 1], Phenox, Bochum, Germany; Solitaire Platinum 4 × 40 mm [n = 2], Medtronic, Dublin, Ireland; Trevo XP ProVue 4 × 30 mm [n = 1], Stryker Neurovascular) were applied. In 2 procedures, the operator switched from the APH to a conventional predecessor Aperio 4.5 × 40 and 3.5 × 28 mm (Acandis) due to anticipated increased pushability. In case of rescue maneuver, final mTICI ≥ 2b could be achieved in 85.7% (6 of 7) of the patients. In one case of basilar artery occlusion, PTA and stent implantation after MT were necessary due to a high-grade atherosclerotic stenosis.

Safety, Complications, and Clinical Outcome

No clinically relevant device-related procedural complications were encountered (Table 1). Angiographically apparent SAH did not occur. Periprocedural embolization into previously unaffected territories by fragmented or lost clots did not appear. In follow-up CT or magnetic resonance imaging 16–24 hours after MT, asymptomatic hemorrhagic transformation or parenchymal hematoma (HI-1, HI-2, PH-1) was observed in 6 patients (12.5%) and asymptomatic, mild SAH, Fisher 1, in 3 patients (6.3%). Three (6.3%) parenchymal hematomas (PH-2), as a result of a reperfusion injury, were symptomatic, and conductance of a craniectomy was required in 1 case. There were no device-related adverse events. Forty-six patients (95.8%) were available for follow-up at discharge; 2 were lost to follow-up (4.3%). A favorable clinical outcome at discharge according to the mRS (0–2) was achieved in 32.6% (15 of 46) and in 36.7% (11 of 30) of the patients available for 90-day follow-up (Table 1). Overall mortality during hospital stay was 21.7% (10 of 46). Procedure-related deaths did not occur.

DISCUSSION

The aim of this multicentric trial was to evaluate the efficacy, safety, and clinical outcome of the APH for the treatment of LVO in the anterior and posterior circulation in patients with acute ischemic stroke. The device was designed to achieve improvements in visibility by implementing radiopaque DFT wires that allow full-length visibility of the device. This quality may increase control during the procedure and reflect thrombus position within the stent frame itself during the retrieval. This new visibility concept was combined with the proven hybrid design[13] of the established predecessor Aperio. In this retrospective, multicentric trial, an overall mTICI 2b–3 revascularization rate was achieved in 95.8%. The rate of final favorable reperfusion (mTICI ≥ 2b) accounted already for 83.4% (40 of 48) when the APH was used exclusively. These results compare favorably with data from the TRACK registry in which Trevo devices were used with reported mTICI ≥ 2b recanalization in 68.8% of patients for the only use of the Trevo device[15] and with the reported rates of 71.1% for the sole use of EmboTrap in a recent core laboratory-audited single-center experience or a previous EmboTrap multicenter series with 73% recanalization rate.[16,17]

The rate of excellent final reperfusion (mTICI ≥ 2c) by the exclusive use of the APH was 52.1% in the present study and is slightly inferior to the outcome data of excellent reperfusion (mTICI ≥ 2c) in the Analysis of Revascularization in Ischemic Stroke with EmboTrap (ARISE II) study (64.7%) where EmboTrap was used.[18] First-pass recanalization rate mTICI ≥ 2b for procedures in which the APH was used solely was achieved in 52.1% and was comparable with EmboTrap in the recently published ARISE II trial (51.5%) and was higher compared with Trevo (40.8%) and Solitaire (32%) in a non–randomized controlled trial (RCT), whereas the rate of excellent first-pass recanalization (mTICI ≥ 2c) was slightly lower in our study compared with EmboTrap in ARISE II (33.4% vs. 40.1%).[18,19]

The mean number of passes (mean, 3.0 ± 3) with the APH was in line with results from a recent nonrandomized comparative trial for Trevo (mean, 2.1; interquartile range, 1–6) and Solitaire

Table 1. Baseline Data, Angiographic Results, Clinical Outcome, and Complications

	Overall Patients	Aperio Hybrid Only	Patients with Rescue
Sample Size	N = 48 Patients	N = 41 Patients	N = 7 Patients
Age, mean (±SD)	73 (±15)	74 (±16)	72 (±8)
Sex, n (%)	f = 26 (54.2), m = 22 (45.8)	f = 21 (51.2), m = 20 (48.8)	f = 5 (71.4), m = 2 (28.6)
Medical history			
Hypertension, n (%)	40 (87.0)	31 (84.6)	7 (100.0)
Diabetes mellitus, n (%)	6 (13.0)	4 (10.3)	2 (28.6)
Atrial fibrillation, n (%)	23 (47.9)	18 (46.2)	5 (71.4)
Previous stroke, n (%)	11 (23.9)	10 (25.6)	1 (14.3)
ASA, n (%)	10 (23.3)	8 (22.2)	2 (28.6)
Clopidogrel, n (%)	1 (2.3)	1 (2.8)	0 (0.0)
Phenprocoumon, n (%)	4 (9.3)	4 (11.1)	0 (0.0)
DOAC, n (%)	7 (16.3)	6 (16.7)	1 (14.3)
IVT, n (%)	25 (52.1)	21 (51.2)	4 (57.1)
NIHSS pre, median, n (%)	15 (2–36)	14 (2–36)	18 (16–20)
mRS pre, median, n (%)	5 (2–5)	5 (2–5)	5 (5–5)
Prestroke imaging			
Hemisphere, n (%)	r = 24 (50.0), l = 19 (39.6), v = 5 (10.4)	r = 21 (51.2), l = 15 (36.6), v = 5 (12.2)	r = 3 (42.9), l = 4 (57.1), v = 0 (0.0)
T-type occlusion, n (%)	8 (16.7)	5 (12.2)	3 (42.9)
M1 occlusion, n (%)	31 (64.6)	27 (65.9)	4 (57.1)
M2 occlusion, n (%)	4 (8.3)	4 (9.8)	0 (0.0)
Basilary occlusion, n (%)	5 (10.4)	5 (12.2)	0 (0.0)
Vessel diameter, mean (±SD)	2.8 (±0.8)	2.8 (±0.8)	3.1 (±0.9)
ASPECTS, median	9 (2–10)	9 (2–10)	8 (5–10)
Procedural data			
Onset-to-needle time (minutes), mean (±SD)	124 (±90)	132 (±94)	72 (±28)
Door-to-needle (minutes), mean (±SD)	70 (±175)	74 (±188)	46 (±33)
Onset-to-groin puncture (minutes), mean (±SD)	221 (±112)	224 (±117)	200 (±72)
Door-to-groin puncture (minutes), mean (±SD)	99 (±151)	99 (±154)	96 (±112)
Onset-to-recanalization (minutes), mean (±SD)	273 (±119)	275 (±127)	256 (±54)
Door-to-recanalization (minutes), mean (±SD)	149 (±163)	148 (±167)	159 (±128)
Groin-to-recanalization (minutes), mean (±SD)	54 (±33)	51 (±33)	69 (±31)
Number of passes, mean (±SD)	3 (±3)	2 (±3)	3 (±2)
Number of device passes to TICI2b/3 recanalization, mean (±SD)	3 (±3)	2 (±3)	3 (±2)

Continues

Table 1. Continued

	Overall Patients		Aperio Hybrid Only	Patients with Rescue
IA tPA, n (%)	1 (2.1)		1 (2.8)	0 (0.0)
Rate of Recanalization After Stent-retriever First Pass				
TICI 0, n (%)	8 (16.7)	7 (17.1)		1 (14.3)
TICI 1, n (%)	3 (6.3)	3 (7.3)		0 (0)
TICI 2a, n (%)	8 (16.7)	6 (14.6)		2 (28.6)
TICI 2b, n (%)	13 (27.1)	10 (24.4)		3 (42.9)
TICI 2c, n (%)	4 (8.3)	3 (7.3)		1 (14.3)
TICI 3, n (%)	12 (25.0)	12 (29.3)		0 (0)
Final Angiographic and Postprocedural Imaging Outcomes			Percentage on Overall Sample (N = 48)	
TICI 0, n (%)	0 (0)	0 (0)	0 (0)	0 (0)
TICI 1, n (%)	0 (0)	0 (0)	0 (0)	0 (0)
TICI 2a, n (%)	2 (4.2)	1 (2.4)	1 (2.1)	1 (14.3)
TICI 2b, n (%)	17 (35.4)	15 (36.6)	15 (31.3)	2 (28.6)
TICI 2c, n (%)	6 (12.5)	4 (9.8)	4 (8.3)	2 (28.6)
TICI 3, n (%)	23 (47.9)	21 (51.2)	21 (43.8)	2 (28.6)
ASPECTS, median	6 (0—10)	7 (0—10)		6 (1—8)
Clinical outcome	(N = 46)		(N = 39)	(N = 7)
Number of patients (%) of mRS ≤2 (at discharge)	15 (32.6)		15 (38.5)	0 (0)
mRS 0, n (%)	3 (6.5)		3 (7.7)	0 (0)
mRS 1, n (%)	9 (19.6)		9 (23.1)	0 (0)
mRS 2, n (%)	3 (6.5)		3 (7.7)	0 (0)
mRS 3, n (%)	3 (6.5)		3 (7.7)	0 (0)
mRS 4, n (%)	8 (17.4)		5 (12.8)	3 (42.9)
mRS 5, n (%)	10 (21.7)		8 (20.5)	2 (28.6)
Mortality (discharge), mRS 6, n (%)	10 (21.7)		8 (20.5)	2 (28.6)
NIHSS discharge	7 (0—42)		5 (0—42)	16 (7—42)
Number of patients (%) of mRS ≤2 (at 90-day FU)	11 (36.7)		10 (41.7)	1 (16.7)
mRS 0, n (%)	4 (13.3)		3 (12.5)	1 (16.7)
mRS 1, n (%)	6 (20.0)		6 (25.0)	0 (0)
mRS 2, n (%)	1 (3.3)		1 (4.2)	0 (0)
mRS 3, n (%)	1 (3.3)		1 (4.2)	0 (0)
mRS 4, n (%)	3 (10.0)		1 (4.2)	2 (33.3)
mRS 5, n (%)	6 (20.0)		4 (16.7)	2 (33.3)
Mortality (90-day FU), mRS 6, n (%)	9 (30.0)		8 (33.3)	1 (16.7)

SD, standard deviation; ASA, acetylsalicylic acid; DOAC, new oral anticoagulants; IVT, intravenous thrombolysis; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; ASPECTS, Alberta Stroke Program Early Computed Tomography Score; IA tPA, intra-arterial tissue plasminogen activator; TICI, thrombolysis in cerebral infarction; FU, follow-up; SAH, subarachnoid hemorrhage; sICH, symptomatic intracranial hemorrhage.

Continues

Table 1. Continued

	Overall Patients	Aperio Hybrid Only	Patients with Rescue
Complications			
None, n (%)	36 (75.0)	29 (70.7)	7 (100.0)
SAH, n (%)	3 (6.3)	3 (7.3)	0 (0)
HI-1, n (%)	3 (6.3)	3 (7.3)	0 (0)
HI-2, n (%)	2 (4.2)	2 (4.9)	0 (0)
PH-1, n (%)	1 (2.1)	1 (2.4)	0 (0)
PH-2, n (%)	3 (6.3)	3 (7.3)	0 (0)
sICH, n (%)	3 (6.3)	3 (7.3)	0 (0)

SD, standard deviation; ASA, acetylsalicylic acid; DOAC, new oral anticoagulants; IVT, intravenous thrombolysis; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; ASPECTS, Alberta Stroke Program Early Computed Tomography Score; IA tPA, intra-arterial tissue plasminogen activator; TICI, thrombolysis in cerebral infarction; FU, follow-up; SAH, subarachnoid hemorrhage; sICH, symptomatic intracranial hemorrhage.

(mean, 2.9; interquartile range, 1–8),[19] with Trevo from the TRACK registry (mean, 1.9 ± 1.2) or EmboTrap from ARISE II (average, 2.6; range, 1–10).[15,18,19]

If MT with the APH was regarded as unsuccessful and aborted, another competing stent retriever was chosen. The rate of 14.6% for rescue maneuvers was consistent with results reported from other non-RCT stent-retriever studies ranging between 15% and 28%.[15-18,20]

An early favorable clinical outcome (mRS, 0–2) at discharge was achieved in 32.6% of our patient sample and is superior to the discharge mRS of the TRACK study (mean [standard deviation], 17.4% [6.7%]).[15]

Being well aware of limited outcome follow-up data in the present study, a 3-month mRS rate of 36.7% seems to be in line with self-reported rates for EmboTrap (35%)[17] and with non-RCT trials for the Aperio (41.2%)[13] and Solitaire (42.1%)[19] as well as rates in the NASA (42%)[20] and Endostroke registry (41%).[21] Better 3-month follow-up rates in further non-RCT trials are reported for EmboTrap[16] and Trevo[15,19] (**Table 2**).

The safety of the APH in the current study is within the range of recent stent-retriever trials (**Table 2**). The rate of 6.3% for sICH is comparable with 5% in the ARISE II trial[18] and 7.1% and 9.9% sICH rates in TRACK[15] and NASA,[20] respectively. Clot fragment embolization into previously unaffected territories did not occur. The all-cause mortality rate at 30 days was 21.7%, which is comparable with TRACK data (19.8%)[15] and NASA,[20] and is higher compared with ARISE II (9%)[18] and in non-RCT trials for EmboTrap (12.9%)[16] and Solitaire and Trevo (6.8% and 4%).[19] No case of death in our patients was procedural related. These safety results support an acceptable benefit-risk profile for the device.

The preceding model of the APH, the Aperio, was evaluated in 2 trials with patients with stroke with LVO of the cerebral circulation. In the first trial, 119 patients from 9 centers, where 42% had the occlusion in the M1 segment, were treated by MT.[22] Rate of mTICI ≥ 2b–3 was 71% at a median of device passes of 2.[22] The handling and effectiveness of the predecessor APH was evaluated regarding trackability, visualization, positioning, and deployment. Trackability was rated as very good and good in 82%, visualization in 91%, deployment in 91%, and positioning in 89%. In the present study, we assessed an improvement in the rating of the new APH in device deployment, positioning of a stent retriever, and visibility.

In 2 cases of the current study, impeded device pushability was observed, but no correlation with a particular microcatheter was ascertainable. In both cases, a tortuous vessel anatomy of the cavernous or terminal internal carotid artery segment, or curved vessels of the M1 segment and its division were assumed as likely causes for increased resistance. In addition, another explanation might be increased friction inside the microcatheter during stent-retriever advancement due higher volume of material evoked by the new embedded DFT wires into the APH. This extra material may become noticeable in the aforementioned challenging anatomic conditions with elongated and curved extra- and intracranial vessels.

These challenges might be overcome by using the new generation of the dedicated neuroslider microcatheter (NeuroSlider DLC; Acandis) for delivery that is expected to offer more stability. In the aforementioned cases, the predecessor Aperio as a rescue device was used assuming a smoother pushability due to less friction within the microcatheter.

The second single-center study evaluated the safety and efficacy of the first-generation Aperio in 82 patients with stroke with LVO of the anterior circulation.[13] mTICI ≥ 2b rate was achieved in 85.3% and first-pass mTICI ≥ 2b in 43.9% at a mean of device passes of 2.6 ± 1.7. Compared with the present study an increase in recanalization rates by the use of the APH with mTICI ≥ 2b in 95.8% and first-pass mTICI ≥ 2b in 52.1% at a mean of 3 ± 3 passes could be assessed.[13] Complication rates were reported with rates of 10% including embolization in new territory in 1.2% (vs. 0% in the present study) and 7.3% sICH (vs. 6.3% in the present study).[13,22] As in the present APH study, serious device-related complications did not occur with the precursor Aperio. Hence, the performance and safety of the APH compares favorably with the predecessor model. Although both stent retrievers have the same hybrid cell design, higher

Table 2. Clinical and Angiographic Outcome of Selected Stent-Retriever Trials

Study	Endovascular Treatment (n)	Device	Baseline NIHSS (Median)	Overall TICI 2b–3 (%)	First Pass TICI (%)	Postinterventional NIHSS (Median)	mRS 0–2 at 90 Days (%)	Mortality (%)	sICH (%)
Singer et al. 2013[21]	309*	Various	16	77	N.A.	N.A.	41	27	15
Kallenberg et al. 2016[22]	119	Aperio	N.A.	71	N.A.	N.A.	N.A.	0	0
Kabbasch et al. 2016[17]	40	EmboTrap	16	95	TICI 3: 38	N.A.	35	17	15
Zaidat et al. 2018[15]	634	Trevo	17	80	TICI 3: 54.3	Mean (SD) Discharge: 17.4 (6.7); 90 day: 18.1 (18.7)	47.9	19.8	7.1
Kaschner et al. 2019[13]	82	Aperio	14	85.3	TICI 2b–3: 43.9	N.A.	41.2	17.1	7.3
Zaidat et al. 2018[18]	227	EmboTrap	Mean (SD) 15.8 (5)	92.5	TICI 2b–3: 51.5 TICI ≥2c: 40.1	N.A.	67	9	5.3
Zaidat et al. 2014[20]	354	Solitaire	17	73	N.A.	N.A.	42	30.2	9.9
Brouwer et al. 2018[16]	201	EmboTrap	15	84.6	N.A.	N.A.	52.8	12.9	N.A.
Yi et al. 2018[19]	102	Solitaire	11.3	82.3	TICI 2b–3: 32	At 30 days: 6.2	42.1	6.8	N.A.
	98	Trevo	11.7	89.7	TICI 2b–3: 40.8	At 30 days: 5.4	48.9	4	N.A.
This study	48	Aperio Hybrid	15	96	TICI 2b–3: 60.4 TICI ≥2c: 33.4 TICI 3: 25	At discharge: 7	36.7	22	6

NIHSS, National Institutes of Health Stroke Scale; N.A., not available; SD, standard deviation; TICI, thrombolysis in cerebral infarction; mRS, modified Rankin Scale; sICH, symptomatic intracranial hemorrhage.

*Number of patients with available TICI scoring.

recanalization rates of the APH were achieved in the current study compared with the Aperio. An explanation might be higher expansion forces of the APH due to the additional DFT wires that may improve clot incorporation. This hypothesis is currently under investigation by the manufacturer, but data from laboratory experiments are still pending.

The major limitations of this study are the nonrandomized retrospective nature, a missing reference group, and the relatively small sample particularly for the posterior circulation.

In addition, angiographic images were evaluated by blinded neurointerventionalists at their own center and not core laboratory adjudicated that can potentially bias the interpretation results. In this study, it was up to the individual operator's discretion when to abstain from the APH and switch to another rescue device. Therefore, it is not known whether a continuation with the APH would have still led to a success in the 7 cases in which rescue devices have been chosen. A further consideration in the present study is the primary use of a concomitant lesional local aspiration technique during stent-retriever retrieval, termed the Solumbra technique.[14] It is important to note that the overall endovasular treatment techniques have evolved. Particularly in Solumbra the aspiration component is very important and effective and might be at least in part an explanation for the good revascularization results that are superior to some of the prementioned RCTs. In this context, it is conceivable that different thrombectomy techniques for different circumstances may impact the rate of excellent reperfusion and first-past complete revascularization, for example, using a balloon guide–assisted proximal aspiration under flow reversal. Further RCTs may help define subgroups of patients, in which the APH, in combination with a specific thrombectomy method, based on the occlusion pattern, would yield the most effective recanalization results.

Follow-up clinical outcome after 90 days is limited to 30 of 48 (63%) patients and therefore has to be interpreted with caution. However, a German multicentric registry is being initiated by our group and will provide more extensive data.

In this initial evaluation, there was no major criticism toward the overall handling of the device. The improved visibility concept of the APH was rated to be "good" or "very good" in 100% of its first clinical trial. Technically, its use seems feasible and safe, and the high rates of successful

recanalization appear to be in the range of comparable stent-retriever publications.

Full structural radiopacity would allow a more targeted deployment of the APH and delineation of the stent retriever. From a procedural point of view, visualization of just the distal markers would be sufficient but a reliable detection of clot integration and clot displacement requires full-length visibility of the stent structures. Moreover, during retrieval there is no visual control of the clot-stent interaction in conventional nitinol retrievers as the predecessor Aperio. Compared with the Aperio, the APH is one of few stent retrievers that allow visualization of the clot-strut interaction during both deployment and retrieval.[11,12] As a result of full-length visibility, a potential failure of the thrombectomy maneuver might be detected at an early stage and enables us to adapt or modify the procedure, for example, obvious nonintegration of the clot within the stent retriever just sliding past it or visible straightening of the target vessel without relative movement of the stent retriever that may indicate increased force transmitted to the vessel, with the risk of structural damage. In our cases in which pushability of the device was rated as "poor" and "very poor" (4.2%, 2 of 48) and positioning of the APH as "poor" (2.1%, 1 of 48), the added DFT wires were supposed to increase the resistance during the delivery and deployment of the APH stent retriever via the microcatheter. This assumption is in accord with reports of an international survey performed among the members of the World Federation of Interventional and Therapeutic.[23] In this context, a final assessment of friction or resistance during delivery and deployment of the device, and evaluation of the used material in combination with the APH (e.g., microcatheters, aspiration catheters), should be subject to a prospective evaluation.

CONCLUSIONS

This early multicenter experience demonstrated that the recently introduced APH yielded high rates of favorable and excellent reperfusion in cerebral LVO in conjunction with lesional aspiration in the setting of acute stroke. Clinical outcome after 90 days seems to be in line with published literature. The absence of device-related procedural complications reflects a high safety profile. Full-length visibility of the APH may allow the detection of the alignment of the device with the clot and may guide procedural adaptation by control of the actual stent-clot or stent-vessel interaction. These promising initial results will be further evaluated in a German multicentric registry.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Marius Kaschner: Writing - original draft, Data curation, Investigation. **Thorsten Lichtenstein:** Writing - original draft, Data curation, Investigation. **Daniel Weiss:** Data curation, Formal analysis. **Bernd Turowski:** Data curation, Formal analysis. **Lukas Goertz:** Data curation, Formal analysis. **Claudia Kluner:** Data curation, Formal analysis. **Marc Schlamann:** Data curation, Formal analysis. **Christian Mathys:** Writing - review & editing, Data curation, Project administration, Investigation, Validation, Supervision. **Christoph Kabbasch:** Conceptualization, Writing - review & editing, Data curation, Project administration, Investigation, Validation, Supervision.

REFERENCES

1. Turc G, Bhogal P, Fischer U, et al. European Stroke Organisation (ESO)—European Society for Minimally Invasive Neurological Therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischemic stroke [e-pub ahead of print]. *J Neurointerv Surg* https://doi.org/10.1136/neurintsurg-2018-014569, accessed February 16, 2020.

2. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2018;49:E46-E110.

3. Berkhemer OA, Fransen PSS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372:11-20.

4. Campbell BCV, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372:1009-1018.

5. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. 2015;372:1019-1030.

6. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med*. 2015;372:2285-2295.

7. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372:2296-2306.

8. Riedel CH, Zimmermann P, Jensen-Kondering U, Stingele R, Deuschl G, Jansen O. The importance of size. *Stroke*. 2011;42:1775-1777.

9. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med*. 2018;378:11-21.

10. Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med*. 2018;378:708-718.

11. Pfaff J, Rohde S, Engelhorn T, Doerfler A, Bendszus M, Möhlenbruch MA. Mechanical thrombectomy using the new Solitaire™ Platinum stent-retriever: reperfusion results, complication rates and early neurological outcome. *Clin Neuroradiol*. 2019;29:311-319.

12. Kabbasch C, Mpotsaris A, Chang D-H, et al. Mechanical thrombectomy with the Trevo ProVue device in ischemic stroke patients: does improved visibility translate into a clinical benefit? *J Neurointerv Surg*. 2016;8:778-782.

13. Kaschner MG, Weiss D, Rubbert C, et al. One-year single-center experience with the Aperio thrombectomy device in large vessel occlusion in the anterior circulation: safety, efficacy, and clinical outcome. *Neurol Sci*. 2019;40:1443-1451.

14. Humphries W, Hoit D, Doss VT, et al. Distal aspiration with retrievable stent assisted thrombectomy for the treatment of acute ischemic stroke. *J Neurointerv Surg*. 2015;7:90-94.

15. Zaidat OO, Castonguay AC, Nogueira RG, et al. TREVO stent-retriever mechanical thrombectomy for acute ischemic stroke secondary to large vessel occlusion registry. *J Neurointerv Surg*. 2018;10:516.

16. Brouwer PA, Yeo LLL, Holmberg A, et al. Thrombectomy using the EmboTrap device: core laboratory-assessed results in 201 consecutive patients in a real-world setting. *J Neurointerv Surg*. 2018;10:964.

17. Kabbasch C, Mpotsaris A, Liebig T, et al. First-in-man procedural experience with the novel EmboTrap® revascularization device for the treatment of ischemic stroke—a European multicenter series. *Clin Neuroradiol*. 2016;26:221-228.

18. Zaidat OO, Bozorgchami H, Ribó M, et al. Primary results of the multicenter ARISE II study (Analysis

of Revascularization in Ischemic Stroke with EmboTrap). *Stroke*. 2018;49:1107-1115.

19. Yi HJ, Lee DH, Kim SU. Effectiveness of Trevo stent retriever in acute ischemic stroke. *Medicine*. 2018;97:e10747.

20. Zaidat OO, Castonguay AC, Gupta R, et al. North American Solitaire Stent Retriever Acute Stroke registry: post-marketing revascularization and clinical outcome results. *J Neurointerv Surg*. 2014;6:584.

21. Singer OC, Haring H-P, Trenkler J, et al. Age dependency of successful recanalization in anterior circulation stroke: the ENDOSTROKE study. *Cerebrovasc Dis*. 2013;36:437-445.

22. Kallenberg K, Solymosi L, Taschner CA, et al. Endovascular stroke therapy with the Aperio thrombectomy device. *J Neurointerv Surg*. 2016;8:834.

23. Berg R van den, Mayer TE. International survey on neuroradiological interventional and therapeutic devices and materials. *Interv Neuroradiol*. 2015;21:646-652.

Conflict of interest statement: C. Kabbasch reports personal fees from Acandis and personal fees from Microvention, outside the submitted work. The remaining authors have no conflicts to report.

All data will be made available on request in an anonymized manner.

Received 24 March 2020; accepted 12 May 2020

Citation: World Neurosurg. (2020). https://doi.org/10.1016/j.wneu.2020.05.104

*Journal homepage: **www.journals.elsevier.com/world-neurosurgery***

*Available online: **www.sciencedirect.com***

A Retrospective Single-Center Case Series of Direct Aspiration Thrombectomy as First-Line Approach in Ischemic Stroke and Review of the Literature

Marius Georg Kaschner, MD,* Christian Rubbert, MD,* Julian Caspers, MD,* Jennifer Karsten,* Bastian Kraus, MD,* John-Ih Lee, MD,† Michael Gliem, MD,† Sebastian Jander, MD,† and Bernd Turowski, MD*

Introduction: The benefit of the direct aspiration thrombectomy (ADAPT) technique for the treatment of ischemic stroke due to large vessel occlusion are challenged after publishing of the ASTER trial that failed to show superiority of ADAPT compared to stent retriever. Aim of the present single-center study was a retrospective evaluation of the ADAPT technique comparing our results with literature. *Material/methods*: We retrospectively analyzed institutional data of stroke procedures in patients with mainstem occlusion of the middle cerebral artery treated between November 2016 and December 2017 with an initial attempt of manual thrombaspiration. Reperfusion rate (thrombolysis in cerebral infarction), procedural times, early clinical outcome and complications were recorded. *Results*: Forty patients were treated by using direct thrombaspiration in middle cerebral artery mainstem occlusion. Median age was 67.5 (±17.8) years (m = 27.5%). Median Baseline National Institutes of Health Stroke Scale score was 12 (IQR 7) preintervention and 3 (IQR 11) postintervention. Twenty-eight (70%) patients received intravenous thrombolysis. Successful recanalization (modified thrombolysis in cerebral infarction $\geq$ 2b) could be achieved in 85% with direct aspiration alone. Mean time from groin puncture to recanalization was 25.2 ± 14.3 minutes. Embolization to new territories occurred in 1 of 40 (2.5%) cases and symptomatic intracranial hemorrhage in 3 of 40 (7.5%). Nineteen of 40 (47.5%) patients achieved favorable outcome (modified Rankin scale 0-2) at discharge. *Conclusions*: The ADAPT technique presented as a safe and efficient first-line recanalization strategy with good clinical outcome for treatment of acute ischemic stroke resulting from large vessel occlusions in this single-center study and review of the literature. However, the concept of ADAPT as an equivalent first-line approach to stent retriever thrombectomy has to be proven by future randomized studies.

Key Words: Stroke—middle cerebral artery occlusion—aspiration thrombectomy—ADAPT

From the *University Düsseldorf, Medical Faculty, Department of Diagnostic and Interventional Radiology, Moorenstr. 5, D-40225, Düsseldorf, Germany; and †Department of Neurology, Heinrich Heine University Duesseldorf, Medical Faculty, Duesseldorf, Germany.

Received June 3, 2018; revision received September 29, 2018; accepted November 4, 2018.

Compliance with ethical standards:

Funding: No funding was received for this study.

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent: Patients were informed about the approach, benefit and risks of the planned procedure in the emergency setting and informed consent was obtained prior to intervention. Consent for retrospective data analysis was waived.

Correspondence to: Marius Kaschner, MD, Department of Neuroradiology, Heinrich Heine University Duesseldorf, Moorenstr.5, 40225 Duesseldorf, Germany. E-mail: marius.kaschner@med.uni-duesseldorf.de.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.11.004

Introduction

The previous studies using ADAPT (a direct first pass aspiration technique) as first-line approach in large vessel occlusion (LVO) reported promising results regarding to recanalization rate, procedural times and costs.[1-6] The ASTER study is the first published prospective, randomized, multicenter, controlled open-label design with blinded outcome evaluation that compared the direct aspiration thrombectomy to stent retriever technique as first-line approach. The study was powered to show superiority of ADAPT over the stent retriever technique regarding efficacy and adverse events.[7] The study enrolled 381 patients from 8 comprehensive stroke centers in France who presented with acute ischemic stroke in the anterior circulation. Superiority of the ADAPT technique over first-line stent retriever could not be demonstrated. Hence, stent retriever thrombectomy remains first-line technique for treatment of LVO in ischemic stroke. The current study presents the results of a single-center patient collective with acute ischemic stroke resulting from middle cerebral artery (MCA) mainstem occlusion that were treated by the ADAPT technique as first-line approach, and a critical review of the literature.

Material and Methods

Our study was approved by our hospital's institutional review board. Data evaluation was approved by the local ethics committee. From November 2016 to December 2017, n = 125 consecutive patients with anterior circulation ischemic stroke due to M1/M2 occlusion, as diagnosed by computed tomography angiography (CTA) or magnetic resonance tomography, were treated by thrombectomy. We further analyzed all patients, in which an aspiration thrombectomy as first-line approach was conducted (n = 40).

According to the guidelines of the local ethics committee, consent for retrospective data analysis was waived.

Inclusion Criteria

The study enrolled adults with occlusion of the M1 and M2 branches of the MCA receiving direct aspiration thrombectomy as first-line endovascular treatment; no age limit, no baseline National Institutes of Health Stroke Scale (NIHSS) score limit at admission, and no time limit from symptom onset to treatment were applied to restrict study inclusion. Standardized stroke imaging at our institution included non−contrast-enhanced cranial computed tomography (NECCT), computed tomography perfusion (CTP), and CTA. If time from symptom onset to admission was uncertain, patients were scanned with magnetic resonance imaging (MRI), applying diffusion-weighted imaging (DWI), perfusion weighted imaging (PWI), and fluid-attenuated inversion recovery (FLAIR) image to discern between salvageable and terminally infarcted tissue. Patients who qualified for treatment with intravenous thrombolysis (IVT), received this treatment according to the guidelines of the German Society of Neurology. Extensive early ischemic signs or hemorrhage could be excluded in preinterventional imaging by CT or MRI assessment. There were no ASPECTS treshholds for exclusion from thrombectomy. Eligibility for thrombectomy in patients with acute M1/M2 occlusion, as established in CTA or time-of-flight magnetic resonance tomography, was determined individually for each patient in consensus between neurologists and neurointerventionalists. The decision is primarily based on the infarct-core/penumbra mismatch, estimated procedural risk, probability of recanalization by IVT, contraindication for IVT, comorbidities, and social and medical prestroke conditions. Exclusion criteria were intracranial hemorrhage and occlusion of the cervical carotid artery.

CTP was acquired with 2 adjacent slices of 1 cm thickness angled parallel to the Frankfurt horizontal line at the level of the cella media over 50 seconds with 1 image per second. Perfusion maps including time to maximum (T_{max}), mean transit time, relative cerebral blood volume (rCBV), and relative cerebral blood flow were calculated using singular value decomposition (STROKETOOL-CT, Version 2.0, H.-J. Wittsack, DIS, Frechen, Germany). Perfusion restriction was detected by visual inspection and region of interest (ROI) measurement in the T_{max} map. A difference exceeding 6 seconds in T_{max} values between ischemic and contralateral unaffected hemisphere was suggested as critical ischemia. To differentiate irreversibly infarcted tissue (infarct core) and salvageable ischemic tissue (penumbra), and to estimate collateralization, NECCT and rCBV were used. Tissue showing infarct typical hypoattenuation in NECCT or/and rCBV close to 0 was considered as irreversibly infarcted brain parenchyma that corresponds to the infarct core. Tissue showing significant T_{max} prolongation outside the infarct core was considered as the penumbra. Dynamic contrast-enhanced magnetic resonance PWI was performed with the duration of the gradient-echo sequence about 1 minute and whole brain coverage (4 mm slice thickness). Perfusion maps including time to peak, mean transit time, CBV, and cerebral blood flow. In MR imaging infarct core was distincted from penumbra by DWI/PWI mismatch. DWI affected tissue was considered as infarct core. Tissue showing perfusion deficit in time to peak without DWI alteration was considered as penumbra.

If substantial penumbra was detected on CTP by NECCT/CTP mismatch or MRI by DWI/PWI mismatch analysis, decision for thrombectomy was made. Furthermore, as portions of DWI abnormalities may represent penumbra with the potential of normalization when perfusion is restored, a phenomenon described "DWI reversal," thrombectomy was also performed in cases where DWI affected tissue clearly exceeded FLAIR demarcation (FLAIR/DWI mismatch).[8,9] For all cases, the estimation of substantial penumbra was to the discretion of the interventionalist.

Interventional Procedure

The interventional procedures were performed under analgesia (1-2 g Novaminsulfone as short infusion) and local anesthesia of the groin. General anesthesia was performed in patients with need for endotracheal intubation (Glasgow coma scale < 8) or in case of extreme agitation. Access was performed using a long 8F sheath or additional guiding catheter positioned in the distal internal carotid artery. A .027-in. inner lumen microcatheter was advanced up to (no touch technique) or past the thrombus over a microwire and then an aspiration catheter (5F or 6F SOFIA, MicroVention Inc, Tustin, CA) was advanced to the proximal aspect of the thrombus. In cases of nonelongated or minorelongated arteries, the aspiration catheter could be directly advanced to the site of occlusion without using a microcatheter and microwire. When applied, microcatheter (Neuroslider 21, Acandis, Pforzheim, Germany) and microguidewire were removed and aspiration catheter was directly locked to a 20 mL syringe. Manual aspiration was started and as soon as absence of flow was noted, the resulting vacuum was maintained for at least 60 seconds, before the catheter was slowly retracted under additional aspiration at the guide catheter.[10] If first aspiration attempt failed completely (defined as no extraction of any thrombus material), a rescue maneuver with a stent retriever (APERIO; Acandis, Pforzheim, Germany) under local aspiration through the aspiration catheter (Solumbra technique) was performed immediately. In case of partial clot extraction the aspiration attempt was either (1) repeated up to 3 times, (2) an additional thrombectomy device was used under local aspiration, or (3) the intervention was terminated when residual clot could not be reached without increased risk of procedural complications. The choice of procedure was at the discretion of the interventionalist.

Imaging and procedural data collection: time from symptom onset to stroke imaging, to groin puncture, and to recanalization were captured. The location of the occlusion and thrombus length were assessed on CT or MR angiographic images. Collateral supply of the occluded MCA territory from preinterventional CTA scans was scored based on collateral grading system of Tan et al on a scale of 0-3.[11] Devices and medication used during the interventional procedures, duration, and intraprocedural complications were evaluated from the treatment protocols. Angiographic outcome was graded by the modified thrombolysis in cerebral infarction (TICI) scale.[12] Pretreatment cerebral infarction, according to the Alberta Stroke Program Early CT score (ASPECTS) was assessed by cardiovascular computed tomography or MRI. Post-treatment ASPECTS and symptomatic intracerebral hemorrhage, according to the European Cooperative Acute Stroke Study classification, were assessed by follow-up cardiovascular computed tomography imaging that was routinely performed 6-24 hours after treatment.[13]

Statistical Analysis

Statistical analysis was performed using R version 3.4.3. R is a programming language widely used for data analysis. Stroke severity as measured by NIHSS, clinical outcome according to modified Rankin Scale (mRS), and ASPECTS between admission and discharge were compared by means of Mann-Whitney U tests. The Mann-Whitney U test is a nonparametric test of the null hypothesis, which allows 2 groups, conditions, or treatments to be compared without making the assumption that the values are normally distributed. A paired test was conducted, since the values were compared in the same patient at the time of admission and discharge. Results were considered statistically significant at a level of $P < .05$.

Results

Patients

Forty patients with M1/M2 segment occlusion were identified who underwent an endovascular therapy by the ADAPT technique as first revascularization attempt between November 2016 and December 2017. Twenty-eight patients (70%) received intravenous tissue plasminogen activator (IVT) prior to endovascular procedure. Mean age of the patients was 67.5 years (SD 17.8), 72.5% were women. Median baseline NIHSS was 12, and median pretreatment mRS was 4. Baseline median ASPECTS was 10 and median collateral score was 3 (Table 1).

Technical Success

An overall final revascularization result of (TICI ≥ 2b) was achieved in all 40 cases. The ADAPT technique with aspiration alone was successful in 85% (34/40) of cases; the remaining 6 (15%) cases required stent retriever thrombectomy to reach TICI 2b/3 recanalization. TICI3 revascularization rate was 52.9% (18/34) with the ADAPT technique alone and 66.7% (4/6) in ADAPT cases with adjunctive use of a stent retriever (Table 1). In 80% (32/40) primary site of occlusion was located in the M1 segment and 20% (8/40) of cases involved the M2 segment. Overall mean time to final recanalization proceeding from femoral access to final revascularization was 25.2 minutes (SD ± 14.3) over all cases and 20.7 minutes (SD ± 8.4) for the ADAPT technique alone cases. In those cases where an adjunctive stent retriever was required time to final recanalization increased significantly to 50.6 minutes (SD ± 15.2, $P = .005$). Median of overall aspiration attempts was 1 in the whole sample, 1 in the ADAPT alone, and 2 in the ADAPT rescue group. In the 34 cases where successful recanalization was achieved by ADAPT as stand-alone technique we found red thrombus material, in the 6 cases with rescue stentretriever treatment hard white fragment clots were extracted.

Table 1. *Baseline data, angiographical results, clinical outcome, and complications*

	All (n = 40)	Aspiration alone (n = 34)	Aspiration + stent retriever (n = 6)
Age (mean, ±SD)	67.5 ± 17.8	65.7 ± 17.8	79 ± 15.1
Sex (n)	m = 11, w = 29	M = 11, w = 23	W = 6
CTA-collateral score (0-3), median	3	3	3
IVT n(%)	28(70)	22(64.7)	6(100)
Onset to groin puncture (min., mean SD±)	202.5 ± 161.6	215.9 ± 171	142 ± 78.2
Time from groin puncture to final recanalization (min., mean ± SD)	25.2 ± 14.3	20.7 ± 8.4	50.6 ± 15.2
TICI 2b n(%)	11(27.5)	9(26.5)	2(33.4)
TICI 2c n(%)	7(17.5)	7(20.6)	0(0)
TICI 3 n(%)	22(55)	18(52.9)	4 (66.6)
ASPECTS premedian, (IQR)	10 (1)	10 (.75)	10 (1.5)
ASPECTS postmedian, (IQR)	8 (2.25)	8 (2)	9 (2.75)
NIHSS premedian, (IQR)	12 (7)	12 (7)	12 (3.75)
NIHSS postmedian, (IQR)	3 (11)	2 (8.25)	12 (8.25)
mRS premedian, (IQR)	4 (1)	4 (1)	5 (1)
mRS postmedian, (IQR)	3 (3)	2 (3)	4 (.75)
mRS ≤ 2 post n(%)	19 (47.5)	19(55.8)	0(0)
Emboli to new territories n(%)	1(2.5)	0(0)	1(17.1)
sICH n(%)	3(7.5)	2(5.8)	1(16.7)
Mortality n(%)	1(2.5)	1(2.9)	0(0)

Abbreviations: CTA, CT angiography; IVT, intravenous thrombolysis; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage; TICI, thrombolysis in cerebral infarction.

Clinical Outcome, Follow-up Imaging and Complications

The post-treatment median NIHSS improved significantly from 12 (at admission) to 3 at discharge ($P < .005$). Median mRS improved from 4 to 3 ($P < .05$). The post-treatment median mRS in the ADAPT alone group was statistically significantly lower compared to patients with stent retriever rescue treatment (2 versus 4, $P < .05$). Forty-seven percent of patients achieved a mRS score of 0-2 at discharge. In the cases where ADAPT alone was successful, 55.8% of patients achieved a mRS score of 0-2. In the cases with stent retriever rescue treatment no patient (0/6) achieved mRS 0-2, 33.3% (2/6) resulted in mRS 5, 33.3% (2/6) in mRS 4, and 16.7% (1/6) resulted in mRS 3. Median pretreatment ASPECTS was 10 in both groups. Median ASPECTS after treatment was 8 in the ADAPT alone cases and 9 in cases with rescue stent retriever maneuver without statistically significance between the groups ($P > .05$). Differences in pre- to post-treatment median ASPECTS shift were significant in the overall and ADAPT alone group (10 versus 8; $P < .05$). Overall mortality was 2.5% (1/40) with a mortality rate of 2.9% (1/35) in the ADAPT alone group and 0% in the ADAPT rescue group. Postprocedure symptomatic intracerebral hemorrhage occurred in 3 cases (7.5%), 2/34 (5.8%) in the ADAPT alone and 1/6 (16.7%) in the ADAPT and stent retriever group. Embolization to new territories occurred in 1 patient (2.5%, 1/40) who received ADAPT plus rescue stent retriever (Table 1).

Discussion

ADAPT or contact aspiration technique has gained growing popularity as it is thought to achieve revascularization safely, quickly and with a small amount of material resources. [5,14,16,10] There are numerous single-center reports suggesting the aspiration approach to be less traumatic in vessel wall damage and consecutive symptomatic hemorrhages.[1,3] Nonrandomized retrospective trials comparing direct aspiration to stent retriever thrombectomy have reported increased successful recanalization rates when using ADAPT as first-line approach.[4,15,16]

The results of our single-center trial are in line with the good results of the preceded observational studies. Our overall rates of 100% (40/40) successful recanalization (TICI2b, 27.5%; TICI2c/3, 72.5%) and 85% (34/40) successful recanalization (TICI 2b;26.5%, TICI 2c/3; 73.5%) when ADAPT used alone were high compared to results of recently published studies (Table 2).[1,3,5-7,10,14,15,17,18] Rates of rescue stent retriever use were comparable in our study group (15%). In all cases of necessary stent retriever maneuvers in addition to ADAPT hard fragment clots were the reason of vessel occlusion, which hints to a possible limitation of the ADAPT technique. The percentage of patients with mRS 0-2 at discharge were comparable to data in recently published studies (47% versus 46%-50.6%).[3,10,14] Our overall rate of symptomatic intracranial hemorrhage of 7.5% is in line with data from other ADAPT studies.[14,15] Embolization to new territories was

comparable to the reported rates in the literature (2.5% versus 2%-6%).[1,3,7,10,14] There was no significant difference between the median ASPECT score in the ADAPT group compared to the ADAPT+rescue group (8 versus 9) post-treatment, but postinterventional median mRS was significantly lower in the ADAPT group compared to the ADAPT+rescue group. Even if the results from literature and our own are encouraging there is a paucity of randomized trials for efficacy of ADAPT as first-line approach in LVO stroke and most of the nonrandomized trials are biased by group definition.

The currently published ASTER-trial is the first randomized comparative trial that has studied the aspiration technique versus the stent retriever thrombectomy as first-line strategy in LVO in acute ischemic stroke but the results indicated that there was no difference between the 2 techniques.[7]

The ASTER trial was designed to demonstrate superiority of aspiration as first-line therapy over stent retriever in achieving the primary end point of successful recanalization (TICI2b/3) at the end of angiography after all endovascular treatment. The study failed to achieve this result with a recanalization rate below the expected level of 15% increased successful recanalization rates by the aspiration attempt. Even if revascularization rate is a major early indicator of treatment success, clinical outcome such as the 90-day mRS score is more relevant. Clinical outcome with a 90-day mRS 0-2 was comparable between the 2 groups but ASTER also failed to demonstrate equivalence or noninferiority in clinical outcome because it was not designed to prove these aspects and hence underpowered. Numerous single-center studies suggest aspiration to be less traumatic regarding vessel damage, which may be because of aspiration thrombectomy having less of a shearing effect, that is why many interventionalists may favor this approach in the first place. The safety profile at the ASTER trial was equal for both treatment strategies with comparable rates of procedure-related adverse events (16.2% aspiration versus 15.9% stent retriever). Thus, ASTER also failed to confirm a potential safety superiority.

The problem of comparing aspiration and the stent retriever technique is the lack of randomized trials for aspiration thrombectomy. The only randomized trial in this analysis using ADAPT as first-line technique was ASTER that demonstrated high revascularization rates with rates of good functional outcome (mRS 0-2) of 45%. In THERAPY, an international, multicenter, prospective, randomized trial comparing aspiration thrombectomy after intravenous alteplase administration with intravenous alteplase alone, high revascularization rates (TICI2b/c) of 70% were achieved but the rate of 38% with 90-day good functional outcome was relatively low. Moreover, the study was underpowered, because it has been terminated early and failed to show significant results.[19]

A patient-level meta-analysis of 5 randomized trials (MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, and an EXTEND IA) that used predominantly stent retrievers for first-line revascularization approach revealed an overall good clinical outcome rate of 46%, but a rate of mRS less than or equal to 2 up to 60% in SWIFT-PRIME and 71% mRS less than or equal to 2 in EXTEND IA could be achieved (Fig 1).[5,7,19-28] At last the heterogeneity in the ADAPT meta-analysis limits the comparability to the stent-retriever technique. Theoretically ADAPT might lower the risk of embolic complications, because passage of the thrombus before aspiration is not necessary and the thrombus is frequently extracted en bloc. However, an in-vitro study has found that more angiographically not visible emboli occur with the ADAPT technique, than with stent retriever. This higher number of microemboli in soft elastic clots might be the reason for the poor rate of favorable functional outcome.[29] The frequency of small distal emboli following recanalization is unknown, and it is unclear whether the risk of small distal embolization differs between recanalization techniques in vivo.

At this point in time, the question if aspiration is equivalent to stent retriever as first-line approach to clot removal is unresolved while uncertainty about clinical effectiveness of the technique remains. On the other hand results of a current meta-analysis indicate that ADAPT might be an effective first-line approach in the treatment of LVO. Wei et al conducted a meta-analysis of 16 studies that used ADAPT as first-line approach and 5 studies that limited endovascular procedures to aspiration thrombectomy only. The reported rate of 90-day mRS less than or equal to 2 in the 16 ADAPT studies was 52.7% (95% confidence interval, 48.0%-57.4%).[16] Moreover, the results from the COMPASS trial, that ought to be published soon, have been presented at the International Stroke Conference (ISC; 24-26 January, Los Angeles, CA) and revealed noninferiority of ADAPT as first-line thrombectomy therapy for acute ischemic stroke with regard to functional outcomes when compared to the stent-retriever-first approach.[30] The major limitation of our study is the relatively small sample size that might be the reason for the relatively high revascularization success. Further, the use of ADAPT technique was at the discretion of the interventionalist, which might have created a selection bias. For example, in very tortuous and complex vessel anatomy the interventionalist may have chosen to use a stent retriever as a first-line therapy, instead of escalating from ADAPT to stent retriever therapy. The detectable significance level of the Mann-Whitney U test is not expected to suffer from the sample size of n = 40.

At last the question arises, if any of the thrombectomy methods are superior to others. Choosing a method for a specific patient depends on a number of different variables, for example vessel anatomy, operator experience, or, as our results show, clot composition. The ADAPT method alone might be more promising in short, soft,

Table 2. *An overview of published studies on thrombectomy using the ADAPT technique as first-line approach*

Study	First-line technique	Number patients/ cases	NIHSS	TICI2b-3 n (%)	ADAPT+ Resc, n (%)	Onset to groin puncture, min.	Time groin puncture-recanalization, min.	90-day mRS≤2, (%)	sICH, n (%)	ENT, n (%)	Mortality, n (%)
Turk 2014 (ADAPT-FAST)[5]	ADAPT	All: 100 ADAPT alone: 78	All: median 17 ADAPT alone: NA	All: 95/100 (95) ADAPT alone: 78/100 (78)	22/100 (22)	All: mean 507 ADAPT alone: NA	All: mean 36.6 ADAPT alone: mean 31.6	All: 32/81 (39.5) ADAPT alone: 37/78 (47.4)	0	0	All: 15/77 (19.5) ADAPT alone: 11/78 (14.1)
Jankowitz 2015[10]	ADAPT	All: 112 ADAPT alone: 66	All: median 17 ADAPT alone: NA	All: 97/112 (87) ADAPT alone: 66/112 (59)	46/112 (41.1)	All: median 267 ADAPT alone: NA	All: median 70 ADAPT alone: NA	All: 52/112 (46.4) ADAPT alone: NA	All: 7/112 (6.2) ADAPT alone: NA	All: 4/112 (3.5) ADAPT alone: 2/66 (3)	All: 35/112 (31.3) ADAPT alone: NA
Romano 2016[14]	ADAPT	All: 152 ADAPT alone: 96	All: mean 19.0 ADAPT alone: mean 19.2	All: 115/152 (75.6) ADAPT alone: 83/152 (54.6)	56/152 (36.8)	All: mean 227 ADAPT alone: NA	All: mean 57.8 ADAPT: mean 44.7	All: 77/152 (50.6) ADAPT: 55/96 (57.3)	All: 12/152 (7.8) ADAPT alone: 4/96 (4.1)	All: 3/152 (1.9) ADAPT alone: 2/96 (2.1)	All: 12/152 (7.8) ADAPT alone: 6/96 (6.2)
Kowoll 2016[3]	ADAPT	All: 54 ADAPT alone: 30	All: median 15 ADAPT alone: mean 14	All: 50/54 (93%) ADPAT alone: 30/54 (55.5)	24/54 (44.4)	All: median 179 ADAPT alone: median 174	All: mean 41 ADAPT alone: median 30	All: 25/54 (46.3)$^{+}$ ADAPT alone: 16/30 (53.3)	All: 2/54 (3.7) ADAPT alone: 1/30 (3)	All: 3/54 (6) ADAPT alone: 2/30 (7)	All: 6/54 (11.1) ADAPT alone: 1/30 (3)
Vargas 2016[17]	ADAPT	All: 191 ADAPT alone: 146	All: mean 15.4 ADAPT alone: mean 15.3	All: 180/191 (94.2) ADAPT alone: 145/191 (75.9)	45/191 (23.6)	All: mean 468.3 ADAPT alone: mean 483.9	All: mean 37.3 ADAPT alone: mean 30.1	All: 98/181 (54.1) ADPAT alone: 79/137 (57.7)	All: 13/191 (6.8) ADAPT alone: NA	0	All: 27/181 (14.9) ADAPT alone: 19/137 (13.9)
Blanc 2017[1]	ADAPT	All: 347 ADAPT alone: 209	All: median 17 ADAPT alone: NA	All: 288/347 (83) ADAPT alone: 193/347 (55.6)	138/347 (39.7)	All: Median 255 ADAPT alone: NA	All: NA ADAPT alone: median 37	All: 144/323 (44.5) ADAPT alone: NA	All: 10/347 (2.9) ADAPT alone: NA	All: 22/347 (6.3) ADAPT alone: NA	All: 73/323 (22.6) ADAPT alone: NA

Study	First-line technique	Number cases/ patients ADAPT	NIHSS	TICI2b-3 n (%)	ADAPT+ Resc, n (%)	Onset to groin puncture, min.	Time groin puncture-recanalization, min.	90d mRS≤2, n (%)	sICH overall, n (%)	ENT, n (%)	Mortality, n (%)
Turk 2015[6]	ADAPT versus SRLA versus PS	ADAPT all: 64 ADAPT alone:NA	ADAPT: median 16.5 ADAPT alone: NA	ADAPT all: 61/64 (95.3) ADAPT alone: 50/64 (78.1)	NA	ADAPT all: NA ADAPT alone: NA	ADAPT all: mean 37.1 ADAPT alone: NA	ADAPT all: 28/60 (46.7) ADAPT alone: (54.6)§	ADAPT all: NA ADAPT alone: NA	ADAPT all: NA ADAPT alone: NA	ADAPT all: NA ADAPT alone: NA
Lapergue 2017 (ASTER)[7]	ADAPT versus SR	ADAPT all: 192 ADAPT alone: 129	ADAPT all: mean 16.3 ADAPT alone: NA	ADAPT all: 164/192 (85.4) ADAPT alone: 121/ 192 (63)	63/192 (32.8)	ADAPT all: median 217 ADAPT alone: NA	ADAPT all: median 38 ADAPT alone: NA	ADAPT all: 82/181 (45.3) ADAPT alone: NA	ADAPT all: 10/188 (5.3) ADAPT alone: NA	ADAPT all: 7/192 (3.7) ADAPT alone: NA	ADAPT all: 35/181 (19.3) ADAPT alone: NA
Delgado Almandoz 2017[18]	ADAPT versus Solumbra	ADAPT all: 45 ADAPT alone: 32	ADAPT all: mean 19.2 ADAPT alone: NA	ADAPT all: 40/45 (89) ADAPT alone: NA	13/45 (28.9)	ADAPT all: mean 224 ADAPT alone: NA	ADAPT all: mean 50 ADAPT alone: NA	ADAPT all: 25/45 (55.6) ADAPT alone: NA	ADAPT all: 1/45 (2.2) ADAPT alone: NA	ADAPT all: 2/45 (4.4) ADAPT alone: NA	ADAPT all: 8/45 (17.8) ADAPT alone: NA
Stapleton 2018[15]	ADAPT versus SR	ADAPT all: 47 ADAPT alone: 27	ADAPT all: mean 16.5 ADAPT alone: mean 16.7	ADAPT all: 39/47 (83) ADAPT alone: 22/47 (46.8)	20/47 (42.5)	ADAPT all: mean 241.9 ADAPT alone: mean 219.3	ADAPT all: mean 54.0 ADAPT alone: mean 41.8	ADAPT all: 23/47 (48.9) ADAPT alone: 14/27 (51.9)	ADAPT all: 6/47 (12.8) ADAPT alone: 1/27 (3.7)	ADAPT all: NA ADAPT alone: NA	ADAPT all: 6/47 (12.8) ADAPT alone: 1/27 (3.7)
Present study 2018	ADAPT	All: 40 ADAPT alone: 34	All: median 12 ADAPT alone: median 12	All: 40/40 (100) ADAPT alone: 34/40 (85)	6/40 (15)	All: mean 202.5 ADAPT alone: mean 215.9	All: mean 25.2 ADAPT alone: mean 20.7	All: 19/40 (47.5)† ADAPT alone: 19/34 (55.8)†	All: 3/40 (7.5) ADAPT alone: 2/34 (5.8)	All: 1/40 (2.5) ADAPT alone: 0/34 (0)	All: 1/40 (2.5) ADAPT alone: 1/34 (2.9)
*Total: Weighted average ratios**	*ADAPT all ADAPT alone*	1344 847		ADAPT all: *86.9%* ADAPT alone: *63.7%*	*33%*			ADAPT all: *47.3%* ADAPT alone: *54.6%*	ADAPT all: *5%* ADAPT alone*: 4.2%*	ADAPT all: *3.2%* ADAPT alone: *1.4%*	ADAPT all: *18.1%* ADAPT alone: *9.8%*

Abbreviations: ADAPT alone, ADAPT without adjunctive thrombectomy techniques; ADAPT + Resc, ADAPT with stent retriever rescue; ENT, embolization to new territories; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; PS, traditional penumbra system; SR, stent retriever; SLRA; stent retriever with local aspiration; sICH, symptomatic intracerebral hemorrhage;TICI, thrombolysis in cerebral infarction; § = number of patients is not available.

*Average ratios weighted to number of patients.

†mRS at discharge.

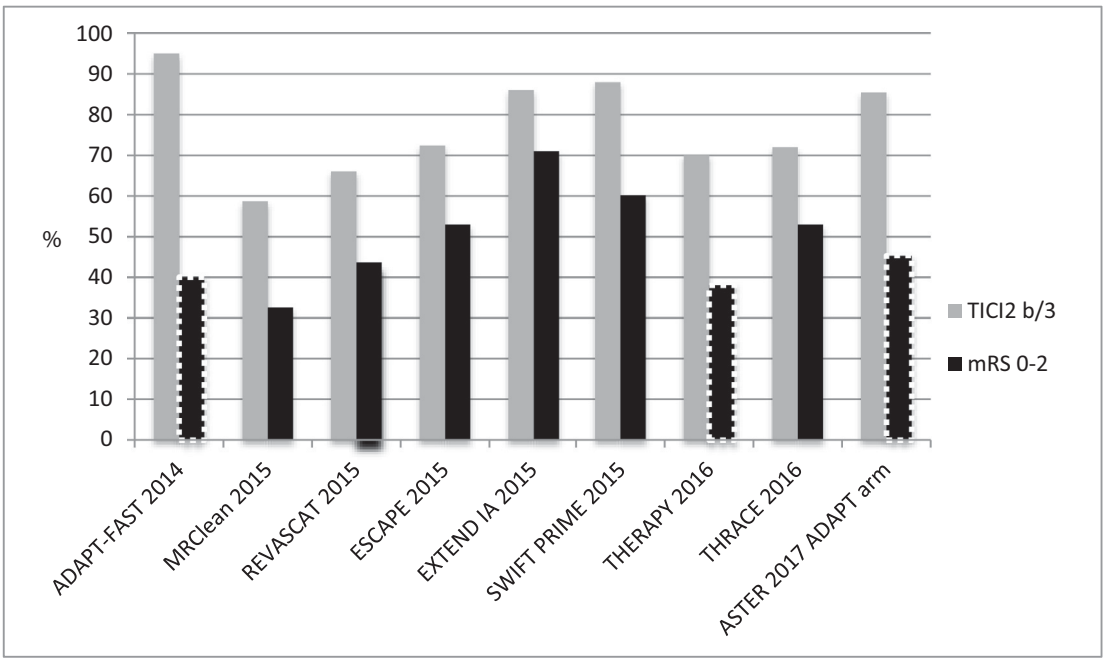


Figure 1. *Summary of major stent retriever and aspiration thrombectomy trials. White-dashed bar graphs represent mRS in trials with ADAPT as first-line revascularization approach. Abbreviations: ADAPT, direct aspiration thrombectomy; mRS, modified Rankin scale.*

elastic clots which can be completely aspirated into large-bore catheters. In longer soft-elastic thrombus, an additional proximal flow-arrest might reduce thrombus fragmentation and microembolies. In contrast, hard, clots are often too rigid to be completely aspirated and may shear of the catheter tip when maneuvering the thrombus along narrow bends or when retracting the aspiration catheter into the sheath or guiding catheter. In such a case, a local aspiration technique in combination with a stent retriever may be the more suitable method, for example the SAVE technique.[31] At this point in time, there are no randomized controlled trials available evaluating the outcome of different stent retriever techniques.

The present series continues to show that the ADAPT technique is very competitive as a first-line treatment modality despite the fact that the randomized study (ie, ASTER) did not show any differences between aspiration and stent retriever thrombectomy. In this context and in regard to this apparent dissonance, it is conceivable that different techniques for different circumstances is probably the most realistic future of thrombectomy.

Conclusions

The existing evidence of ADAPT as a first-line approach may not reach the level of Class IA, but it is increasingly available and our study adds to that body of knowledge. Results from the COMPASS trial, which ought to be published soon, may provide more definitive evidence, that aspiration thrombectomy may be considered as an equally effective therapy when compared to stent retrievers. Choosing the thrombectomy method suitable for a respective patient depends on a number of different variables and further randomized trials may define subgroups of patients, in which a single method or a combination of methods may be more suitable than other approaches.

References

1. Blanc R, Redjem H, Bartolini B, et al. Predictors of the Aspiration Component Success of a Direct Aspiration First Pass Technique (ADAPT) for the endovascular treatment of stroke reperfusion strategy in anterior circulation acute stroke. Stroke 2017;48:1588-1593.
2. Kabbasch C, Möhlenbruch M, Stampfl S, et al. First-line lesional aspiration in acute stroke thrombectomy using a novel intermediate catheter: initial experiences with the SOFIA. Interv Neuroradiol 2016;22:333-339.
3. Kowoll A, Weber A, Mpotsaris A, et al. Direct aspiration first pass technique for the treatment of acute ischemic stroke: initial experience at a European stroke center. J Neurointerv Surg 2016;8:230-234.
4. Lapergue B, Blanc R, Guedin P, et al. A direct aspiration, first pass technique (ADAPT) versus stent retrievers for acute stroke therapy: an observational comparative study. AJNR Am J Neuroradiol 2016;37:1860-1865.
5. Turk AS, Frei D, Fiorella D, et al. ADAPT FAST study: a direct aspiration first pass technique for acute stroke thrombectomy. J Neurointerv Surg 2014;6:260-264.
6. Turk AS, Turner R, Spiotta A, et al. Comparison of endovascular treatment approaches for acute ischemic stroke: cost effectiveness, technical success, and clinical outcomes. J Neurointerv Surg 2015;7:666-670.
7. Lapergue B, Blanc R, Gory B, et al. Effect of endovascular contact aspiration vs stent retriever on revascularization in patients with acute ischemic stroke and large vessel occlusion: the ASTER Randomized Clinical Trial. JAMA 2017;318:443-452.

8. Loh PS, Butcher KS, Parsons MW, et al. Apparent diffusion coefficient thresholds do not predict the response to acute stroke thrombolysis. Stroke 2005;36:2626.
9. Kidwell CS, Saver JL, Mattiello J, et al. Thrombolytic reversal of acute human cerebral ischemic injury shown by diffusion/perfusion magnetic resonance imaging. Ann Neurol 2000;47:462.
10. Jankowitz B, Aghaebrahim A, Zirra A, et al. Manual aspiration thrombectomy: adjunctive endovascular recanalization technique in acute stroke interventions. Stroke 2012;43:1408-1411.
11. Tan IYL, Demchuk AM, Hopyan J, et al. CT angiography clot burden score and collateral score: correlation with clinical and radiologic outcomes in acute middle cerebral artery infarct. AJNR Am J Neuroradiol 2009;30:525-531.
12. Goyal M, Fargen KM, Turk AS, et al. 2C or not 2C: defining an improved revascularization grading scale and the need standardization of angiography outcomes in stroke trials. J Neurointerv Surg 2014;6:83-86.
13. Fiorelli M, Bastianello S, von Kummer R, et al. Hemorrhagic transformation within 36 hours of a cerebral infarct: relationships with early clinical deterioration and 3-month outcome in the European Cooperative Acute Stroke Study I (ECASS I) cohort. Stroke 1999;30:2280-2284. 1999.
14. Romano DG, Cioni S, Vinci SL, et al. Thromboaspiration technique as first approach for endovascular treatment of acute ischemic stroke: initial experience at nine Italian stroke centers. J Neurointerv Surg 2017;9:6-10.
15. Stapleton J, Leslie-Mazwi TM, Torok CM, et al. A direct aspiration first-pass technique vs stentriever thrombectomy in emergent large vessel intracranial occlusions. J Neurosurg 2018;128:567-574.
16. Wei D, Mascitelli JR, Nistal DA, et al. The use and utility of aspiration thrombectomy in acute ischemic stroke: a systematic review and meta-analysis. AJNR Am J Neuroradiol 2017;38:1978-1983.
17. Vargas J, Spiotta A, Fargen K, et al. Long term experience using the ADAPT technique for the treatment of acute ischemic stroke. J NeuroInterv Surg 2017;9:437-441.
18. Delgado Almandoz JE, Kayan Y, et al. Comparison of clinical outcomes in patients with acute ischemic strokes treated with mechanical thrombectomy using either Solumbra or ADAPT techniques. J NeuroInterv Surg 2016;8:1123-1128.
19. Mocco J, Zaidat OO, Rüdiger von Kummer R, et al. Aspiration thrombectomy after intravenous alteplase versus intravenous alteplase alone. Stroke 2016;47:2331-2338.
20. Zaidat OO, Castonguay AC, Gupta R, et al. North American Solitaire Stent Retriever Acute Stroke registry: post-marketing revascularization and clinical outcome results. J NeuroInterv Surg 2014;6:584-588.
21. Pereira VM, Gralla J, Davalos A, et al. Prospective, multicenter, single-arm study of mechanical thrombectomy using solitaire flow restoration in acute ischemic stroke. Stroke 2013;44:2802-2807.
22. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 2015;372:11-20.
23. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 2015;372:2296-2306.
24. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 2015;372:1019-1030.
25. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 2015;372:1009-1018.
26. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med 2015;372:2285-2295.
27. Bracard S, Ducrocq X, Mas JL, et al. Mechanical thrombectomy after intravenous alteplase versus alteplase alone after stroke (THRACE): a randomised controlled trial. Lancet Neurol 2016;15:1138-1147.
28. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 2016;387:1723-1731.
29. Chueh JY, Puri AS, Wakhloo AK, et al. Risk of distal embolization with stent retriever thrombectomy and ADAPT. J NeuroInterv Surg 2016;8:197-202.
30. Turk AS, Siddiqui AH, Mocco J. A comparison of direct aspiration versus stent retriever as a first approach ('COMPASS'): protocol. J NeuroInterv Surg 2018. https://doi.org/10.1136/neurintsurg-2017-013722. Published Online First.
31. Maus V, Behme D, Kabbasch C, et al. Maximizing first-pass complete reperfusion with SAVE. Clins Neuroradiol 2017. https://doi.org/10.1007/s00062-017-0566-z.

Original Article

INR INTERVENTIONAL NEURORADIOLOGY

Interventional Neuroradiology
0(00) 1–7

DOI: 10.1177/1591019918760747
journals.sagepub.com/home/ine

SAGE

Mechanical thrombectomy in MCA-mainstem occlusion in patients with low NIHSS scores

Marius Georg Kaschner, Julian Caspers, Christian Rubbert, Raul Lande, Bastian Kraus, John-Ih Lee, Michael Gliem, Sebastian Jander and Bernd Turowski

Abstract

Introduction: While effectiveness of mechanical thrombectomy (MTE) in M1 segment occlusion is approved for patients with severe impairment, there is a lack of evidence for a potential benefit of MTE in patients with minor to moderate symptoms. The purpose of this study was to evaluate neurological outcome and occurrence of periprocedural complications after MTE in patients with low National Institutes of Health Stroke Scale (NIHSS) scores.

Materials and methods: A retrospective analysis of 1081 consecutive patients with anterior circulation ischemic stroke due to M1 occlusion detected by computed tomography angiography and treated with MTE at our hospital between February 2012 and November 2017 was performed. NIHSS, Barthel Index (BI) and modified Rankin Scale (mRS) scores between admission and discharge were compared with paired Mann–Whitney test, and recanalization rate and complications were assessed in patients with NIHSS ≤ 5 at admission.

Results: Thirty patients were included with a median NIHSS score of 4. NIHSS score (median: 4 vs. 1; $p < 0.001$), BI (median: 43 vs. 80; $p < 0.001$) and mRS (2 vs. 1; $p < 0.001$) showed significant improvement from admission to discharge after MTE. Recanalization rate was Thrombolysis in Cerebral Infarction (TICI) 2b to 3 in 29 of 30 patients (96.7%). One case of an intracerebral reperfusion hematoma (ECASS: PH2) required surgical treatment.

Conclusion: MTE might lead to a significantly improved clinical outcome also for patients with low NIHSS score due to M1 segment occlusion. Periprocedural complications appeared infrequently. These results encourage further evaluation of the benefit-risk profile of MTE compared to standard treatment in patients with low NIHSS scores in future randomized trials.

Keywords

Low NIHSS, M1 segment occlusion, mechanical thrombectomy

Received 10 December 2017; accepted 28 January 2018

Introduction

Patient populations of previously published larger randomized trials, proving the efficacy of mechanical thrombectomy (MTE) in large-vessel occlusion (LVO) of the anterior circulation, predominantly included patients with severe stroke symptoms. Although the study protocol of the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) and the Extending the Time for Thrombolysis in Emergency Neurological Deficits-Intra-Arterial (EXTEND-IA) study also involved patients with minor neurologic deficit (National Institutes of Health Stroke Scale (NIHSS) 2–42 MR CLEAN, NIHSS 0–42 EXTEND-IA), the median NIHSS score for patients who underwent acute endovascular thrombectomy was approximately 15 to 17 in all major stroke trials.[1–5] There is a paucity of data from randomized clinical trials on the efficacy and safety of MTE in patients with lower NIHSS as a main study population. However, there is no clear definition of minor or moderate stroke. Also in case of low NIHSS scores in underlying LVO, patients can have a severe functional deficit like aphasia, hemianopia or monoplegia.[6] On the contrary many patients with low NIHSS scores have relatively mild clinical symptoms, and thus the question arises whether the risk of an endovascular procedure is justified in these patients.

There are some considerations as to why MTE in patients with low NIHSS scores might be useful.

Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany

Corresponding author:
Marius Georg Kaschner, Heinrich-Heine-University Duesseldorf, Moorenstr. 5, Duesseldorf, NRW 40225 Germany.
Email: marius.kaschner@med.uni-duesseldorf.de

Despite a low NIHSS score, an LVO of the middle cerebral artery (MCA) might be found, with a probability of recanalization by intravenous thrombolysis (IVT) of $< 1\%$ when thrombotic clot length exceeds 8 mm.[7] Nine percent to 10% of patients with initially minor stroke may be affected by early progression of symptoms and infarct growth in association with LVO.[8–10] In a retrospective analysis of 7621 patients with NIHSS score ≤ 5 treated with IVT, absence of recovered independent ambulatory ability was observed in only 30.3% at discharge.[11] However, procedural risk of MTE in low-NIHSS patients has to be critically balanced against the benefit, because the advantage of MTE compared to pharmacological treatment has not yet been proved. Based on the major MTE trials, the American Heart Association guidelines provided level 1a evidence for MTE for patients with NIHSS scores of 6 or more, so that our selected NIHSS range ≤ 5 includes a patient collective about whom less is known. Some current studies already reported good clinical outcome after MTE in patients with mild symptoms harboring LVO in the anterior circulation.[12,13] In this single-center study, we intend to evaluate whether these results can be confirmed in patients with M1 occlusion and low baseline NIHSS scores at our institution.

Material and methods

Patient selection

We retrospectively assessed all patients with an NIHSS score ≤ 5 who were treated by MTE between February 2012 and November 2017 at the University Hospital Duesseldorf. Data evaluation was approved by the local ethics committee. For each patient, neurological examination was performed at admission by the attending neurologist in the emergency department, including detailed assessment of NIHSS, modified Rankin Scale (mRS) and Barthel Index (BI) scores. Standardized stroke imaging at our institution included non-contrast-enhanced cranial computed tomography (NECCT), CT-perfusion (CTP) and CT angiography (CTA). In admitted patients who received stroke imaging in external hospitals prior to admission, CTP imaging was absent in some cases. In patients with unknown symptom onset, magnetic resonance (MR) stroke imaging including diffusion-weighted imaging (DWI), fluid-attenuation inversion recovery, and susceptibility-weighted imaging sequences were performed. Extensive early ischemic signs or hemorrhage could be excluded in pre-interventional imaging by CT- and DWI-Alberta Stroke Program Early CT score (ASPECTS) assessment.

Eligibility for MTE in patients with acute M1 occlusion established in CTA or time-of-flight-magnetic resonance angiography (TOF-MRA) was determined individually for each patient in consensus between neurologists and neurointerventionalists, depending on estimated procedural risk, probability of recanalization by IVT, contraindication for IVT, social and medical pre-stroke conditions, and comorbidities. IVT was applied as bridging therapy according to national and international guidelines in eligible patients when treatment was initiated within 4.5 hours after symptom onset.

Endovascular treatment

Stent retriever thrombectomy (4.5×40 mm or 3.5×28 mm Aperio; Acandis, Pforzheim, Germany) combined with local thromboaspiration via a 5-Fr or 6-Fr intracranial intermediate catheter (Sofia 5-Fr; MicroVention or 6-Fr Navien Intracranial Support Catheter; formerly the ReFlex Intracranial Catheter; Covidien Vascular Therapies, Mansfield, MA, USA) at the MCA mainstem was performed. During stent retrieval, aspiration was applied through the intermediate catheter via a 20 ml syringe. Arterial punctures were closed by vascular closure devices (Angio-Seal VIP; St. Jude Medical, Minnetonka, MN, USA). MTE was performed under permanent monitoring of vital parameters and analgesia (local anesthesia in the groin, 1 g of metamizole as short infusion), and without general anesthesia or sedation in all cases. In case of vital deterioration, stand-by support by intensive care physicians was obtainable. After intervention, patients were admitted to the stroke unit of our hospital and treated according to in-house standard operating procedures. Patients who received acute stenting of extracranial arteries in addition to endovascular thrombectomy were treated with the gpIIb/IIIa antagonist tirofiban (1.250 mg bolus during intervention followed by a continuous infusion of 0.1 μg/kg body weight/minute) from time of acute stenting until a switch to oral aspirin and clopidogrel was performed, usually within 12–24 hours, with 12-hour overlap. Follow-up imaging CCT was routinely performed 6–24 hours after treatment. Postinterventional NIHSS, mRS and BI were assessed by the treating neurologist at discharge.

Imaging and procedural data collection

Time from symptom onset to stroke imaging, to start of angiography, and to recanalization were captured. The location of the occlusion and thrombus length were assessed on CTA or TOF-MRA images. Collateral supply of the occluded MCA territory from pre-interventional CTA scans was scored on the basis of the collateral grading system of Tan et al. on a scale of 0–3.[14] A score of 0 corresponds to absent collateral supply, a score of 1 corresponds to collateral supply filling $<50\%$ but $>0\%$, and a score of 2 corresponds to collateral supply filling $>50\%$ but $<100\%$ of the occluded MCA territory. One hundred percent collateral supply of the occluded MCA territory was

scored as 3. Devices and medication used during the interventional procedures, procedural duration, and intra-procedural complications were evaluated from the treatment protocols. Angiographic outcome was graded by the modified Thrombolysis in Cerebral Infarction (TICI) scale.[15] Pre- and post-treatment cerebral infarction, according to the ASPECTS and post-treatment intracerebral hemorrhage, according to the European Cooperative Acute Stroke Study classification (ECASS[16]), were assessed by routine follow-up imaging as described above.

Statistical analysis

Statistical analysis was performed by using R, version 3.4.3. Stroke severity as measured by NIHSS, clinical outcome according to mRS, and BI at admission and discharge were compared by paired Mann–Whitney test. Correlation between ASPECTS and time to successful recanalization (TTSR), and ASPECTS and collateral score was assessed by Spearman correlation. Results were considered statistically significant at a level of $p < 0.05$.

Results

A total of 1081 patients with M1 occlusion were treated by MTE between February 2012 and November 2017. Of these, 30 patients presented with a pre-therapeutic NIHSS score of 1 to 5. Thrombus location in all included patients is summarized in Table 1. Twenty-four patients received intravenous (i.v.) bridging lysis. All patients were treated by stent retriever thrombectomy under local aspiration. In five patients carotid artery stent implantation because of arteriosclerotic carotid artery stenosis for intracranial access was necessary. CTA-based collateral status assessment was available in 21 patients (score 0, $n = 0$; 1, $n = 2$; 2, $n = 5$; 3, $n = 14$). In nine patients, preinterventional cranial imaging was performed by MR and thus were not eligible for collateral score assessment.

Overall median thrombus length, measured by CTA, was 14 mm (range: 5 to 22 mm), and 14 mm for patients receiving i.v. bridging lysis as well.

A favorable recanalization rate (TICI 2b–3), was achieved in 29 patients, with TICI 2b in nine, TICI 2c in four, and TICI 3 in 16 patients. Embolization to other vascular territories was not observed. In the one patient with unsuccessful recanalization (TICI2a) of a right-sided M1 occlusion, a good collateralization could be confirmed by digital subtraction angiography. Despite a pre- and postinterventional ASPECTS of 5, this patient's NIHSS improved from 5 to 0 and mRS from 3 to 1 at discharge. The patient with TICI2a was excluded from the following subgroup analysis because of poor statistical significance.

The median NIHSS score of the 30 included patients was 4 before MTE. At discharge, median NIHSS score

Table 1. Baseline characteristics, treatment details and clinical outcome of patients with low NIHSS scores due to M1-segment occlusion who received mechanical thrombectomy.

Participant sample $n = 30$		
Sociodemographic characteristics		
Age (years), mean ± SD	71.5 ± 11	
Female	$n = 17$	(56.7%)
Coronary artery disease	$n = 6$	(20%)
Myocardial infarction	$n = 2$	(6.7%)
Atrial fibrillation	$n = 11$	(36.7%)
Arterial hypertension	$n = 24$	(80%)
PAOD	$n = 0$	(0%)
Diabetes mellitus	$n = 3$	(10%)
Dyslipidemia	$n = 11$	(36.7%)
COPD	$n = 4$	(13.4%)
Coumarin treatment	$n = 2$	(6.7%)
Previous stroke	$n = 1$	(3.3%)
Baseline ASPECTS median (IQR)	10	(10–10)
Treatment details		
Admission NIHSS median (IQR)	4	(2–5)
Admission mRS median (IQR)	2	(2–3)
Admission BI median (IQR)	43	(25–75)
Occlusion location		
- M1 isolated	$n = 16$	(53.4%)
- M1 + M2	$n = 5$	(16.7%)
- Cervical ICA + M1	$n = 5$	(16.7%)
- Carotid T (including M1)	$n = 4$	(13.4%)
Thrombus length (mm) median (range)	14	(5–22)
IV rtPA	$n = 24$	(80%)
IA rtPA	$n = 15$	(50%)
Collateral status median (IQR)	3	(2–3)
Median time (minutes) median (mean ± SD)		
- from symptom onset to imaging	79	(146 ± 175)
- from symptom onset to groin puncture	203	(243 ± 164)
- to final recanalization M1	244	(300 ± 167)
Treatment and clinical outcome		
TICI 2b–3	$n = 29$	(96.7%)
TICI 2a	$n = 1$	(3.3%)
TICI 2b	$n = 9$	(30%)
TICI 2c/TICI 3	$n = 20$	(66.7%)
Discharge NIHSS median (IQR)	1	(0–2)
Discharge mRS (0–2)	$n = 28$	(93.4%)
Discharge mRS median (IQR)	1	(1–2)
Discharge BI median (IQR)	80	(60–100)
Symptomatic intracranial hemorrhage (ECASS:PH2)	$n = 1$	(3.3%)
Post-treatment ASPECTS median (IQR)	9	(7–10)

ASPECTS: Alberta Stroke Program Early CT score; BI: Barthel Index; COPD: chronic obstructive pulmonary disease; ECASS: European Cooperative Acute Stroke Study classification; IQR: interquartile range; IV: intravenous; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; PAOD: peripheral arterial occlusive disease; rtPA: recombinant tissue plasminogen activator; TICI: Thrombolysis in Cerebral Infarction.

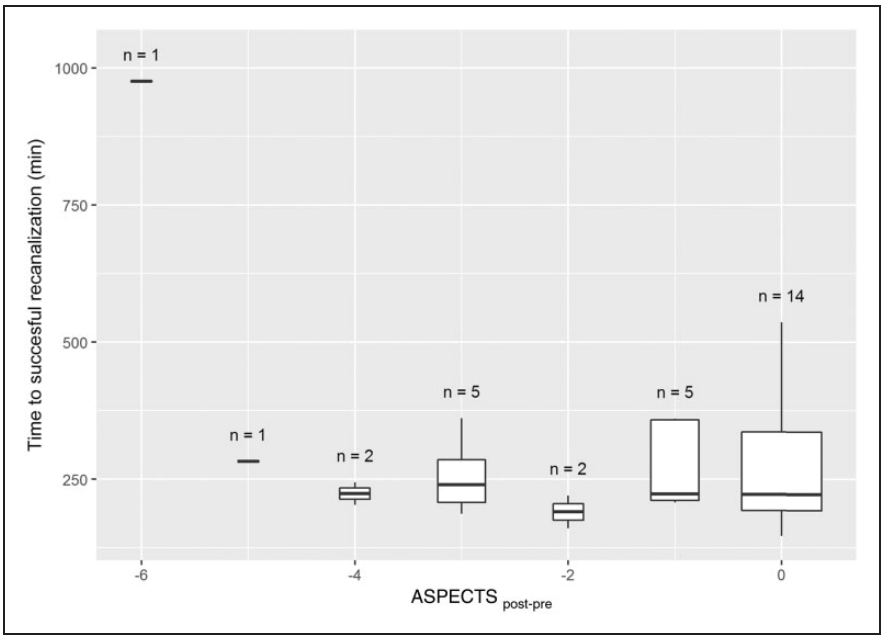


Figure 1. Alberta Stroke Program Early CT score (ASPECTS) in relation to time to successful recanalization, $ASPECTS_{post\text{-}pre}$ = differences between pre- and postinterventional ASPECTS.

changed from 4 to 1 ($p < 0.001$), median mRS decreased from 2 to 1 ($p < 0.001$), and median BI improved from 43 to 80 ($p < 0.001$). Patients were discharged or moved to another hospital after 2 to 25 days (median: 9). At that time clinical outcome according to the mRS scale in detail was 0: $n = 5$, 1: $n = 13$, 2: $n = 10$, 3: $n = 1$, 4: $n = 0$, 5: $n = 1$. In one patient (3.3%) a reperfusion hematoma (ECASS: PH2) of the basal ganglia occurred after M1 revascularization (TICI 3) and additional carotid stenting for severe carotid stenosis.

Small or confluent petechial infarction without space-occupying effect and without clinical deterioration was found in 5/30 patients (16.7%). No deaths occurred. Median ASPECTS of the 30 patients was 10 in the preinterventional NECCT imaging and 9 at the 24-hour follow-up imaging.

Subgroup analysis between TICI2b and TIC2c/3 patients regarding pre- and post-treatment ASPECTS differences was performed. Median pretreatment ASPECTS was 10 in both groups. Median post-treatment ASPECTS was 10 in TICI2b patients and 8 in TICI2c/3 patients without statistically significant differences in pre- to post-treatment ASPECTS shift between the groups ($p = 0.23$).

Changes between pre- and post-treatment ASPECTS did not correlate to TTSR ($\rho = -0.12$, $p = 0.51$; after removal of one outlier, $\rho = -0.02$, $p = 0.89$, Figure 1).

The relation between ASPECTS difference and collateralization was assessed in a correlation analysis. There was a significant correlation between the range of pre- compared to post-treatment ASPECT scores and collateralization score, i.e. a higher collateral score resulted in a lower decrease of posttreatment ASPECTS compared to baseline ASPECTS ($\rho = 0.53$, $p < 0.005$, Figure 2).

Discussion

MTE is the standard of care for ischemic stroke patients with LVO of the anterior circulation in addition to IVT or as first-line therapy for patients who are not eligible for IVT.[20–22] Thrombectomy results in significantly better clinical outcomes compared to IVT only in patients with acute occlusion of the intracranial M1 segment of the MCA.[1–5] While MTE is considered a highly effective procedure with a low risk of complications for LVO in the anterior circulation, there are only a few non-randomized study series for MTE in patients initially presenting with mild stroke symptoms (Table 2).[12,13,17,18,19]

Substantiating the encouraging results from these reports, we could confirm a favorable clinical outcome in patients with low NIHSS scores after MTE in the present study (mRS 0–2 93.4%) that are in accordance with these previous studies. Successful recanalization (modified TICI 2b–3) in 96.7%, no embolization to new territories, and symptomatic intracranial hemorrhage rate of 3.3%, in our study complied with the suggested threshold levels for recanalization and complication rates from the current guidelines.[23] To date there is little information about the effectiveness of endovascular treatment in patients with anterior LVO compared to IVT (Table 2) but there are some reasons why MTE in low-NIHSS score patients should be considered.[17–19] Previous studies showed that patients with mild stroke and LVO who did not receive acute recanalization therapy experienced a poor clinical outcome at 90 days.[24,25] This might be explained by the observation that thrombus length exceeding 8 mm has a limited potential of thrombolysis.[7,26] These findings are in accordance with our own results. In all 24 patients who

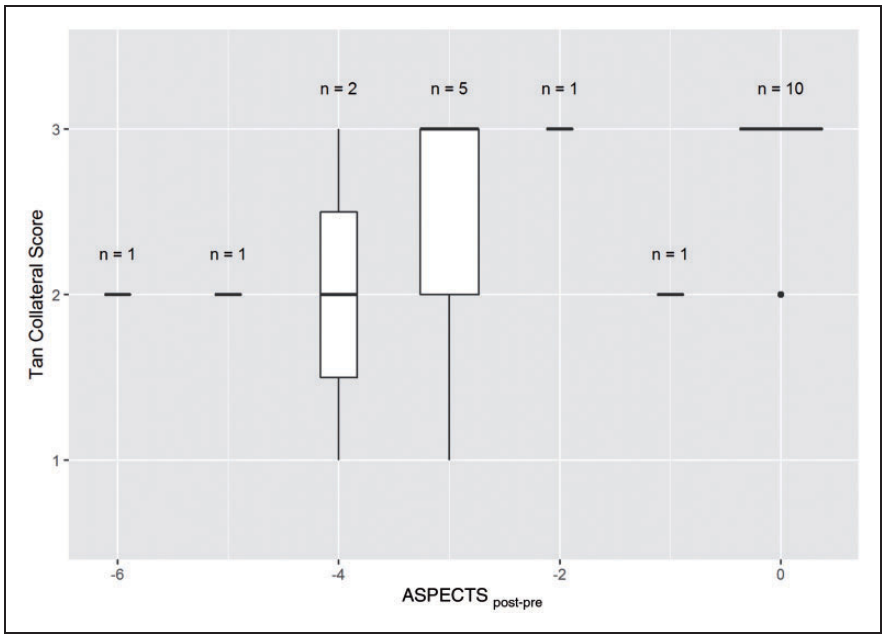


Figure 2. Alberta Stroke Program Early CT (ASPECT) score in relation to collateral score, $ASPECTS_{post\text{-}pre}$ = difference between pre- and postinterventional ASPECT score.

Table 2. Studies including patients with low NIHSS due to LVO of the anterior circulation.

Study	Description	NIHSS	TICI (2b-3)	Outcome	Complications
Bhogal et al. 2016[13]	MTE $n=41$	≤ 5	87.8%	90-day mRS (0-2): 75%	sICH: 4.9%
Pfaff et al. 2016[12]	MTE $n=33$	≤ 8	78.7%	90-day mRS (0-2): 63.6%	sICH: 6% Mortality: 9.1%
Urra et al. 2014[17]	MTE vs. IVT ($n=78$); MTE, $n=34$ vs. IVT, $n=44$	≤ 5	MTE, 91.2% vs. IVT, 63.4% ($p=0.006$)	90-day mRS (0-1): MTE, 58.8% vs. IVT, 68.2% ($p=0.393$)	sICH: MTE,11.8% vs. IVT, 0% ($p=0.003$) Death: MTE,11.8% vs. IVT, 4.5% ($p=0.395$)
Haussen et al. 2017[18]	MTE vs. IVT ($n=32$); MTE, $n=10$ vs. IVT, $n=22$	≤ 5	MTE, 100% IVT, NA	90-day mRS (0-2): MTE, 100% vs. IVT, 77% ($p=0.15$)	sICH: $n=0$ Mortality: MTE, 0% vs. IVT, 14% ($p=0.38$)
Messer et al. 2017[19]	MTE vs. IVT ($n=54$); MTE-I, $n=8$ vs. delayed MTE-END, $n=6$ vs. IVT, $n=40$	≤ 5	MTE-I, 75% vs. MTE-END, 100% (NA) IVT, NA	mRS (0-1): MTE-I, 75% vs. MTE-END, 33.3% vs. IVT, 55%	sICH: $n=0$ Mortality: $n=3$ (overall group)

LVO: large-vessel occlusion; MTE: mechanical thrombectomy; IVT: intravenous thrombolysis; MTE-I: MTE immediately; MTE-END: MTE early neurologic deterioration; sICH: symptomatic intracranial hemorrhage; mRS: modified Rankin Scale score; NIHSS: National Institutes of Health Stroke Scale; TICI: Thrombolysis in Cerebral Infarction; NS: not statistically significant; NA: not available.

received i.v. bridging lysis, a persistent thrombus (median thrombus length: 14 mm) was observed in subsequent catheter angiography. The above-mentioned studies and our own results demonstrate limited effectiveness of IVT in broad M1 segment thrombus. Also patients with mild clinical symptomatology are at risk for neurological deterioration because of a decrease in their collateralization status.[18] For instance, there were two patients in our sample with M1 segment thrombus and good collateralization proven by CTA showing nearly complete regression of neurological symptoms after IVT, but who presented with neurological deterioration after several hours due to persistent thrombus. Both patients had successful recanalization and favorable clinical outcome.

Campbell et al. demonstrated that deterioration in collateral status between baseline and subsequent imaging was strongly associated with infarction volume growth in patients without recanalization.[27] Correlation between good collateral status and favorable clinical outcome has been shown in several clinical trials.[28–30] But good collateralization alone without recanalization might not prevent an unfavorable outcome. The role of successful recanalization in acute

ischemic stroke patients with LVO was demonstrated in a study by Miteff et al. Among patients with good collaterals, favorable outcome was achieved in those who received MTE, whereas in patients without recanalization, only 38% had a favorable outcome.[28] Our findings that better collateralization scores were associated with less ASPECTS worsening between pre- and post-treatment ASPECTS supports the presumption that good collateralization is related to favorable treatment outcome. In the current study the extent of infarction assessed by differences between pre- and post-treatment ASPECTS was independent from TTSR. Although time is still obviously very important and the earlier recanalization is achieved the better the results, we have shown in our case series that time should not be the only factor that determines endovascular therapy decisions. Moreover, these findings let us assume that the so-called ''time window'' is not stationary. Instead it might be a dynamic period of time that is determined by several factors including the complex interplay between LVO, blood pressure, collateral status, and individual cerebral ischemic tolerance.

In our sample, MTE was often initiated after a prolonged period after symptom onset for different reasons. First, many patients were referred from external hospitals to our institution, which could delay initiating of endovascular treatment. Some patients showed fluctuating symptoms and were readmitted to the hospital after a prolonged time. Because of clinical deterioration after fluctuating symptoms, MTE and carotid stent implantation were initiated after a prolonged time period in one patient with a very poor outcome (mRS 5) because of a symptomatically reperfusion hematoma. Although procedural-related complications in MTE like reperfusion hematoma, angiographically apparent vessel perforation, symptomatic subarachnoid hemorrhage with an appearance of 0.5%–4.9%, and embolization to new territories with a reported incidence of 4.9%–8.6% are serious complications, this might be an acceptable complication rate compared to the expected stroke severity as a consequence of a persistent LVO.[1–5] On the contrary, although we assume impairment with a high probability in patients with moderate symptoms due to LVO, it is not evidenced that the natural course of disease or standard treatment would not result in a comparable outcome like endovascular treatment. Therefore, in patients with a low NIHSS score, a markedly lower procedural complication rate than recommended in guidelines should be targeted.

Sufficient stroke imaging might improve patient selection. CTA or MRA are required for proof of LVO and thrombus extent. If there is a flowed-around short-range thrombus, IVT has a high feasibility of recanalization.[7] Evaluation of anatomic complexity of supra-aortic access is necessary to estimate risk of procedural complications. The collateral status may give indications to brain condition and outcome. Optimally, stroke imaging should include CT perfusion imaging to estimate penumbra and severity of perfusion restriction. An obvious limitation of this study is the lack of a control group with low-NIHSS score patients treated by standard of care with or without IVT.

This was a non-randomized, retrospective study with a small case series that naturally limits the statistical significance of results. Clinical follow-up was ascertained at a nine-day median, and there is a lack of long-term outcome. On the other hand, the good short-term results indicate the effectiveness of MTE in this trial. The patient number was too low for subgroup analysis to define valid lower NIHSS score thresholds for treatment decisions.

However, the limited current state of research for MTE in patients with mild to moderate stroke symptoms in LVO makes it challenging to determine if MTE as rescue therapy after neurological deterioration or IVT is the most beneficial therapy for this subgroup. The results from previous studies and the current study indicate a benefit of early MTE with regard to good clinical outcome without increased procedural risk. The need for randomized trials still remains, to select patients with mild stroke symptoms who mostly benefit from immediate MTE.

Conclusion

In patients presenting with low NIHSS score due to M1 occlusion, MTE could be performed safely, technically very successfully, and with a favorable outcome. Deterioration in M1 segment occlusion after i.v. lysis can be observed, despite low NIHSS score. Therefore, although data from randomized controlled trials are still lacking, early endovascular recanalization has to be taken into consideration in these patients.

Acknowledgments

All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Patients were informed about the approach, benefit and risks of the planned procedure in the emergency setting and informed consent was obtained prior to intervention. Consent for retrospective data analysis was waived.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

References

1. Berkhemer OA, Fransen PS, Beumer D, et al. MR CLEAN Investigators. A randomized trial of intraarterial

treatment for acute ischemic stroke. *N Engl J Med* 2015; 372: 11–20.
2. Goyal M, Demchuk AM, Menon BK, et al. ESCAPE Trial Investigators. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med* 2015; 372: 1019–1030.
3. Campbell BC, Mitchell PJ, Kleinig TJ, et al. EXTEND-IA Investigators. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med* 2015; 372: 1009–1018.
4. Saver JL, Goyal M, Bonafe A, et al. SWIFT PRIME Investigators. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med* 2015; 372: 2285–2295.
5. Jovin TG, Chamorro A, Cobo E, et al. REVASCAT Trial Investigators. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med* 2015; 372: 2296–2306.
6. Köhrmann M, Nowe T, Huttner HB, et al. Safety and outcome after thrombolysis in stroke patients with mild symptoms. *Cerebrovasc Dis* 2009; 27: 160–166.
7. Riedel CH, Zimmermann P, Jensen-Kondering U, et al. The importance of size: Successful recanalization by intravenous thrombolysis in acute anterior stroke depends on thrombus length. *Stroke* 2011; 42: 1775–1777.
8. Rajajee V, Kidwell C, Starkman S, et al. Early MRI and outcome of untreated patients with mild or improving ischemic stroke. *Neurology* 2006; 67: 980–984.
9. Coutts SB, Hill MD, Eliasziw M, et al. VISION Study Group. Final 2 year results of the vascular imaging of acute stroke for identifying predictors of clinical outcome and recurrent ischemic events (VISION) study. *BMC Cardiovasc Disord* 2011; 11: 18.
10. Asdaghi N, Hill MD, Coulter JI, et al. Perfusion MR predicts outcome in high-risk transient ischemic attack/minor stroke: A derivation-validation study. *Stroke* 2013; 44: 2486–2492.
11. Romano JG, Smith EE, Liang L, et al. Outcome in mild acute ischemic stroke treated with intravenous thrombolysis: A retrospective analysis of Get With the Guidelines-Stroke registry. *JAMA Neurol* 2015; 72: 423–431.
12. Pfaff J, Herweh C, Pham M, et al. Mechanical thrombectomy in patients with acute ischemic stroke and lower NIHSS score: Recanalization rates, periprocedural complications, and clinical outcome. *AJNR Am J Neuroradiol* 2016; 37: 2066–2071.
13. Bhogal P, Bücke P, Ganslandt O, et al. Mechanical thrombectomy in patients with M1 occlusion and NIHSS score $\leq$5: A single-centre experience. *Stroke Vasc Neurol* 2016; 1: 165–171.
14. Tan IYL, Demchuk AM, Hopyan J, et al. CT angiography clot burden score and collateral score: Correlation with clinical and radiologic outcomes in acute middle cerebral artery infarct. *AJNR Am J Neuroradiol* 2009; 30: 525–531.
15. Goyal M, Fargen KM, Turk AS, et al. 2C or not 2C: Defining an improved revascularization grading scale and the need for standardization of angiography outcomes in stroke trials. *J Neurointerv Surg* 2014; 6: 83–86.
16. Fiorelli M, Bastianello S, von Kummer R, et al. Hemorrhagic transformation within 36 hours of a cerebral infarct: Relationships with early clinical deterioration and 3-month outcome in the European Cooperative Acute Stroke Study I (ECASS I) cohort. *Stroke* 1999; 30: 2280–2284.
17. Urra X, San Román L, Gil F, et al. Medical and endovascular treatment of patients with large vessel occlusion presenting with mild symptoms: An observational multicenter study. *Cerebrovasc Dis* 2014; 38: 418–424.
18. Haussen DC, Bouslama M, Grossberg JA, et al. Too good to intervene? Thrombectomy for large vessel occlusion strokes with minimal symptoms: An intention-to-treat analysis. *J Neurointerv Surg* 2017; 9: 917–921.
19. Messer MP, Schonenberger S, Möhlenbruch MA, et al. Minor stroke syndromes in large-vessel occlusions: Mechanical thrombectomy or thrombolysis only? *AJNR Am J Neuroradiol* 2017; 38: 1177–1178.
20. Jayaraman MV, Hussain MS, Abruzzo T, et al. Embolectomy for stroke with emergent large vessel occlusion (ELVO): Report of the Standards and Guidelines Committee of the Society of NeuroInterventional Surgery. *J Neurointerv Surg* 2015; 7: 316–321.
21. Powers WJ, Derdeyn CP, Biller J, et al. American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2015; 46: 3020–3035.
22. Wahlgren N, Moreira T, Michel P, et al. Mechanical thrombectomy in acute ischemic stroke: Consensus statement by ESO-Karolinska Stroke Update 2014/2015, supported by ESO, ESMINT, ESNR and EAN. *Int J Stroke* 2016; 11: 134–147.
23. Lavine SD, Cockroft K, Hoh B, et al. Training guidelines for endovascular ischemic stroke intervention: An international multi-society consensus document. *AJNR Am J Neuroradiol* 2016; 37: E31–E33.
24. Smith EE, Fonarow GC, Reeves MJ, et al. Outcomes in mild or rapidly improving stroke not treated with intravenous recombinant tissue-type plasminogen activator: Findings from Get With The Guidelines-Stroke. *Stroke* 2011; 42: 3110–3115.
25. Mokin M, Masud MW, Dumont TM, et al. Outcomes in patients with acute ischemic stroke from proximal intracranial vessel occlusion and NIHSS score below 8. *J Neurointerv Surg* 2014; 6: 413–417.
26. Behrens L, Möhlenbruch M, Stampfl S, et al. Effect of thrombus size on recanalization by bridging intravenous thrombolysis. *Eur J Neurol* 2014; 21: 1406–1410.
27. Campbell BC, Christensen S, Tress BM, et al. Failure of collateral blood flow is associated with infarct growth in ischemic stroke. *J Cereb Blood Flow Metab* 2013; 33: 1168–1172.
28. Miteff F, Levi CR, Bateman GA, et al. The independent predictive utility of computed tomography angiographic collateral status in acute ischaemic stroke. *Brain* 2009; 132: 2231–2238.
29. Maas MB, Lev MH, Ay H, et al. Collateral vessels on CT angiography predict outcome in acute ischemic stroke. *Stroke* 2009; 40: 3001–3005.
30. Berkhemer OA, Jansen IG, Beumer D, et al. MR CLEAN Investigators. Collateral status on baseline computed tomographic angiography and intra-arterial treatment effect in patients with proximal anterior circulation stroke. *Stroke* 2016; 47: 768–776.

Neurological Sciences
https://doi.org/10.1007/s10072-020-04430-5

ORIGINAL ARTICLE

Mechanical thrombectomy in acute middle cerebral artery M2 segment occlusion with regard to vessel involvement

Vivien Lorena Ivan[1] · Christian Rubbert[1] · Julian Caspers[1] · John-Ih Lee[2] · Michael Gliem[2] · Sebastian Jander[2] · Bernd Turowski[1] · Marius Kaschner[1]

Received: 6 November 2019 / Accepted: 13 April 2020

Abstract

Background Endovascular treatment (EVT) is an established procedure in patients with acute ischemic stroke due to occlusion of the proximal M1-segment of middle cerebral artery. The assessment of distal thrombectomy in daily clinical routine has not yet been sufficiently evaluated.

Methods Patients with M2-segment-occlusions treated by EVT in the local department (January 2012–December 2017) were included ($n = 57$, mean National-Institutes-of-Health-Stroke-Scale of 11, range 0–20). Patients were grouped according to localization of M2-occlusion (Cohort A ($n = 14$): central region only, B ($n = 24$): central region and involvement of frontal vessels, C ($n = 19$): parietal, occipital, and/or temporal vessels). Differences in proximal (M2-trunk, $n = 34$) and distal (M2-branches, $n = 23$) occlusions were also examined. Reperfusion (Thrombolysis-In-Cerebral-Infarction (TICI)), early clinical outcome at discharge (modified Rankin Scale (mRS)), and complications (hemorrhage, new emboli) were noted.

Result Successful reperfusion (TICI2b–3) was found in 49 patients (86.0%). Favorable early clinical outcome (mRS0–2) was achieved in $n = 19$ (37.7%). Compared to admission, mRS at discharge improved significantly (median (admission) 5 vs. median (discharge) 4, $p < 0.001$). Early clinical outcome was more favorable in patients with better reperfusion (TICI2b-3: mean mRS 3 ± 1.7 vs. TICI0–2a: mean mRS 4.4 ± 1.4, $p = 0.037$). Six (10.5%) patients suffered from symptomatic intracranial hemorrhage during treatment or hospitalization. Four patients died (7.0%). No significant differences in favorable clinical outcome (mRS ≤ 2: Cohort A 42.9%, B 50.0%, C 16.7%, $p = 0.4$; χ^2-test) or periinterventional complications were found with regard to vessel involvement.

Conclusion EVT in patients with acute M2-occlusion is safe and leads to a significant clinical improvement at discharge. No significant differences in clinical outcome or complications were found with regard to the localization of the M2-occlusion.

Keywords Thrombectomy · Endovascular treatment · M2-segment occlusions

Introduction

The five major studies for the treatment of acute ischemic stroke in the anterior circulation from 2015 (MR CLEAN, EXTEND IA, ESCAPE, REVASCAT, SWIFT PRIME) demonstrated a significant benefit of treatment with endovascular therapy (EVT) and intravenous thrombolysis (IVT) versus IVT alone. Owing to these results, the endovascular recanalization became an established procedure and part of international guidelines for treatment of middle cerebral artery (MCA) occlusions of the proximal M1 segment [1–5].

Whether more distal occlusions of the M2-segments should be treated with EVT as well remains uncertain. Endovascular access can be more challenging and risky because of decreasing vessel diameter, more tortuous anatomy, and, in elderly patients, increasing vessel fragility in the distal parts of the anterior circulation. Initial studies from 2014 failed to show a positive effect of successful early reperfusion on clinical outcome in M2-occlusions [6], but more recent studies showed an increasing trend towards safety and efficacy of EVT in distal vessel occlusions [7–11]. For example, Sheth et al. evaluated patients with M2-occlusions and found that

✉ Vivien Lorena Ivan
vivien.ivan@med.uni-duesseldorf.de

[1] Department of Diagnostic and Interventional Radiology, University Dusseldorf, Medical Faculty, D-40225 Dusseldorf, Germany

[2] Department of Neurology, Heinrich-Heine-University, Medical faculty, Düsseldorf, Germany

Published online: 30 April 2020

successful reperfusion was associated with improved functional outcome at discharge [9]. Another recent study from 2017 found similar recanalization rates in M1- vs. M2-occlusions, but found more favorable outcome in patients with M2-occlusions [11]. However, a 2017 systematic review of eight studies concluded that the benefit of EVT in comparison to the natural course of M2-occlusions still remains unclear [12].

Nonetheless, comparable to M1-occlusions, especially proximal M2-occlusions may lead to clinically massive strokes with moderate to severe neurological symptoms or even death [9]. The hypothesis of the current work is that with ongoing development of thrombectomy techniques, distal access catheters and microcatheters, as well as stent retrievers, EVT in M2-occlusions should be overall favorable, especially in patients with occlusion of the larger M2-vessels supplying the central region territories. Our aim is to critically evaluate the efficacy and safety of mechanical recanalization in daily clinical routine as treatment for M2-occlusions, especially with regard to the M2-vessles occluded, i.e., the M2-territories affected.

Materials and methods

We retrospectively selected patients from the local department's stroke registry, which monitors quality of all EVT performed in our center under routine practice conditions. All patients with an acute ischemic stroke due to an initial occlusion of the MCA M2-segment, as demonstrated by noninvasive imaging, that underwent EVT between January 2012 and December 2017 were included ($n = 57$). The study was approved by the local ethics committee, and need for written informed consent was waived.

M2-segment occlusions were defined as occlusions of M2-branches arising from the distal M1-division (frontobasal, frontoopercular, precentral, central or rolandic, postcentral, angular, parietal posterior, temporooccipital branches). Additional carotid T-closures or hemodynamically relevant, arteriosclerotic carotid stenoses were exclusion criteria. The patients were divided into three cohorts depending on the localization of the M2-occlusion. Cohort A encompasses all patients with occlusion of vessels in the central region only (Aa. precentralis, centralis, postcentralis). Cohort B includes patients with occlusion of vessels in the central region and involvement of frontal vessels (Aa. frontobasalis, frontoopercularis). Cohort C finally encompasses patients with occlusion of vessels in the central region and involvement of parietal and/or temporal vessels (Aa. parietalis posterior, temporooccipitalis, gyri angularis). Furthermore, we grouped the patients depending on whether the M2-occlusion is located in the M2-trunk (including MCA-division into M2-trunks) or in distal M2-branches.

At the local department, all patients with a clearly known onset of neurological stroke symptoms undergo CT including non-enhanced imaging of the brain, CT-angiography starting from the aortic arch, as well as CT perfusion imaging. If the onset is unclear, magnetic resonance imaging (MRI) with perfusion weighted imaging is performed, which is in accordance with the national stroke guidelines [13]. Baseline clinical characteristics of all patients were noted and included the following: age, sex, associated conditions (atrial fibrillation, diabetes mellitus, hypertension, dyslipidemia, chronic pulmonary diseases, and peripheral arterial occlusive disease), suspected cause of stroke (cardiac, periinterventional, meaning stroke in the context of an elective groin intervention, or embolism of unknown origin), side of occlusion, and the status of intravenous lysis therapy. In addition, National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) at admission and Alberta stroke program early CT score (ASPECTS) [14] in the initial non-enhanced cranial CT or the DWI-MRI were documented.

In each case, the final indication for EVT of M2-occlusions was made in consensus by the attending stroke neurologist and interventional neuroradiologist on call based on the findings of the previously mentioned major randomized EVT studies. Indication is essentially based on the patient's neurological status, clinical history, and an experience-based assessment, whether the closed vessel is accessible without risk of significant harm. Except for one case of sole direct aspiration, a combination of distal access catheters and stent retriever thrombectomy in conjunction with distal aspiration was routinely performed. Eleven different interventionalists performed EVT within the selected period of time and had considerable experience in endovascular procedures like the thrombectomy with a median experience of 3.2 years.

If intravenous thrombolysis was performed, it was discontinued at the time of groin puncture based on our in-house standards to minimize the risk of interventional hemorrhage. The procedures were performed under analgesia (1–2 g Novaminsulfon as short infusion). In cases of extreme agitation or patients with Glasgow coma scale score ≤ 8, general anesthesia was performed. After local anesthesia of the groin, access was established using 80 cm 8F-sheath or additional guiding catheter positioned in the distal internal carotid artery. Generally, stent retriever thrombectomy (Aperio 4.5 × 40 mm, 4.5 × 30 mm, or 3.5 × 28 mm, Acandis, Pforzheim, Germany) combined with distal aspiration via 5F or 6F intracranial distal access catheter (SOFIA, MicroVention, Düsseldorf, Germany) at the affected M2-segment was performed. After passing the clot with a 0.014 microwire, a microcatheter was advanced beyond the distal end of the clot, and the position was verified by an angiographic control run. The proximal part of the stent retriever was lined up with the clot to (a) achieve an overlap of the stent retriever and the clot and (b) to catch potentially torn off fragments. The stent retriever was

deployed by first withdrawing the microcatheter and then by gently pushing the stent retriever to improve expansion into the clot ("active push deployment") [15]. Subsequently, the stent retriever was withdrawn into the intracranial distal access catheter under manual local aspiration via a 20-ml syringe (termed Solumbra-technique) [16]. Biplane follow-up angiograms were performed to document revascularization results. In case of persistent thrombus, the procedure was repeated, with modifications of the techniques at the interventionalist's digression. Arterial puncture sites were closed by vascular closure devices (Angio-Seal, Terumo, Tokyo, Japan). After the intervention, patients were transferred to the stroke unit of our hospital and treated according to in-house standard operating procedures in accordance with the national guidelines.

The duration of procedure, time from onset to groin puncture and time from stroke onset to recanalization, were documented. Follow-up imaging was then performed within 24 h after EVT or due to a worsening of neurological symptoms. As outcome measurements, mRS and NIHSS at discharge as well as mortality were documented. The clinical parameters at discharge from hospital (such as mRS, NIHSS) were determined by qualified neurologist as part of an in-house standardized neurological examination. We are aware that there are studies that critically question the neurologist's qualification in stroke cases depending on the level of education and emergency care infrastructure. However, the neurologists in our department are trained in particular in the recognition and assessment of a stroke from the start of their careers [17]. A mRS of 0–2 at discharge was considered a favorable outcome. Quality of recanalization was measured using the Thrombolysis in Cerebral Infarction (TICI) score. A good recanalization was defined as TICI 2b-3 on the final angiographic run. We determined the incidence of hemorrhagic transformation on the control CT scan within the first 24 h after EVT and categorized it as hemorrhagic infarction (HI) or parenchymal hematoma (PH) according to the ECASS classification [18, 19]. Furthermore, the presence of subarachnoid or intraventricular hemorrhage and emboli to new arterial territory was documented. Symptomatic intracranial hemorrhage (sICH) was defined as any of these intracranial hemorrhages associated with clinical deterioration within the first 24 h of EVT, i.e., any clinical worsening of at least one point in the NIHSS has been considered. Additionally, we determined the ASPECT score in the postinterventional non-enhanced cranial CT.

Statistical analysis was performed using R Core Team (2018) [20]. Paired Student's t test was used to evaluate all metric variables. The Kruskal-Wallis test was used to evaluate all scores (NIHSS, mRS, ASPECTS) and one way ANOVA for times and differences in age. χ^2-test was used to test for differences in frequencies.

Categorical variables are presented as absolute values and percentages, and continuous variables as median ± standard deviation (SD) or median. All tests were conducted two sided, and $p < 0.05$ was considered statistically significant for all tests.

Results

A total of 23 (40.4%) male and 34 (59.6%) female patients with M2-occlusions ($n = 57$) were included in this study. The mean age was 73 ± 13.3 years. 75.4% ($n = 43$) underwent IVT. The baseline characteristics are shown in Table 1.

There were 14 patients in cohort A with a mean age of 76 ± 13.8 years. Twenty-four patients had an occlusion of M2-branches supplying the central and frontal region (cohort B, mean age 74 ± 11 years). Nineteen patients had an occlusion of vessels supplying the central and parietal/temporal region (cohort C) with a mean age of 71 ± 16 years. No statistical difference in age was found among the three cohorts ($p = 0.44$). Most patients had an occlusion on the left side with no significant difference among the subgroups (78.6% vs. 75% vs. 63.2%, $p = 0.57$). Furthermore, distribution of the administration of IVT showed no significant difference (57.1% vs. 83.3% vs. 78.9%, $p = 0.18$). Associated medical conditions were equally distributed in all three cohorts with hypertension being the most prevalent associated condition (92.9% vs. 87.5% vs. 77.8%, $p = 0.46$) and dyslipidemia also seen in half or more of the patients in all groups (57.1% vs. 79.2% vs. 50%, $p = 0.16$). The preinterventional ASPECTS, showing early ischemic damage, revealed a mean of 9.5 ± 1.1 with no statistical difference among the cohorts (median 10 vs. 10 vs. 10, $p = 0.68$). The included patients showed a similar level of physical impairment after stroke regardless of exact localization of the M2-occlusion with similar baseline NIHSS (median 12 vs. 10 vs. 11, $p = 0.68$) and a similar mRS-score at admission (median 4 vs. 5 vs. 5, $p = 0.5$).

Mean time from stroke onset to groin puncture and to recanalization are listed in Table 1. Mean time from stroke onset to groin puncture was 227 ± 70 min and was not statistically different between the cohorts (180 ± 50 vs. 268 ± 84 vs. 188 ± 55, $p = 0.68$). Mean time from stroke onset to recanalization was 259 ± 85 min with no statistical differences among the cohorts (218 ± 58 vs. 261 ± 99 vs. 274 ± 72, $p = 0.33$). The average duration of the procedure (from groin puncture to final angiographic run) did not differ significantly between the cohorts (51 ± 33, 58 ± 35, 81 ± 46, $p = 0.07$). The overall mean procedure time was 68 ± 42 min.

Technical success

Table 2 provides an overview of the patient's postoperative data. Successful partial or complete reperfusion (TICI 2b-3) was achieved in 49 patients (86%), whereas four patients (7%)

Table 1 Baseline characteristics of patients

Characteristics	All patients ($n = 57$)	Cohort A ($n = 14$)	Cohort B ($n = 24$)	Cohort C ($n = 19$)
Mean age ± SD, years	73 ± 13.3	76 ± 13.8	74 ± 11	71 ± 16
Male	23 (40.4)	4	11	8
Associated Conditions*				
Atrial fibrillation	27 (48.2)	9 (64.3)	9 (37.5)	11 (61.1)
Diabetes mellitus	13 (23.2)	4 (28.6)	5 (20.8)	4 (22.2)
Hypertension	46 (82.1)	13 (92.9)	21 (87.5)	14 (77.8)
Dyslipidemia	34 (60.7)	8 (57.1)	19 (79.2)	9 (50.0)
Chronic pulmonary disease	6 (10.7)	1 (7.1)	3 (12.5)	2 (11.1)
PAOD	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Suspected cause				
Cardiac embolism	31 (54.4)	10 (71.4)	8 (33.3)	13 (72.2)
Periinterventional**	1 (1.8)	0 (0.0)	1 (4.2)	0 (0.0)
Unknown	25 (43.9)	4 (28.6)	15 (62.5)	6 (27.8)
IVT	43 (75.4)	8 (57.1)	20 (83.3)	15 (78.9)
Side of occlusion: right	16 (28.1)	3 (21.4)	6 (25.0)	7 (36.8)
NIHSS score at admission				
0	1 (1.9)	0 (0.0)	1 (4.3)	0 (0.0)
1–4	2 (3.7)	1 (7.7)	1 (4.3)	0 (0.0)
5–15	36 (66.7)	8 (61.5)	16 (69.6)	12 (66.7)
16–20	15 (27.8)	4 (30.8)	4 (17.4)	6 (33.3)
21–42	0 (0.0)	0 (0.0)	1 (4.3)	0 (0.0)
Mean ± SD	11.5 ± 5	11.5 ± 5.3	10.9 ± 5.5	12.3 ± 4.5
Median	11	12	10	11
mRS at admission				
3–6	48 (88.9)	13 (100)	18 (81.8)	17 (94.4)
≤ 2	6 (11.1)	1 (7.7)	4 (18.2)	1 (5.6)
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	2 (3.7)	0 (0.0)	2 (9.1)	0 (0.0)
2	4 (7.4)	1 (7.7)	2 (9.1)	1 (5.6)
3	5 (9.3)	2 (15.4)	2 (9.1)	1 (5.6)
4	15 (27.8)	5 (38.5)	5 (22.7)	5 (27.8)
5	28 (51.9)	6 (46.2)	11 (50.0)	11 (61.1)
Mean ± SD	4.2 ± 1.1	4.1 ± 0.9	4 ± 1.4	4.4 ± 0.9
Median	5	4	5	5
Mean preinterventional ASPECT score ± SD	9.5 ± 1.1	9.5 ± 0.9	9.5 ± 1.3	9.7 ± 1
Median preinterventional ASPECT score	10	10	10	10
Mean duration of procedure ± SD, min	68 ± 42	51 ± 33	58 ± 35	81 ± 46
Mean time from stroke onset to groin puncture ± SD, min	227 ± 70	180 ± 50	268 ± 84	188 ± 55
Mean time from stroke onset to recanalization ± SD, min	259 ± 85	218 ± 58	261 ± 99	274 ± 72

Figures are numbers with percentages in parentheses unless otherwise indicated

SD, standard deviation; *NIHSS*, National Institutes of Health Stroke Scale; *ASPECT score*, Alberta Stroke Program Early Computed Tomographic score; *PAOD*, peripheral arterial occlusive disease; *IVT*, intravenous lysis therapy; *mRS*, modified Rankin Scale

*Comorbidities were not available for one patient in Cohort C

**Periinterventional stroke in the context of an elective groin intervention

Cohort A: Occlusion of the vessels in the central region (Aa. precentralis, centralis, postcentralis)

Cohort B: Occlusion of the vessels in the central region and involvement of the frontal vessels (Aa. frontobasalis, frontoopercularis)

Cohort C: Occlusion of the vessels in the central region and involvement of the parietal and/or temporal vessels (Aa. parietalis posterior, temporooccipitalis, gyri angularis)

Table 2 The post-operative outcome

Characteristics	All patients ($n = 57$)	Cohort A ($n = 14$)	Cohort B ($n = 24$)	Cohort C ($n = 19$)
Mean postinterventional ASPECTS score ± SD	6.8 ± 2.5	7.1 ± 2.8	6.8 ± 2.3	6.4 ± 2.7
Median postinterventional ASPECTS score	7	7	7	7
Post-operative hemorrhage*				
None	35 (62.5)	10 (71.4)	17 (70.8)	10 (55.6)
SAH	8 (14.3)	1 (7.1)	3 (12.5)	4 (22.2)
HI-1	1 (1.8)	1 (7.1)	0 (0.0)	0 (0.0)
HI-2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
PH-1	6 (10.7)	0 (0.0)	2 (8.3)	4 (22.2)
PH-2	5 (8.9)	3 (21.4)	1 (4.2)	1 (5.6)
Intraventricular hemorrhaging	1 (1.8)	0 (0.0)	1 (4.2)	0 (0.0)
SICH within 24 h	6 (10.5)	2 (14.3)	3 (12.5)	1 (5.3)
Emboli to new territories	3 (5.4)	0 (0.0)	2 (8.3)	1 (5.6)
TICI				
0	4 (7.0)	1 (7.1)	3 (12.5)	0 (0.0)
1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2a	4 (7.0)	2 (14.4)	2 (8.3)	0 (0.0)
2b	18 (31.6)	5 (35.7)	6 (25.0)	7 (36.8)
2c	12 (1.8)	3 (21.4)	4 (16.7)	5 (26.3)
3	19 (33.3)	3 (21.4)	9 (37.5)	7 (36.8)
2b-3	49 (86.0)	11 (78.6)	19 (79.2)	19 (100)
NIHSS score at discharge				
0	3 (5.9)	1 (7.7)	2 (10.0)	0 (0.0)
1–4	20 (39.2)	6 (46.2)	8 (40.0)	6 (33.3)
5–15	22 (43.1)	3 (23.1)	8 (20.0)	11 (61.1)
16–20	6 (11.8)	3 (23.1)	2 (10.0)	1 (5.6)
21–42	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mean ± SD	6.8 ± 5.7	7 ± 7.1	6.1 ± 5.8	7.6 ± 4.6
Median	5	2	5	7
mRS at discharge				
3–6	32 (62.7)	8 (57.1)	10 (50.0)	15 (83.3)
≤ 2	19 (37.3)	6 (42.9)	10 (50.0)	3 (16.7)
0	4 (7.8)	1 (7.1)	2 (10.0)	1 (5.6)
1	8 (15.7)	3 (21.4)	5 (25.0)	0 (0.0)
2	7 (13.7)	2 (14.3)	3 (15.0)	2 (11.1)
3	5 (9.8)	0 (0.0)	2 (10.0)	3 (16.7)
4	18 (35.3)	5 (35.7)	5 (25.0)	8 (44.4)
5	9 (17.6)	2 (14.3)	3 (15.0)	4 (22.2)
Mean ± SD	3.2 ± 1.7	3 ± 1.9	2.9 ± 1.9	3.6 ± 1.3
Median	4	4	3	4
Mortality	4 (7.0)	2 (14.3)	2 (8.3)	0 (0.0)

Figures are numbers with percentages in parentheses unless otherwise indicated

SD, standard deviation; *NIHSS*, National Institutes of Health Stroke Scale; *ASPECT score*, Alberta Stroke Program Early Computed Tomographic score; *SAH*, subarachnoid hemorrhage; *HI*, haemorrhagic infarction; *PH*, parenchymal hematoma; *SICH*, symptomatic intracranial hemorrhage; *TICI*, Thrombolysis in Ischemic Stroke score; *mRS*, modified Rankin Scale

*Complications were not available for one patient in Cohort C

had persistent occlusion after multiple attempts of EVT. Partial or complete recanalization (TICI 2b-3) was more frequently achieved in patients with occlusion of M2-vessles supplying the central and parietal/temporal areas ($n = 19$,

cohort C 100%) compared to other cohorts (cohort A 78.6%, cohort B 79.2%) without statistical difference ($p = 0.8$).

Clinical outcome and complications

Median mRS at admission was 5 and improved to 4 at discharge ($p < 0.001$). The NIHSS score decreased significantly from a median preinterventional score of 11 to 5 during the time of hospitalization (postinterventional NIHSS taken on average 4.7 days after EVT, $p < 0.001$). Favorable clinical outcome (mRS ≤ 2) at discharge was not significantly different between the three cohorts (42.9% vs. 50.0% vs. 16.7%, $p = 0.09$). The NIHSS score at discharge was lower in the cohort with central M2-occlusions alone (cohort A, median 2) than in the other two cohorts (median cohort B 5 vs. cohort C 7, $p = 0.43$), however, not statistically significantly different.

The postoperative ASPECT score showed similar results in all subgroups (Table 2, median of 7, $p = 0.67$). The postinterventional ASPECT score was significantly lower compared to the preinterventional ASPECT score (7 vs. 10, $p < 0.001$).

In 35 (62.5%) patients, no kind of post-operative hemorrhage arose during the treatment or the hospital stay. The prevalence of post-operative hemorrhage was largely similar between the three cohorts (Table 2, $p = 0.61$). sICH was observed in 6 patients (10.5%). In our cohort, besides ICH and post-operative bleeding, three cases of embolism in other territories occurred. Beyond that, no further therapeutically relevant complications arose.

Table 3 summarizes complications and functional outcomes grouped by successful and unsuccessful EVT as determined by TICI reperfusion results. The mean mRS at discharge between the two groups differed significantly in favor of higher reperfusion rates (mean mRS of 4.43 ± 1.40, median 4, for TICI 0–2a vs. mean mRS of 3.00 ± 1.68, median 4, for TICI 2b-3; $p = 0.037$). No statistically significant difference in the rates of post-operative hemorrhage ($p = 0.36$), sICH ($p = 0.88$) was observed. Perioperative mortality, meaning all deaths during the period of hospitalization until discharge from hospital, showed no significant differences between the two groups ($p = 0.35$).

Furthermore, we examined whether a more proximal (M2-trunk/division of the MCA into M2-trunks) or more distal (M2-branches) localization of the occlusion affects the outcome. As shown in Table 4, 34 patients presented with a proximal occlusion (59.6%) and 23 patients with a distal occlusion (40.4%). No significant differences in the outcome (median mRS proximal 4 vs. distal 4, $p = 0.81$; median NIHSS proximal 6 vs. distal 5, $p = 0.53$) or the complications during the intervention were found between the two groups.

Discussion

Five major randomized trials (MR CLEAN, EXTEND IA, ESCAPE, REVASCAT, SWIFT PRIME) from 2015 showed significantly better recanalization rates for M1-occlusions using an additional treatment with EVT versus IVT alone (for example in MR CLEAN study absence of residual occlusion was 75.4% in the intervention group vs. 32.9% in the control group [1]), but the benefit of EVT in M2-occlusions remains unclear [1–5].

As of today, there is a lack of randomized, controlled trials focusing on EVT of M2-occlusions vs. best medical treatment alone, and recent findings of non-randomized studies are still inconclusive on whether EVT is safe and efficient in these cases. A number of studies have reported high recanalization rates in M2-occlusions with good clinical outcome and a low rate of procedural complications [7, 8, 11]. Underlining these results, our study found that patients with ischemic stroke in the M2-segment of MCA benefited from recanalization therapy. The European Society of Minimally Invasive Neurological Therapy (ESMINT) and the European Stroke

Table 3 Complications and outcome (mRS) depending on the success of reperfusion

Reperfusion *n* (%)		Complications *n* (%)		mRS at discharge mean ± SD (median)
TICI 2b-3	48 (86)	Post-operative hemorrhage SICH	15 (31.3)* 5 (10.4)	3.00 ± 1.68 (4)
		Perioperative death***	2 (4.2)	
TICI 0–2a	8 (14)	Post-operative hemorrhage SICH	4 (50.0)** 1 (12.5)	4.43 ± 1.40 (4)
		Perioperative death***	2 (25.0)	

Figures are numbers with percentages in parentheses unless otherwise indicated

SD, standard deviation; *SAH*, subarachnoid hemorrhage; *SICH*, symptomatic intracranial hemorrhage; *TICI*, Thrombolysis in Ischemic Stroke score; *mRS*, modified Rankin Scale

*most prevalent were PH-2 and SAH, $n = 6$ (12.2)

**most prevalent was SAH, $n = 2$ (25.0)

***perioperative death, meaning mortality during the period of hospitalization

Table 4 Complications and outcome (mRS, NIHSS) depending on the occlusion's localization

Occlusion's localization *n* (%)		Complications *n* (%)		mRS at discharge mean ± SD (median)
M2 trunk	34 (59.6)	Post-operative hemorrhage	8 (23.5)*	3.16 ± 1.61 (4)
		SICH	1 (2.9)	
		Perioperative death***	1 (2.9)	
M2 branch	23 (40.4)	Post-operative hemorrhage	8 (34.8)**	3.23 ± 1.88 (4)
		SICH	5 (21.7)	
		Perioperative death***	3 (13.0)	

Figures are numbers with percentages in parentheses unless otherwise indicated

SD, standard deviation; *SAH*, subarachnoid hemorrhage; *SICH*, symptomatic intracranial hemorrhage; *TICI*, Thrombolysis in Ischemic Stroke score; *mRS*, modified Rankin Scale

*most prevalent was SAH, $n = 5$ (14.7)

**most prevalent was PH-2, n = 5 (21.7)

***perioperative death, meaning mortality during the period of hospitalization

Organization (ESO) published the new European guidelines on mechanical thrombectomy in February 2019. Regarding M2 occlusion, there is a consensus from the guideline group that mechanical thrombectomy is useful for these patients, although there is still a lack of evidence [21]. Should M2 EVT become an integral part of the aforementioned guidelines, a widespread adoption would add to the generally high workload of existing comprehensive stroke centers and might lead to shifting at least some of the endovascular procedures to primary stroke centers [22].

To our knowledge, this is the first study evaluating safety, efficacy, and functional outcome with regard to the (group of) M2-vessles occluded, i.e., M2-territories affected. It is apparent that there is lack of studies examining the anatomical characteristics of M2-branches. Different ways to categorize the distal vessels make it even harder to compare the results from different analyses, so more research with larger cohorts regarding M2-occlusions is still necessary.

We did not find any significant differences with regard to the successful reperfusion rate, even if partial or complete recanalization was more frequently achieved in patients with an occlusion of the M2-vessles supplying the central and parietal/temporal area.

The baseline characteristics of the patients included in the current study were in line with other studies. The baseline median ASPECTS in our study was 10, while the median NIHSS was 11. Both are comparable to the ranges reported by Chen et al. in their review of eight studies, published 2014 to 2017, investigating M2-vessel occlusions (median NIHSS 10 to 16 and median ASPECTS of 9 to 10) [12]. Data for mRS at admission was not available in the current literature. Mean time from onset to recanalization was shorter in our study (259 ± 85 min) than reported by Bhogal et al. (399 ± 7.5 min [11]) but still in line with data by Dorn et al. (247 ± 132 min [8]). Mean duration of the procedure in our stroke center were comparable with data from other studies (68 ± 42 min versus 103 ± 7.8 min [11] and 49 ± 28 min [8]).

Successful revascularization of M2-segment occlusions (TICI 2b-3) ranges between 78.0 and 93.3% in the current literature [7, 8, 11, 23, 24]. The review by Chen et al. [12] found a rate of successful revascularization of 78% [12], which was lower than in our study (86%). However, a post hoc analysis of pooled data from the STAR (Solitaire Flow Restoration Thrombectomy for Acute Revascularization), SWIFT （Solitaire With the Intention For Thrombectomy), and SWIFT PRIME (Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment) trials, also part of the review by Chen et al., found a rate of 85%, comparable to our results [23]. In another recent example, Bhogal et al. reviewed 585 patients (106 with M2- and 479 with M1-occlusions) [11]. Their rates of successful recanalization (M2 90.5% vs. M1 88.5%, $p = 0.612$) are similar to ours. Additionally, the authors found no significant difference between M2- and M1-recanalization rates, suggesting that M2-revascularizations could be as effective as EVT of M1-segment occlusions. More unfavorable revascularization rates were found in a pooled analysis of three older interventional stroke trials (PROACTII, IMS, and IMSII) by Rahme et al. [6] (TICI 2–3, 58.1% vs. TICI 0–1, 53.1%; $p = 0.80$) and in a post hoc analysis of older data from the IMSIII trial by Tomsick et al. [10] (TICI 2b-3, 39%). This is most likely attributable to the inclusion of data from 1999 through 2013 [6, 10], after which both interventional techniques and materials advanced profoundly.

For analysis of functional outcome, we chose mRS scores at discharge and defined a good clinical outcome as mRS 0–2, i.e., "not reliant on outside help" (in our study $n = 19$, 37.7%). Recent studies reported favorable outcome rates of 60–63% at a 3-month-follow-up [7, 8, 12, 23, 24]. However, more disadvantageous rates of 41–56% have also been reported [6, 10, 11]. It has to be noted that most recent studies recorded the mRS at a 3-month-follow-up and are therefore not directly comparable to our results. However, it is likely that functional

outcome of the patients in the current sample should have improved after 3 months due to neurorehabilitation efforts. Furthermore, we assessed the NIHSS at discharge and detected a significant decrease comparing the pre- and postinterventional findings. Dorn et al. also reported the NIHSS at admission (mean 13.73 ± 8.3) and discharge (mean 7.43 ± 9.84), which is in line with our findings (mean NIHSS at admission 11.5 ± 5 vs. 6.8 ± 5.7 at discharge) [8].

Our findings show significantly better clinical outcome (mRS 0–2) at discharge in patients with higher reperfusion rates. In contrast, Rahme et al. failed to find a positive relation between successful early reperfusion and clinical outcome for 63 patients with M2-occlusion (mRS 0–2 at 3 months with TICI 2–3, 58.1% vs. TICI 0–1, 53.1%; $p = 0.80$) [6].

We observed sICH in 10.5% of the cases, which is comparable to a sICH rate of 9.0% by Flores et al. [7]. However, the review by Chen et al., which also included the data of Flores et al., found an overall lower sICH rate of 5% [12], which is also in line with data by Bhogal et al. (5.0%) [11]. Only the pooled analysis of older data (PROACTII, IMS, IMSII) by Rahme et al. found a higher rate of sICH (17.4%) [6], which might be traced back to the fact that EVT did not have a comparable quality in the past. In contrast to the sICH findings, our mortality rate was lower than the average mortality rate reported by Chen et al. (7% vs. 11%) [12], or in other studies (12% by Tomsick et al. [10] or 17.5% by Rahme et al. [6]). Compared to the five large randomized trials examining EVT in proximal occlusions of the anterior circulation (MR CLEAN, EXTEND IA, ESCAPE, REVASCAT, SWIFT PRIME), we found a slightly higher rate of sICH (4.4% vs. 10.5%) but less mortality (15.3% vs. 7%) [1–5, 24]. Bhogal et al. also describes a lower mortality rate for M2- (6.7%) than for M1-occlusions (21%) [25]. This might be attributable to the fact, that M2-vessels might be more fragile and prone to bleeding, than the larger M1-segment. On the other hand, only a smaller territory is affected, and therefore, complications might be less severe than in proximal occlusions of the M1-segment.

In our study, limitations occur which are explained in the following. The retrospective, single-center design we have chosen here is itself a limitation and does not allow final conclusion. However, our study shows us tendencies to perform thrombectomy in M2 closures, which shall be confirmed in follow-up studies. Due to small power size, it is partly not possible to achieve statistical significance and is therefore a further limitation. In the period from January 2012 to December 2017, EVT techniques have evolved in the local department—although in accordance with the experiences from other centers. Also, the final indication, technique, and choice of materials were at the discretion of the interventional neuroradiologist on call. Due to the small number of patients, we have not further analyzed the impact of additional IVT, although the majority was treated with EVT and IVT (75.4%). There is evidence that the administration of intravenous thrombolysis is associated with recanalization success [26]. At our local department, we tend to more readily attempt EVT in patients who cannot undergo IVT, although this approach is, as noted, at the discretion of the neuroradiologist on call. It is possible that IVT may have a greater relative contribution to recanalization in distal M2 branches than in M1 branches, which will be investigated in a follow-up study. It should also be noted that possible concomitant medications, concomitant diseases, degree of collateral circulation, mismatch, and endpoint infarction volume were not included in the analysis Unfortunately, due to methodological barriers, we could not collect a 90-day mRS. Thus, it is difficult to estimate the long-term benefit of patients from the intervention and to compare the results with other studies. At this point, we are planning a follow-up study in our institute with a larger cohort and long-term parameters such as the 90-day mRS for a better assessment of clinical development after distal thrombectomy. Lastly, comparisons of the current results and results from the literature are not easily done, since the definition of the M2-segment anatomy is diverse.

In conclusion, in our current study, we found a significant improvement in functional outcome at discharge after EVT of M2-segment occlusions and no relevant complications. With regard to the M2-vessles/territories or a more proximal or distal occlusions, no significant differences were found in functional outcome, procedure-related complications, or mortality. The results suggest that EVT should be performed in patients with M2-occlusions, although further studies with larger sample sizes, preferably in a randomized design, are needed to substantiate the findings.

Author contributions M.K., B.T., and V.I. conceived of the presented idea. V.I. and M.K developed the theory and V.I. performed the computations and analytic calculations. C.R. and J.C verified the analytical methods. M.K. encouraged V.I. to investigate the outcome and vessel involvement in patients with mechanical thrombectomy in acute middle cerebral artery M2 segment occlusions and supervised the findings of this work. V.I., M.K., C.R., J.C., B.T., J.L., M.G., and S.J. contributed to the interpretation of the results. All authors discussed the results and contributed to the final manuscript. V.I. took the lead in writing the manuscript with input and support from all authors (M.K., C.R., J.C., B.T. J.L., M.G., S.J.). All authors provided critical feedback and helped shape the research, analysis and manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the local ethics committee.

Informed consent The requirement for written informed consent was waived by the local ethics committee.

References

1. Berkhemer OA, Fransen PSS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ et al (2015) A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 372:11–20 [cited 2018 Sep 25]. Available from: https://www.nejm.org/doi/pdf/10.1056/NEJMoa1411587
2. Campbell BCV, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N et al (2015) Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 372:1009–1018 [cited 2018 Sep 29]. Available from: https://www.nejm.org/doi/pdf/10.1056/NEJMoa1414792
3. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J et al (2015) Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 372:1019–1030 [cited 2018 Sep 23]. Available from: www.aspectsinstroke.com
4. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A et al (2015) Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 372:2296–2306 [cited 2018 Sep 29]. Available from: https://www.nejm.org/doi/pdf/10.1056/NEJMoa1503780
5. Saver JL, Goyal M, Bonafe A, Diener H-C, Levy EI, Pereira VM et al (2015) Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med 372:2285–2295 [cited 2018 Sep 29]. Available from: https://www.nejm.org/doi/pdf/10.1056/NEJMoa1415061
6. Rahme R, Yeatts SD, Abruzzo TA, Jimenez L, Fan L, Tomsick TA et al (2014) Early reperfusion and clinical outcomes in patients with M 2 occlusion: pooled analysis of the PROACT II, IMS, and IMS II studies. J Neurosurg 121:1354–1358. https://doi.org/10.3171/2014.7.JNS131430
7. Flores A, Tomasello A, Cardona P, De Miquel MA, Gomis M, Bermejo PG et al (2015) Endovascular treatment for M2 occlusions in the era of stentrievers: a descriptive multicenter experience. J Neurointerv Surg 7:234–237 [cited 2018 Sep 25]. Available from: http://jnis.bmj.com/
8. Dorn F, Lockau H, Stetefeld H, Kabbasch C, Kraus B, Dohmen C et al (2015) Mechanical thrombectomy of M2-occlusion. J Stroke Cerebrovasc Dis 24:1465–1470 [cited 2018 Aug 12]. Available from: https://www.sciencedirect.com/science/article/pii/S1052305715002062
9. Sheth SA, Yoo B, Saver JL, Starkman S, Ali LK, Kim D et al (2015) M2 occlusions as targets for endovascular therapy: comprehensive analysis of diffusion/perfusion MRI, angiography, and clinical outcomes. J Neurointerv Surg 7:478–483 [cited 2018 Sep 27]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24821842
10. Tomsick TA, Carrozzella J, Foster L, Hill MD, Von Kummer R, Goyal M et al (2017) Endovascular therapy of M2 occlusion in IMS III: role of M2 segment definition and location on clinical and revascularization outcomes. Am J Neuroradiol 38:84–89 [cited 2018 Aug 12]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27765740
11. Bhogal P, Bücke P, AlMatter M, Ganslandt O, Bäzner H, Henkes H et al (2017) A comparison of mechanical thrombectomy in the M1 and M2 segments of the middle cerebral artery: a review of 585 consecutive patients. Interv Neurol 6:191–198 [cited 2018 Aug 12]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29118796
12. Chen CJ, Wang C, Buell TJ, Ding D, Raper DM, Ironside N et al (2017) Endovascular mechanical thrombectomy for acute middle cerebral artery M2 segment occlusion: a systematic review. World Neurosurg:684–691 [cited 2018 Aug 12]. Available from: https://www.sciencedirect.com/science/article/pii/S1878875017314092
13. Deutsche Gesellschaft für Neurologie. Leitlinien für Diagnostik und Therapie in der Neurologie. Leitlinien für Diagnostik und Ther der Neurol [Internet]. 2012 [cited 2018 Dec 26]. p 1–17. Available from: www.dgn.org
14. Warwick Pexman JH, Barber PA, Hill MD, Sevick RJ, Demchuk AM, Hudon ME et al (2001) Use of the Alberta Stroke Program Early CT score (ASPECTS) for assessing CT scans in patients with acute stroke. AJNR Am J Neuroradiol Available from: http://www.ajnr.org/content/ajnr/22/8/1534.full.pdf
15. Wiesmann M, Brockmann M-A, Heringer S, Müller M, Reich A, Nikoubashman O (2017) Active push deployment technique improves stent/vessel-wall interaction in endovascular treatment of acute stroke with stent retrievers. J Neurointerv Surg 9:253–256 [cited 2019 Apr 22]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26975839
16. Humphries W, Hoit D, Doss VT, Elijovich L, Frei D, Loy D, Dooley G, Turk AS, Chaudry I, Turner R, Mocco J, Morone P, Fiorella D, Siddiqui A, Mokin M, Arthur AS (2015) Distal aspiration with retrievable stent assisted thrombectomy for the treatment of acute ischemic stroke. J Neurointerv Surg 7:90–94
17. Iodice F, Brunetti V, Nicolini E, Paolucci M, Di Lorenzo F (2019) Endovascular therapy for acute ischemic stroke: which role for neurologists? Neurol Sci: 1737–9
18. Derex L, Nighoghossian N (2008) Intracerebral haemorrhage after thrombolysis for acute ischaemic stroke: an update. J Neurol Neurosurg Psychiatry:1093–1099 [cited 2018 Sep 29]. Available from: http://jnnp.bmj.com/
19. Larrue V, Von Kummer R, Müller A, Bluhmki E (2001) Risk factors for severe hemorrhagic transformation in ischemic stroke patients treated with recombinant tissue plasminogen activator: a secondary analysis of the European-Australasian acute stroke study (ECASS II). Stroke 32:438–441
20. R Core Team (2018) R: a language and environment for statistical computing [Internet]. Vienna, Austria. Available from: https://www.r-project.org/
21. Turc G, Bhogal P, Fischer U, Khatri P, Lobotesis K, Mazighi M et al (2019) European Stroke Organisation (ESO) - European Society for Minimally Invasive Neurological Therapy (ESMINT) guidelines on mechanical thrombectomy in acute ischemic stroke. J Neurointerv Surg:1–30 [cited 2020 Feb 13]. Available from: http://jnis.bmj.com/
22. Ornello R, Carolei A (2019) Primary stroke centers: are they worthy of an upgrade? Intern Emerg Med:333–334
23. Coutinho JM, Liebeskind DS, Slater LA, Nogueira RG, Baxter BW, Levy EI et al (2016) Mechanical thrombectomy for isolated M2 occlusions: a post hoc analysis of the star, swift, and SWIFT PRIME studies. Am J Neuroradiol:667–672 [cited 2018 Aug 12]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26564442
24. Sarraj A, Sangha N, Hussain MS, Wisco D, Vora N, Elijovich L et al (2016) Endovascular therapy for acute ischemic stroke with occlusion of the middle cerebral artery M2 segment. JAMA Neurol 73:1291–1296 [cited 2018 Sep 30]. Available from: http://archneur.jamanetwork.com/article.aspx?doi=10.1001/jamaneurol.2016.2773
25. Bhogal P, Bücke P, AlMatter M, Ganslandt O, Bäzner H, Henkes H et al (2017) A comparison of mechanical thrombectomy in the M1 and M2 segments of the middle cerebral artery: a review of 585 consecutive patients. Interv Neurol 6:191–198 [cited 2018 Aug 12]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29118796
26. Heider DM, Simgen A, Wagenpfeil G, Dietrich P, Yilmaz U, Mühl-Benninghaus R et al (2020) Why we fail: mechanisms and co-factors of unsuccessful thrombectomy in acute ischemic stroke. Neurol Sci:1–9

Original Article

NRJ

The Neuroradiology Journal
2022, Vol. 0(0) 1–7

DOI: 10.1177/19714009211067403
journals.sagepub.com/home/neu
SAGE

Mechanical thrombectomy in stroke patients with acute occlusion of the M1- compared to the M2-segment: Safety, efficacy, and clinical outcome

Daniel Weiss[1], Christian Rubbert[1], Vivien L Ivan[1], John-Ih Lee[2], Michael Gliem[2], Sebastian Jander[2], Julian Caspers[1], Bernd Turowski[1] and Marius G Kaschner[1]

Abstract

Purpose: Endovascular treatment (ET) in occlusions of the M1- and proximal M2-segment of the middle cerebral artery (MCA) is an established procedure. In contrast, ET in distal M2-occlusions has not been sufficiently evaluated yet. The purpose of this study was to assess relevant parameters for clinical outcome, efficacy, and safety of patients undergoing ET in M1-, proximal M2-, and distal M2-occlusions.

Methods: One hundred seventy-four patients undergoing ET in acute ischemic stroke with an occlusion of the M1- or M2-segment of the MCA were enrolled prospectively. Non-parametric analysis of variance in 3-month mRS, TICI scale, and complication rates were performed with Kruskal–Wallis test between M1- and proximal and distal M2-occlusions. Subsequent pairwise group comparisons were calculated using Mann–Whitney U-tests. Binary logistic regression models were calculated for each occlusion site.

Results: There were no significant group differences in 3-month mRS, mTICI scale, or complication rates between M1- and M2-occlusions nor between proximal and distal M2-occlusions. Binary logistic regression in patients with M1-occlusions showed a substantial explanation of variance (NR^2=0.35). NIHSS (p=0.009) and Maas Score as parameter for collateralization (p=0.01) appeared as significant contributing parameters. Binary logistic regression in M2-occlusions showed a high explanation of variance (NR^2=0.50) of mRS but no significant factors.

Conclusions: Clinical outcome and procedural safety of patients with M2-occlusions undergoing ET are comparable to those of patients with M1-occlusions. Clinical outcome of patients with M1-occlusions undergoing ET is primarily influenced by the initial neurological deficit and the collateralization of the occlusions. By contrast, clinical outcome in patients with M2-occlusions undergoing ET is more multifactorial.

Keywords

endovascular treatment, stroke, M1-segment, M2-segment, clinical outcome

Introduction

Endovascular thrombectomy (ET) gained importance as an established treatment of acute ischemic stroke (AIS).[1–5] Especially, for the treatment of occlusions of the M1-segment of the middle cerebral artery (MCA), ET is feasible and safe and has become the standard of care.[6,7] Evidence for ET in more distal parts of MCA is sparser. In this regard, it has to be considered that, if the occlusion is located in the distal M2-branches or beyond, ET may result in difficult revascularization maneuvers. Possibly, these maneuvers are providing a higher risk for complications, for example, by vessel perforation due a smaller diameter and the tortuous and curvy run of the vessels. However, recent studies showed promising results of ET in occlusions of the M2-division regarding safety, complications, and functional outcome.[8] The aim of this study is to evaluate safety and efficacy of ET in M2-occlusions (proximal and distal) compared to ET in M1-occlusions and to identify parameters favoring a good functional outcome. Furthermore, we compared functional outcome after 3 months and occurrence of complications of ET in M2-occlusions compared to ET in M1-occlusions.

Material and methods

174 patients undergoing ET in acute ischemic stroke with an occlusion of the M1- or M2-segment of the MCA were prospectively enrolled at the local Department of Diagnostic and Interventional Radiology between June 2016 and May 2018.

[1]University Dusseldorf, Medical Faculty, Department of Diagnostic and Interventional Radiology, D-40225 Dusseldorf, Germany
[2]Department of Neurology Medical Faculty, Heinrich Heine University Düsseldorf, Düsseldorf, Germany

Corresponding author:
Daniel Weiss, University Dusseldorf, Medical Faculty, Department of Diagnostic and Interventional Radiology, Moorenstraße 5, D-40225 Dusseldorf, Germany.
Email: DanielArvid.Weiss@med.uni-duesseldorf.de

The study was approved by the local institutional review board. Written informed consent for study inclusion was obtained from all patients or their next of kind. When patients passed away during hospitalization, written informed consent was waived.

Thrombectomy technique

The interventional procedures were performed under analgesia (1–2 g novaminsulfone as short infusion) and local anesthesia of the groin. General anesthesia was performed in patients with need for endotracheal intubation (Glasgow coma scale <8) or in case of extreme agitation. Access was performed using a long 8F sheath or additional guiding catheter positioned in the distal internal carotid artery. The thrombectomy procedure in the M1- and proximal and distal M2-segment could be performed using one of two techniques: The stent retriever TE or sole aspiration TE (ADAPT—a direct first pass aspiration technique) as first-line revascularization attempt. Both techniques could be used consecutively if one of them failed.

Stent retriever thrombectomy

The procedures were either performed using the "Solumbra technique," in which the stent retriever is usually retracted into an aspiration catheter placed proximal to the clot, or the SAVE technique in which the clot is tucked between the stent retriever and the tip of the aspiration catheter and both are withdrawn into the sheath or guiding catheter.[9,10]

Under guidance of a standard 0.014″ micro-guidewire or in very small vessels of a 0.014″ microwire with a soft tip (Stryker Neurovascular, Fremont, California, USA), a microcatheter (Neuroslider 17 or 21, Acandis, Pforzheim, Germany) was placed distal to the clot and an aspiration catheter (e.g., 5F or 6F Sofia Plus aspiration, Microvention, Tustin, CA) was placed as proximal as possible to the thrombus. Afterward, the guidewire was replaced by the APERIO stent retriever (APERIO® Thrombectomy Device; Acandis, Pforzheim, Germany). The size of the APERIO was determined considering the length and the cross section of the thrombus and vessel, respectively. The APERIO is composed of repetitive functional segments, that enable adaptation of the device length to the thrombus length by partial deployment of the stent retriever in tortuous M2-vessels. A 20 mL syringe was attached to the aspiration catheter for manual aspiration while the APH and thrombus were withdrawn into the aspiration catheter.

A direct first pass aspiration technique

A 0.027 in. inner lumen microcatheter was advanced up to or if the system was not stable enough, past the thrombus over a microwire and then an aspiration catheter (5F or 6F SOFIA, MicroVention Inc, Tustin, CA) was advanced to the proximal aspect of the thrombus. Then, the microcatheter (Neuroslider 21, Acandis, Pforzheim, Germany) and the guidewire were removed. The aspiration catheter was directly locked to a 20 mL syringe. Manual aspiration was started, and as soon as absence of flow was noted, the resulting vacuum was maintained for at least 60 s. Then, the catheter was slowly retracted under additional aspiration at the guide catheter.

In case of partial clot extraction, the TE attempt was either (i) repeated, (ii) a stent retriever was used under local aspiration, or (iii) the intervention was terminated when residual clot could not be reached without increased risk of procedural complications.

Imaging and post-processing

Patients directly admitted to our local department were examined with a standardized stroke protocol including non-contrast enhanced cranial computed tomography (CT), CT angiography (CT-A), and CT perfusion (CT-P). Coronal and sagittal multiplanar reformations (MPRs) with a slice thickness of maximally 2 mm as well as maximum intensity projections (MIPs) in axial, coronal, and sagittal plane were obtained for further analysis using the local Picture Archiving and Communication System (PACS, IDS7, Sectra, Linköping, Sweden).

Subdivision of MCA-branches was based on angiographic findings. We distinguished between (1) occlusion of the M1-segment; (2) an occlusion of the proximal M2-segment; and (3) an occlusion of the distal M2-segment.

Proximal M2-segment (M2-trunk) is defined as the segment between the division of the M1-segment up to the next division into distal M2-branches.

Distal M2-segment is defined as branches starting from the division of the M2-trunk up to the beginning of M3-segment (Figure 1).

For evaluation of collateralization, Maas Score, a 5-point CT-A collateral score, was assessed retrospectively in 9 mm axial MIP reconstructions of CT-A images parallel to the orbitomeatal line at basal ganglia level.[11–13]

Outcome analysis

Functional outcome of patients was evaluated using the modified Rankin Scale (mRS) 3 months after ET. The mRS was assessed by a standardized telephone interview performed by one investigator (D.W.). Patients were dichotomized by mRS into favorable outcome (mRS ≤2) and poor outcome (mRS ≥3).

Radiographic outcome was measured using the mTICI scale (modified thrombolysis in cerebral infarction) based on angiographic findings. A TICI scale of ≥2b was considered a successful recanalization.

Periprocedural complications including perforation, dissection, and embolism into new territories were analyzed.

Complications within the first 24 h including new infarction on CCT due to embolisms into new territories, subarachnoid hemorrhages, and parenchymal intracerebral hemorrhage were evaluated. Intracerebral hemorrhages were classified according to the Heidelberger bleeding classification and include hemorrhages within and beyond infarcted brain tissue (PH-2) with neurological deterioration (decline in NIHSS ≥4) and hemorrhagic transformation of infarcted brain tissue (HI-1, HI-2, and PH-1).[14]

Statistical analysis

Statistical analysis was performed with SPSS software environment (Statistical Package for Social Science, version 25,

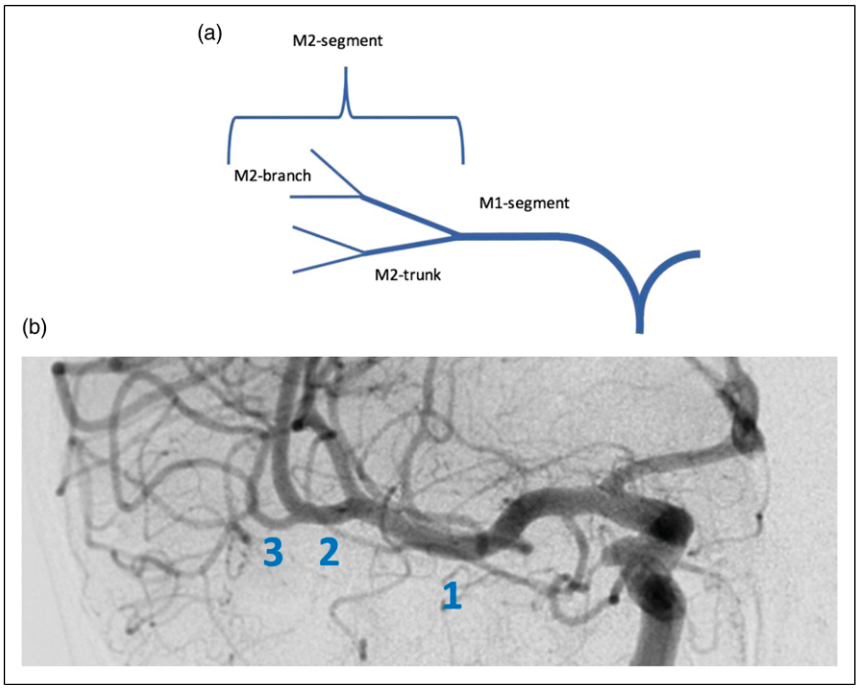


Figure 1. Anatomical schema of MCA-division (a) and angiography of the middle cerebral artery (b)1: M1-segment, 2: M2-trunk = *proximal* M2-segment, 3: M2-branch = *distal* M2-segment.

IBM, Armonk, New York). A p-value <0.05 was considered statistically significant for all analyses.

A priori power analysis was performed for this population for a moderate effect size.

Non-parametric analysis of variance in 3-month mRS, TICI scale, and complication rates (after 24 h) were performed with Kruskal–Wallis test between M1- and proximal and distal M2-occlusions.

Pairwise group comparisons between M1- and M2-occlusions and proximal M2- and distal M2-occlusions were performed using Mann–Whitney U-tests with subsequent Bonferroni correction in case of multiple testing.

Binary logistic regression models were calculated for each occlusion site. Each analysis included age, NIHSS at admission, Maas Score, onset-to-recanalization time, and ASPECTS at admission as independent variables and dichotomized 3-month mRS as dependent variable. Associations between each independent variable and favorable functional outcome adjusted for the other four independent variables were analyzed. For assessment of model quality Nagelkerke's R^2 was used. Furthermore, odds ratios with confidence intervals as well as regression coefficients were calculated.

Results

174 patients met the inclusion criteria for the current analysis. Mean age was 76 (±13) years and 59.2% of all patients were female. M1-division of MCA was the most frequently occluded vessel (n = 141, 81.0%). Proximal M2-segment was occluded in 22 (12.6%) cases and distal M2-segment was occluded in 11 (6.3%) cases. Median ASPECT-Score at admission was 10 (IQR 9–10) and median NIHSS at admission was 14 (IQR 9–17). Most patients achieved a complete or substantial revascularization after mechanical recanalization (TICI scale 2b-3; 87.7%). 64 patients were undergoing ET alone (36.8%) and 110 combined with intravenous thrombolysis (IVT) (63.2%). Of all patients with a M2-occlusion, 8 (24.2%) were initially treated with ADAPT. Overall complication rate (after 24 h) was 28.7% (50 patients). No procedural complications such as perforation, dissection, or emboli to new territories occurred in patients treated with a stent retriever TE and with ADAPT. Seventy-nine (45.4%) patients showed a favorable outcome (mRS ≤2) and ninety-three (54.6%) patients a poor outcome (mRS ≥3) (Table 1). Baseline characteristics, procedural data, and clinical outcome of patients treated with ADAPT are separately summarized in Table 2.

A priori power analysis was performed for this population and showed power of 82% for a moderate effect size.[15]

Non-parametric analysis of variance in 3-month mRS, TICI scale, and complication rate were performed with Kruskal–Wallis test between M1- and proximal and distal M2-occlusions and did not show significant differences between occlusion site and dichotomized 3-month mRS (p = 0.07) nor dichotomized TICI scale (p = 0.44) nor complication rates (p = 0.26).

There was no significant group difference in dichotomized 3-month mRS between M1- and M2-occlusions (p = 0.12, U = 3403). When investigating the subgroups of M2-occlusion sites, there was no significant group difference in dichotomized 3-month mRS between M1- and proximal M2-occlusions (p = 0.07, U = 1023), between M1- and distal M2-occlusions (p = 1.00, U = 753), or between proximal M2- and distal M2-occlusions (p = 0.99, U = 111).

There was no significant group difference in dichotomized TICI scale between M1- and M2-occlusions (p = 0.54, U = 1485), between M1- and proximal M2-occlusions (p = 0.75, U = 1389), between M1- and distal M2-occlusions (p = 1.00, U = 720), or between proximal M2- and distal M2-occlusions (p = 0.96, U = 29).

There was no significant group difference in 24 h complication rates between M1- and M2-occlusions (p = 0.12,

Table 1. Baseline data.

	Total (n = 174)	M1 (n = 141)	pM2 (n = 22)	dM2 (n = 11)
Age, mean (SD, min-max), in years	76 (±13, 35-111)	76 (±13, 35-111)	77 (±11, 48-96)	70 (±14, 46-88)
Female sex, n (%)	103 (59.2)	87 (61.7)	13 (59.1)	3 (27.3)
Left hemisphere, n (%)	103 (59.2)	79 (56.0)	14 (63.6)	10 (90.9)
ASPECTS at admission, median (IQR)	10 (9-10)	10 (9-10)	10 (10-10)	10 (10-10)
ASPECTS shift, median (IQR)	4 (1-6)	4 (1-8)	3 (0-4)	2 (0-6)
NIHSS at admission, median (IQR)	14 (9-17)	14 (10-17)	10 (7-15)	8 (7-16)
NIHSS shift, median (IQR)	6 (3-10)	6 (2-11)	6 (3-13)	5 (3-6)
mRS after 3 months, n (%)				
0	27 (15.5)	21 (14.9)	5 (22.7)	1 (9.1)
1	33 (19.0)	22 (15.6)	7 (31.8)	4 (36.4)
2	19 (10.9)	17 (12.1)	2 (9.1)	0 (0)
3	9 (5.2)	8 (5.7)	1 (4.5)	0 (0)
4	30 (17.2)	26 (18.4)	3 (13.6)	1 (9.1)
5	18 (10.3)	17 (12.1)	0 (0)	1 (9.1)
6	38 (21.8)	30 (21.3)	4 (18.2)	4 (36.4)
Favorable mRS (0-2) after 3 months, n (%)	79 (45.4)	60 (42.6)	14 (63.6)	5 (45.5)
Periprocedural complications, n (%) (perforation, dissection, and emboli to new territories)	0 (0)	0 (0)	0 (0)	0 (0)
Complications after 24 h, n (%)				
None	121 (69.5)	93 (66.0)	19 (86.4)	9 (81.8)
HI-1, HI-2, PH-1	22 (12.6)	20 (14.2)	0 (0.0)	1 (9.1)
sICH (PH-2)	11 (6.3)	10 (7.1)	1 (4.5)	1 (9.1)
SAH	17 (9.8)	15 (10.6)	2 (9.1)	0 (0)
Door-to-IVT, mean (SD, min-max) in min	52 (±26, 10-122)	51 (±24, 11-106)	55 (±28, 22-114)	61 (±43, 10-122)
Onset-to-IVT, mean (SD, min-max) in min	105 (±55, 22-420)	100 (±41, 22-240)	137 (±115, 60-420)	121 (±61, 70-225
Door-to-groin-puncture, mean (SD, min-max) in min	130 (±77, 15-653)	128 (±78, 15-653)	137 (±52, 54-206)	146 (±93, 50-325)
IVT-to-groin-puncture, mean (SD, min-max) in min	76 (±48, 5-188)	76 (±49, 5-188)	84 (±48, 9-150)	57 (±39, 15-110)
Onset-to-groin-puncture, mean (SD, min-max) in min	187 (±79, 50-575)	183 (±75, 50-575)	211 (±114, 84-510)	191 (±79, 120-325)
Door-to-recanalization, mean (SD, min-max) in min	171 (±84, 50-699)	168 (±84, 50-699)	180 (±49, 78-222)	186 (±124, 80-416)
Onset-to-recanalization, mean (SD, min-max) in min	228 (±85, 67-611)	225 (±80, 67-611)	257 (±114, 108-534)	221 (±104, 146-5416)
Groin-to-recanalization, mean (SD, min-max) in min	41 (±26, 8-158)	41 (±26, 8-158)	40 (±22, 22-91)	40 (±26, 21-91)
Maneuver, mean (SD, min-max)	2 (±1, 1-11)	2 (±2, 0-11)	2 (±1, 1-3)	1 (±2, 1-5)
TICI scale, n (%)				
0	9 (5.3)	7 (5.1)	1 (4.5)	1 (9.1)
1	1 (0.6)	1 (0.7)	0 (0)	0 (0)
2a	11 (6.4)	10 (7.2)	0 (0)	1 (9.1)
2b	64 (37.4)	47 (34.1)	10 (45.5)	7 (63.6)
2c	36 (21.1)	29 (21.0)	5 (22.7)	2 (18.2)
3	50 (29.2)	44 (31.9)	6 (27.3)	0 (0.0)

SD: standard deviation, IQR: interquartile range, ASPECTS: Alberta Stroke Program Early CT Score, NIHSS: National Institutes of Health Stroke Scale, mRS: modified Rankin Scale, IVT: intravenous thrombolysis, TICI: thrombolysis in cerebral infarction, SAH: subarachnoid hemorrhage, sICH: symptomatic intracerebral hemorrhage, HI: hemorrhagic infarction, PH: parenchymal hematoma, pM2: proximal portion of M2-segment, dM2: distal portion of M2-Segment.

U = 3003), between M1- and proximal M2-occlusions (p = 0.33, U = 1283), between M1- and distal M2-occlusions (p = 1.00, U = 712), or between proximal M2- and distal M2-occlusions (p = 1.00, U = 80).

Binary logistic regression analysis model for M1-occlusions showed a substantial explanation of variance ($NR^2 = 0.31$). NIHSS at admission ($p = 0.01$) and Maas Score (p = 0.02) were significant factors in this model (Table 3).

Binary logistic regression analysis model for M2-occlusions showed a high explanation of variance (NR^2 = 0.53). There were no significant factors in this model (Table 3).

Discussion

This study has identified NIHSS at admission and collateralization (measured by the Maas Score) as independent parameters that had an impact on clinical outcome in M1-occlusions. For M2-occlusions, no parameters with significant influence on clinical outcome were identified. Favorable clinical outcome was comparable between patients after M1- and M2-thrombectomy. Successful revascularization rates (TICI scale 2b-3) as radiographic outcome did not differ between patients with M1 and M2-occlusions nor between patients with proximal and distal M2-occlusions. The study showed a low complication rate for M1- and M2-occlusion within 24 h and absence of procedural complications that require treatment.

The influence of NIHSS at admission to the clinical outcome after 3 months of patients undergoing ET in AIS may be explained by the impact of the initial neurological deficit and was already shown in former studies.[16] Furthermore, we found that collateralization measured by the

Table 2. Baseline characteristics of patients with M2-segment occlusion treated with ADAPT.

	Total (n = 8)	*pM2 (n = 7)*	*dM2 (n = 1)*
Age *(SD, min-max) in years*	79 (±8, 63-88)	78 (±7, 63-85)	88 (±0, 88-88)
Female sex, *n (%)*	6 (75.0)	6 (85.7)	0 (0)
NIHSS at admission *median (IQR)*	15 (12-19)	14 (9-15)	23 (23-23)
ASPECTS at admission *median (IQR)*	10 (9-10)	10 (10-10)	7 (7-7)
OTRT *(SD, min-max) in minutes*	217 (±56, 108-260)	211 (±60, 108-260)	249 (±0, 249-249)
Favorable TICI scale	8 (100.0)	7 (100.0)	1 (100.0)
2c	2	1 (14.3)	1 (100)
3	6	6 (85.7)	
Favorable mRS (0-2) after 3 months, n (%)	5 (62.5)	5 (71.4)	0 (0)
Periprocedural complications, n (%)	0 (0.0)	0 (0.0)	0 (0.0)
Complications after 24 h, n (%)	2 (25.0)	1 (14.3)	1 (100.0)
Additional stent retriever, *n (%)*	3 (37.5)	3 (42.9)	1 (100.0)

SD: standard deviation, IQR: interquartile range, ASPECTS: Alberta Stroke Program Early CT Score, NIHSS: National Institutes of Health Stroke Scale, mRS: modified Rankin Scale, OTRT: onset-to-recanalization-time, TICI: thrombolysis in cerebral infarction.

Table 3. Binary logistic regression analyses.

	M1 (n = 141)	*M2 (n = 33)*
NR^2	0.31	0.53
Age	p = 0.05, OR = 0.95 (CI = 0.91-1.00)	p = 0.68, OR = 1.03 (CI = 0.89-1.20)
NIHSS	p = 0.01[a], OR = 0.85 (CI = 0.74-0.96)	p = 0.44, OR = 0.83 (CI = 0.52-1.33)
Maas Score	p = 0.02[a], OR = 3.20 (CI = 1.23-8,34)	p = 0.83, OR = 0.70 (CI = 0.27-18.05)
OTRT	p = 0.18, OR = 0.99 (CI = 0.99-1.00)	p = 0.74, OR = 0.99 (CI = 0.99-1.01)
ASPECTS	p = 0.83, OR = 1.05 (CI = 0.66-1.68)	p = 0.99, OR = - (CI = -)[a]

NR^2 = Nagelkerke's R^2, OTRT = onset-to-recanalization-time, ASPECTS: Alberta Stroke Program Early CT score, OR = odds ratio.
[a] Due to minimal significance, no confidence interval can be calculated for methodological reasons.

Maas Score had a significant influence on clinical outcome of patients with M1-occlusion. Collateralization is well known as a relevant parameter for clinical outcome in AIS.[11,17] It even showed a greater impact on the clinical outcome than the onset-to-recanalization time in patients with M1-occlusion. Although the factor time has been proven important for clinical outcome in AIS, collateralization may be decisive as well.[11]

In contrast to patients with M1-occlusion, we could not find any outstanding parameter with impact on the clinical outcome of patients with M2-occlusion. This may be caused by the lower number of patients in this subgroup. Nonetheless, parameters like time-to-recanalization and collateralization still did not show the tendency to be decisive for clinical outcome in this subgroup, though there is a high explanation of variance in the respective regression analysis. Therefore, the impact on clinical outcome in patients with M2-occlusion seems to be rather multifactorial compared to patients with M1-occlusion.

Frequency of favorable clinical outcome between patients with an M1-occlusion did not differ from patients with an M2-occlusion. Similar results were already reported in former studies and underline the comparability of safety and efficacy of ET in M1- and M2-occlusions.[8,18,19] Furthermore, favorable outcome did not differ between proximal and distal M2-occlusions. This indicates that even in distal M2-branches, ET can not only be performed with technical success but also with favorable clinical outcome and is consistent with findings from a few small patient samples.[18,20]

Successful revascularization rates (TICI scale 2b-3) for M1- and M2-occlusions (87 vs 90.9%) were comparable to previous studies.[2–4,7] These results demonstrate that high recanalization rates can be achieved in M1- and M2-occlusions. Furthermore, also in distal M2-branches, successful recanalization was feasible with comparable recanalization rates of ET in the proximal M2-trunk (81.8% vs. 95.5%) and confirmed the results of a recently published study.[20]

Occurrence of complications can impair clinical outcome of patients undergoing ET. We observed comparable numbers of overall complications after ET in patients with different occlusion sites among each other. Furthermore, overall complications are comparable to other studies.[6,21] The number of patients with M1-occlusion (n = 10, 7.1%) and proximal M2-occlusion (n = 1, 9.1%) developing symptomatic intracerebral hemorrhage (sICH) within 24 h in our study is slightly lower compared to previous reports, most likely to be caused by different sample sizes.[22]

Absence of procedural complications like dissection, angiographic detectable SAH or ENT, indicates the safety of the thrombectomy procedure in this study. Non-occurrence of clinically relevant procedural complications may have depended on the used thrombectomy techniques. In M1-occlusions, the stent retriever TE has shown to be an effective and safe technique. Because most proximal M2-vessels have a similar diameter compared to the M1-segment, recanalization rates and safety of the procedure might be equal. There is an increasing evidence for stent retriever TE in the M2-segment as the current study and previous studies

have demonstrated.[8] However, the comparison of results of mechanical TE depending on the anatomy of the M2-segment (proximal vs. distal M2 occlusions) is limited and only retrospectively analyzed.[18,20] Using stent retrievers in very tortuous vessels with sharp angulation implicates the increased risk of laceration of the endothelium resulting in dissection and new thrombus formation due to shear stress and avulsion of perforators by tension to the vessel tree. Nevertheless, in tortuous M2-segments, a contact aspiration maneuver (ADAPT) can be considered, assuming this technique is less traumatic to the endothelium and causes less traction to the vessels. For revascularization success by contact aspiration alone, a direct contact of the intermediate catheter to the thrombus is essential. However, in very tortuous vessels, the thrombus can often not be accessed by the aspiration catheters via coaxial microcatheter/microwire-guiding alone due to insufficient push, or the clot cannot be approached by the aspiration catheter because the target vessel diameter is too small. In these cases, the stent retriever can be used as an anchor to guide the aspiration catheter as close as possible to the thrombus to perform a stent retriever TE with local aspiration. Implementation of the SAVE or Solumbra technique might have preserved from ETN in TE procedures in the current study. To prevent SAH, the stent retriever was released partially to adapt to the thrombus length, that is possible due to the repeating functional segments of the device. Thereby, the angulation of the stent retriever may be reduced to minimize shear stress and traction to the vessels. Perforation might be prevented by using microwires with soft tips instead of a standard tip, especially in distal M2-segments, and by shaping the microwire with a J-configuration.

A potential risk of the ADAPT technique is ETN by thrombus fragmentation. Thus, we prefer the Solumbra or SAVE technique. Based on our results, we estimate that the stent retriever-TE in M2-segments is not more traumatic than ADAPT, but for a final validation of both TE-approaches, larger trials or RCTs are necessary.

We have several limitations to admit. First, this study is limited by the low number of patients, especially in the subgroups of patients with proximal and distal M2-occlusions. Furthermore, there was no randomization by intention. Lastly, definition or terminology of the M2-segment anatomy is diverse in the literature, which may influence direct comparisons to other studies. Both, the ADAPT and the stent retriever TE appear comparable regarding to recanalization rate, procedural complications, and clinical outcome in M1-occlusions, but there are no RCTs that evaluated these techniques in particular for M2-TE.[23] At last, no recommendation for a special TE technique can be made. In our experience, the stent retriever TE techniques is feasible for challenging M2-thrombectomies, but choosing the most suitable technique depends on different factors including device properties, vessel anatomy, pre-interventional ASPECTS, operator experience, or clot composition and length.

Conclusion

The current findings suggest that clinical outcome, procedural safety, and efficacy of ET in patients with M1-occlusions might be comparable to ET in patients with M2-occlusions. Furthermore, ET in distal M2-segments might be as safe and efficient as in proximal M2-segments with comparable clinical outcome. Initial neurological deficits and the collateralization status appeared as significant factors influencing clinical outcome in patients with M1-occlusions undergoing ET. By contrast, clinical outcome in patients with M2-occlusions undergoing ET is more multifactorial. Further investigations with larger samples are needed to identify specific parameters influencing the functional outcome to select eligible patients for M2-thrombectomy.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Daniel Weiss https://orcid.org/0000-0002-3118-7627
Marius Kaschner https://orcid.org/0000-0001-6293-6240

References

1. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *New Engl Journal Medicine* 2015; 372(1): 11–20.
2. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *New Engl Journal Medicine* 2015; 372(11): 1019–1030.
3. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *New Engl J Med* 2015; 372(24): 2296–2306.
4. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *New Engl J Med* 2015; 372(24): 2285–2295.
5. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. *New Engl Journal Medicine* 2017; 378(1): 11–21.
6. Kaschner M. G., Weiss D., Rubbert C., et al. One-year single-center experience with the Aperio thrombectomy device in large vessel occlusion in the anterior circulation: safety, efficacy, and clinical outcome. *Neurol Sci* 2019; 40(7): 1443–1451.
7. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *New Engl Journal Medicine* 2015; 372(11): 1009–1018.
8. Salahuddin H, Ramaiah G, Slawski DE, et al. Mechanical thrombectomy of M1 and M2 middle cerebral artery occlusions. *J NeuroInterventional Surg* 2018; 10(4): 330–334.
9. Humphries W, Hoit D, Doss VT, et al. Distal aspiration with retrievable stent assisted thrombectomy for the treatment of acute ischemic stroke. *J NeuroInterventional Surg* 2015; 7(2): 90–94.
10. Maus V, Behme D, Kabbasch C, et al. Maximizing First-Pass Complete Reperfusion with SAVE. *Clin Neuroradiology* 2018; 28(3): 327–338.
11. Weiss D, Kraus B, Rubbert C, et al. Systematic evaluation of computed tomography angiography collateral scores for

estimation of long-term outcome after mechanical thrombectomy in acute ischaemic stroke. *Neuroradiology J* 2019; 32(4): 277–286.
12. Maas MB, Lev MH, Ay H, et al. Collateral vessels on CT angiography predict outcome in acute ischemic stroke. *Stroke* 2009; 40(9): 3001–3005.
13. Seker F, Potreck A, Möhlenbruch M, et al. Comparison of four different collateral scores in acute ischemic stroke by CT angiography. *J NeuroInterventional Surg* 2016; 8(11): 1116–1118.
14. Von Kummer R, Broderick JP, Campbell BCV, et al. The Heidelberg Bleeding Classification. *Stroke* 2015; 46(10): 2981–2986.
15. Faul F, Erdfelder E, Buchner A, et al. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods* 2009; 41(4): 1149–1160.
16. Wouters A, Nysten C, Thijs V, et al. Prediction of outcome in patients with acute ischemic stroke based on initial severity and improvement in the first 24 h. *Front Neurol* 2018; 9: 308.
17. Seker F., Pereira-Zimmermann B, Pfaff J, et al. Collateral scores in acute ischemic stroke : a retrospective study assessing the suitability of collateral scores as standalone predictors of clinical outcome. *Clin Neuroradiol* 2019.
18. Tomsick TA, Carrozzella J, Foster L, et al. Endovascular therapy of M2 occlusion in IMS III: role of M2 segment definition and location on clinical and revascularization outcomes. *Am J Neuroradiology* 2017; 38(1): 84–89.
19. Sheth SA, Jahan R, Gralla J, et al. Time to endovascular reperfusion and degree of disability in acute stroke. *Ann Neurology* 2015; 78(4): 584–593.
20. Ivan VL, Rubbert C, Caspers J, et al. Mechanical thrombectomy in acute middle cerebral artery M2 segment occlusion with regard to vessel involvement. *Neurol Sci* 2020.
21. Dorn F, Stehle S, Lockau H, et al. Endovascular treatment of acute intracerebral artery occlusions with the solitaire stent: single-centre experience with 108 recanalization procedures. *Cerebrovasc Dis* 2012; 34(1): 70–77.
22. Flores A, Tomasello A, Cardona P, et al. Endovascular treatment for M2 occlusions in the era of stentrievers: a descriptive multicenter experience. *J NeuroInterventional Surg* 2015; 7(4): 234–237.
23. Turk AS, Siddiqui A, Fifi JT, et al. Aspiration thrombectomy versus stent retriever thrombectomy as first-line approach for large vessel occlusion (COMPASS): a multicentre, randomised, open label, blinded outcome, non-inferiority trial. *The Lancet* 2019; 393(10175): 998–1008.

Die Publikation “Single-center experience with the new-generation Derivo embolization device for ruptured and unruptured intracranial aneurysms (2020). J Neurosurg Sci. 64:353-363“ kann gemäß den Bestimmungen des Verlages an dieser Stelle nicht abgedruckt werden. Die Publikation wird zur Einsicht von dem Autor bereitgestellt.

Original article

NRJ

The Neuroradiology Journal
0(0) 1–10

DOI: 10.1177/1971400919847182
journals.sagepub.com/home/neu

SAGE

Systematic evaluation of computed tomography angiography collateral scores for estimation of long-term outcome after mechanical thrombectomy in acute ischaemic stroke

Daniel Weiss[1], Bastian Kraus[1], Christian Rubbert[1], Marius Kaschner[1], Sebastian Jander[2], Michael Gliem[2], John-Ih Lee[2], Carl-Albrecht Haensch[3], Bernd Turowski[1] and Julian Caspers[1]

Abstract

Purpose: This study compares computed tomography angiography-based collateral scoring systems in regard to their inter-rater reliability and potential to predict functional outcome after endovascular thrombectomy, and relates them to parenchymal perfusion as measured by computed tomography perfusion.

Methods: Eighty-four patients undergoing endovascular thrombectomy in anterior circulation ischaemic stroke were enrolled. Modified Tan Score, Miteff Score, Maas Score and Opercular Index Score ratio were assessed in pre-interventional computed tomography angiographies independently by two readers. Collateral scores were tested for inter-rater reliability by weighted-kappa, for correlations with three-months modified Rankin Scale, and their potential to differentiate between patients with favourable (modified Rankin Scale $\leq$2) and poor outcome (modified Rankin Scale $\geq$3). Correlations with relative cerebral blood volume and relative cerebral blood flow were tested in patients with available computed tomography perfusion.

Results: Very good inter-rater reliability was found for Modified Tan, Miteff and Opercular Index Score ratio, and substantial reliability for Maas. There were no significant correlations between collateral scores and three-months modified Rankin Scale, but significant group differences between patients with favourable and poor outcome for Maas, Miteff and Opercular Index Score ratio. Miteff and Maas were significant predictors of favourable outcome in binary logistic regression analysis. Miteff best differentiated between both outcome groups in receiver-operating characteristics, and Maas reached highest sensitivity for favourable outcome prediction of 96%. All collateral scores significantly correlated with mean relative cerebral blood volume and relative cerebral blood flow.

Conclusions: Computed tomography angiography scores are valuable in estimating functional outcome after mechanical thrombectomy and reliable across readers. The more complex scores, Maas and Miteff, show the best performances in predicting favourable outcome.

Keywords

Collateral scores, ischaemic stroke, thrombectomy, computed tomography angiography, computed tomography perfusion

Introduction

In recent years, endovascular thrombectomy (ET) has greatly gained importance in the treatment of acute ischaemic stroke (AIS) due to arterial occlusion.[1–4] In this regard, one of the outstanding goals of current research is to reliably estimate the opportunity to achieve a favourable functional outcome before initiating therapy, to reasonably consider whether ET should be performed. One of the main research topics was the influence of time until recanalization on the long-term outcome. Major studies initially indicated that patients benefited from revascularization within six[1,3] or eight hours[4] after symptom onset. More recently it has been shown that revascularization even after more than 12 h after symptom onset may be of benefit for patients, if certain criteria are met.[5,6] However, in addition to the time since symptom onset, the major factor for

[1]Medical Faculty, Department of Diagnostic and Interventional Radiology, University Duesseldorf, Moorenstr. 5, 40225 Duesseldorf, Germany
[2]Medical Faculty, Department of Neurology, University Duesseldorf, Moorenstr. 5, 40225 Duesseldorf, Germany
[3]Department of Neurology, Krankenhaus St Franziskus, Viersener Str. 450, 41063 Mönchengladbach, Germany

Corresponding author:
Bastian Kraus, Department of Diagnostic and Interventional Radiology, University Hospital Düsseldorf, Medical Faculty, Moorenstr. 5, 40225 Düsseldorf, Germany.
Email: Bastian.Kraus@med.uni-duesseldorf.de

estimating patient outcome in AIS is the residual blood supply of the affected brain tissue provided by collaterals.[7,8] Computed tomography perfusion (CT-P) features, especially mismatch ratio and infarct core, are of major importance in this regard.[9–11]

However, standardised CT-P is strongly dependent on patient compliance regarding head movement and is yet not routinely performed in all institutions. In this regard, it has to be considered that CT-P is an additional time-consuming examination associated with additional radiation exposure and an increased volume of contrast agent compared with non-contrast cranial computed tomography plus computed tomography angiography (CT-A) alone. Especially in the case of a blood-brain-barrier disruption, additional volume of contrast agent may enlarge toxic effects on brain tissue. Nevertheless, if CT-P is performed, it is basically considered as reliable, safe and diagnostically important examination.

CT-A is able to capture intracranial vessel status even in moderately agitated patients and is nowadays broadly available. CT-A allows for an estimation of collateralization and may thus be a cornerstone in the process of indicating mechanical revascularization when CT-P is not performed.[12–15]

Different scoring systems have been introduced to assess and describe the collateralization status.[10,13,15,16] However, no systematic evaluation of these scoring systems has been conducted, yet. In particular, it is unclear, how well these scores reflect parenchymal collateralization and perfusion, and if they can be used as predictors of functional outcome after recanalization in AIS.

The purpose of this study was to systematically evaluate four established and frequently used CT-A collateral scoring systems, namely the Modified Tan (mTan) Score,[11] the Miteff Score,[10] the Maas Score[13] and the more recently introduced Opercular Index Score ratio (OISr).[16]

The inter-rater reliability of each score, their potential to predict functional outcome after ET in AIS and their correlation with CT-P measurements was assessed.

Material and methods

Patient selection

All patients undergoing ET in acute ischaemic stroke at the local department of Diagnostic and Interventional Radiology between June 2016–June 2017 were prospectively enrolled. The inclusion criteria for the current study were: (a) anterior circulation vessel occlusion, i.e. of the internal carotid artery, the sphenoidal or proximal insular segment of the middle cerebral artery (MCA) or tandem occlusions; (b) available and technically sufficient CT-A images (c) available three--month modified Rankin Scale (mRS). The patient sample comprised patients directly admitted to the local department as well as patients initially admitted to an external hospital for evaluation of AIS including neuro-imaging and then referred to the local department for mechanical recanalization. The procedure of ET was performed in a standardised manner.[17,18] The indication for ET was determined by the neuroradiologist and neurologist on duty in accordance with current guidelines.[19] The study was approved by the local institutional review board (ID: 5468R). Written informed consent for inclusion in the study was obtained from all patients or their next of kin. When patients passed away during hospitalization, written informed consent was waived.

Imaging and post-processing

Imaging protocols of the seven referring facilities differed. To ensure comparable image quality throughout the analysis, only patients with sufficiently contrasted CT-A scans and images with a slice thickness of maximally 2.0 mm in axial plane were included in the current analysis. CT-A scans were considered technically sufficient if intracranial arteries of the non-affected side showed good opacification and terminal branches of the external carotid artery were contrasted. If not provided by the referring hospital, coronal and sagittal multiplanar reformations (MPRs) as well as maximum intensity projections (MIPs) in the axial, coronal and sagittal plane were obtained for further analysis using the local Picture Archiving and Communication System (PACS; IDS7, Sectra, Linköping, Sweden).

Patients directly admitted to our local department were examined with a standardised stroke protocol including non-contrast enhanced cranial computed tomography, CT-A and CT-P.

CT-A was performed covering the brain supplying and intracranial arteries from the aortic arch to the vertex with continuous axial sections parallel to the orbitomeatal line. CT-A parameters were 120 kVp, 100 mAs, 128×0.6 mm collimation, 1 s/rotation, table feed of 1 mm/rotation, and active tube current modulation (SOMATOM Definition FLASH, 128-slices, Siemens, Erlangen, Germany), or 120 kVp, 175 mAs, 64×0.6 mm collimation, 1 s/rotation, table feed of 1 mm/rotation, and active tube current modulation (SOMATOM Definition AS with sliding gantry, 64-slices, Siemens, Erlangen, Germany).

An intravenous single bolus contrast agent injection (weight-dependent 70–80 ml iomeprol 400 mg J/ml, Imeron, Bracco, Konstanz, Germany), followed by a 30 ml saline solution bolus was injected by an automated injector via an at least 18-gauge intravenous line in an antecubital vein or a high-flow central intravenous line at 5 ml/s. Image acquisition was started by automatic bolus tracking using a region of interest (ROI) placed in the ascending aorta.

Axial CT-A images of 0.75 and 4 mm, 1 mm coronal and sagittal MPRs as well as 9 mm MIPs in the axial, coronal and sagittal plane were reconstructed.

CT-P was acquired with two adjacent slices of 1 cm thickness angled parallel to the Frankfurt horizontal line at the level of the cella media over 50 s with one image per second. CT-P parameters were 80 kVp, 180 mAs, 1×10 mm collimation (SOMATOM Definition FLASH) or 80 kVp, 120 mAs, 64×0.6 mm collimation (SOMATOM Definition AS). For CT-P, a second bolus of contrast agent of 30 ml iomeprol 400 followed by a 30 ml saline solution bolus was injected at 5 ml/s. Image acquisition started with a three-second delay after injection.

Image analysis

Retrospective assessment of CT-A collateral scores was performed independently by two readers with different levels of experience, i.e. one senior interventional neuroradiologist (BK) with nine years experience in (neuro-) radiology and one specifically trained final-year medical student (DW), extensively instructed and trained in the evaluation of CT-A collaterals on studies not included in the current analysis. An exemplary assessment of collateral scores in two patients is shown in Figure 1.

The assessment of individual scores was based on the definitions given in the respective original publications and conducted as follows:

mTan Score. The mTan Score[11] classifies vessel opacification of the affected MCA territory as $\geq$50% (good) and less than 50% (poor) in comparison with the opposite side [15] (similar to the Miteff and Maas Score).

Miteff Score. The scoring system of Miteff et al.[10] is based on the topography of opacified branches in the affected MCA territory. It is divided into three categories: (a) only distal superficial MCA branches are reconstituted; (b) some vessels in the Sylvian fissure show opacification; (c) the entire MCA distal to the occlusion is reconstituted.[15]

Maas Score. The scoring system of Maas et al.[13] classifies vessel opacification of the affected MCA territory in five categories: (a) there is no vessel opacification in the affected MCA territory; (b) vessel opacification is lower compared with the opposite side; (c) both MCA territories are opacified similarly; (d) opacification of the affected MCA territory is higher compared with the

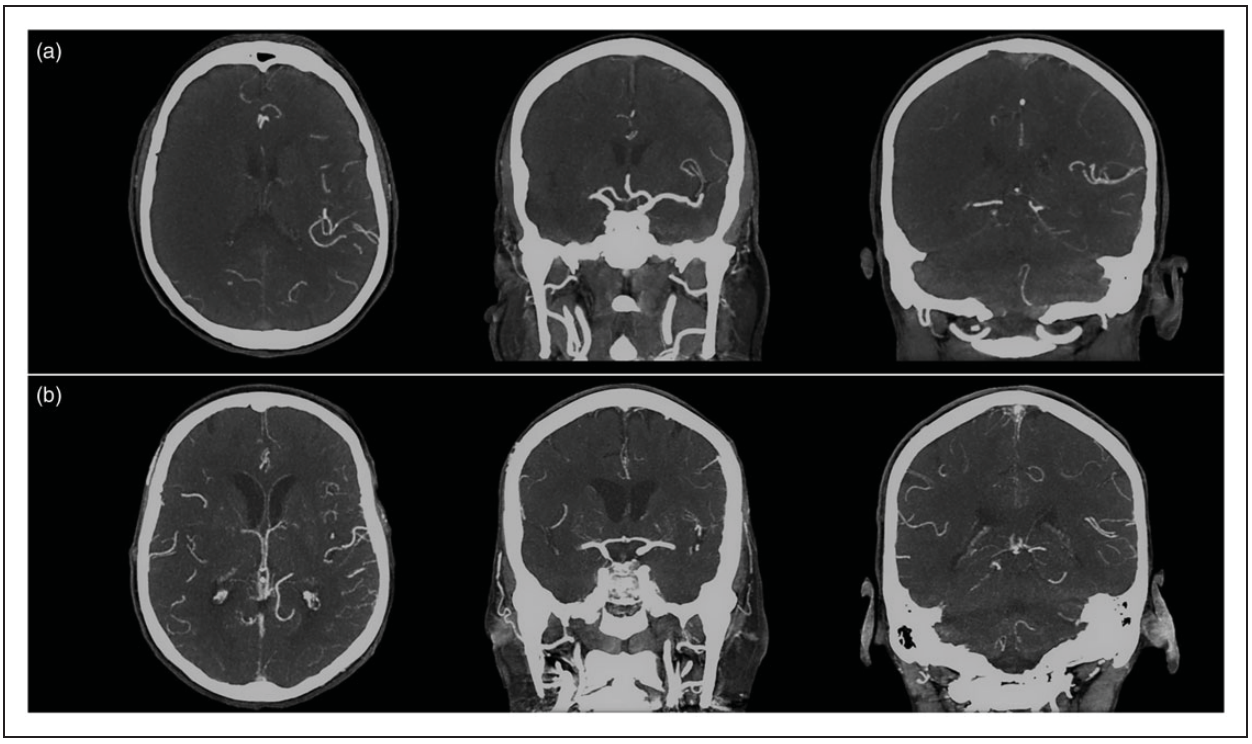


Figure 1. Examples of computed tomography angiography (CT-A) scans and survey of collateral scores. Exemplary CT-A scans of two patients with right middle cerebral artery (MCA) occlusion. A representative axial and two coronal CT-A maximum intensity projections (MIPs) are shown. (a) Patient with insufficient collaterals. Modified Tan (mTan) Score was one, Miteff Score was one, Maas Score was one, Opercular Index Score ratio was >2, modified Rankin Scale (mRS) after three months was six. (b) Patient with good collaterals. mTan Score was two, Miteff Score was three, Maas Score was three, Opercular-Index-Score-ratio was one, mRS after three months was zero.

opposite side; (e) opacification of the affected MCA territory is exuberant.[15]

Opercular Score. The Opercular Index Score (OIS)[16] is based on the number of opacified opercular branches of the affected MCA territory compared with the opposite side in coronal images. Based on the number of opacified branches, the number of the opacified branches of the unaffected MCA territory is divided by the number of the opacified branches of the affected side to determine the OIS ratio (OISr). Two categories of the OISr are discriminated: (a) OISr ≤ 2 (good) and (b) OISr > 2 (poor).[16]

mTan, Miteff and Maas scores were evaluated in 9 mm axial MIP reconstructions of CT-A images parallel to the orbitomeatal line at basal ganglia level. OIS was assessed in 9 mm coronal MIP reconstructions of CT-A images.

For the subgroup of patients with standardised CT-P imaging available perfusion maps including time to maximum (TMax), mean transit time (MTT), relative cerebral blood volume (rCBV), and relative cerebral blood flow (rCBF) were calculated using singular value decomposition (STROKETOOL-CT, Version 2.0, H.-J. Wittsack, DIS, Frechen, Germany). The arterial input function was determined automatically or, if automatic detection failed, manually defined by choosing up to 10 reference points in the most opacified arterial vessels. Subsequent extraction of territorial rCBV and rCBF values from CT-P parameter maps was done using Angiotux CT 2D (ECCET 2006/Beck A, Aurich V, Langenfeld, Germany).[20] Mean values of affected MCA territory were divided by the mean values of the unaffected MCA territory to calculate rCBV ratio and rCBF ratio.

Outcome analysis

The functional outcome of patients was evaluated using the mRS three months after ET. mRS was assessed by a standardised telephone interview performed by one investigator (DW). Patients were dichotomised by mRS into favourable outcome (mRS ≤ 2) and poor outcome (mRS ≥ 3).

Statistical analysis

Statistical analysis was performed with SPSS software environment (Statistical Package for Social Science, version 24, IBM, Armonk, New York, USA). A p value <0.05 was considered statistically significant for all analyses.

Inter-rater reliability between the two readers for each collateral score was assessed by calculating weighted-kappa statistics (k), which takes the level of disagreement between readers into account.

For further statistical analyses, the median between both investigators for each collateral score was used. Correlations between each collateral score and mRS after three months were determined using Spearman's correlation coefficients. Group comparisons between the mRS subgroups were conducted with Mann–Whitney U-tests for each collateral score.

In the subgroup of patients with standardised CT-P available, mean rCBF and mean rCBV of the affected MCA territory, as well as rCBF and rCBV ratios, were correlated with functional outcome and with each collateral score using Spearman correlations. Group comparisons for these CT-P parameters between the mRS subgroups were performed using Student's t-test.

Binary logistic regression models were calculated for each collateral score. The models included the respective collateral score, age, National Institutes of Health Stroke Scale (NIHSS) at admission and onset-to-groin-puncture time as independent variables and dichotomised three-months mRS as dependent variable. Associations between each independent variable and favourable functional outcome adjusted for the other three independent variables were analysed. For assessment of model quality Nagelkerkes R^2 was used. Furthermore, odds ratios with confidence intervals as well as regression coefficients were calculated.

Collateral scores and perfusion parameters were analysed for their test quality for prediction of favourable outcome using receiver-operating characteristic (ROC) analysis with calculation of the area under the curve (AUC) and subsequent determination of Youden's J index to establish cut-off points. For unified presentation of results, ROC analysis for OISr was performed with poor outcome as state variable.

Results

Eighty-four patients were included in the current analysis. Mean age was 75 ($\pm$14) years and 53.6% of all patients were female. MCA was the most frequently occluded vessel (M1 segment, 73.8%). Median Alberta Stroke Program Early CT Score (ASPECT) Score at admission was 10 (interquartile range (IQR) 9–10) and median NIHSS at admission was 14 (IQR 10–18). Most patients achieved a level of reperfusion after mechanical recanalization of thrombolysis in cerebral infarction (TICI) 3 (36.9%). Thirty-one (37%) patients showed a favourable outcome (mRS ≤ 2) and fifty-three (63%) patients a poor outcome (mRS ≥ 3) (Table 1).

Analysis of inter-rater reliability of collateral scores indicated very good inter-rater reliability for mTan Score ($k = 0.86$), Miteff Score ($k = 0.81$) and OISr ($k = 0.91$), as well as a substantial reliability for Maas Score ($k = 0.77$).

There were no significant correlations between collateral scores and three-months mRS. However, there were significant group differences between patients with favourable and poor outcome for all collateral scores, except for mTan (Table 2).

In patients with available CT-P, mean rCBF and mean rCBV showed moderate and statistically

Table 1. Baseline characteristics.

	Total ($n = 84$)	mRS ≤ 2 ($n = 31$)	mRS ≥ 3 ($n = 53$)
Age, mean, (SD, min-max) in years	75 (±14, 27–99)	68 (±14, 27–93)	79 (±12, 45–99)
Female sex, *n*, (%)	45 (53.6)	14 (45.2)	31 (58.5)
Left hemisphere, *n*, (%)	48 (57.1)	16 (51.6)	32 (60.4)
Location of occlusion, *n*, (%)			
ICA	10 (11.9)	3 (9.7)	7 (13.2)
T-type	8 (9.5)	1 (3.2)	7 (13.2)
M1	62 (73.8)	24 (77.4)	38 (71.7)
M2	4 (4.8)	3 (9.7)	1 (1.9)
Local department, *n*, (%)	39 (46.4)	12 (38.7)	27 (50.9)
ASPECTS at admission, median, (IQR)	10 (9–10)	10 (9–10)	10 (9–10)
NIHSS at admission, median, (IQR)	14 (10–18)	11 (8–16)	16 (13–19)
Door-to-groin-puncture, mean, (SD, min-max) in min	145 (±113, 15–775)	172 (±166, 23–775)	130 (±65, 15–385)
Onset-to-groin-puncture, mean, (SD, min-max) in min	188 (±81, 60–495)	189 (±88, 70–495)	188 (±78, 60–385)
TICI Score, *n*, (%)			
0	5 (6.0)	0 (0)	5 (9.4)
1	1 (1.2)	0 (0)	1 (1.9)
2a	3 (3.6)	1 (3.2)	2 (3.8)
2b	28 (33.3)	9 (29.0)	19 (35.8)
2c	16 (19.0)	7 (22.6)	9 (17.0)
3	31 (36.9)	14 (45.2)	17 (32.1)
mTan Score, median, (IQR)[a]	2.0 (1.0–2.0)	2.0 (1.0–2.0)	1.5 (1.0–2.0)
Miteff Score, median, (IQR)[a]	2.5 (1.5–3.5)	3.0 (2.0–3.0)	2.0 (1.0–3.0)
Maas Score, median, (IQR)[a]	2.0 (2.0–2.5)	2.0 (2.0–3.0)	2.0 (2.0–2.5)
Operculum Index Score ratio, median, (IQR)[a]	1.0 (1.0–2.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)
CT-P, *n*, (%)	46 (55)	15 (48)	31 (58)
rCBF ratio, mean, (SD, min-max)	0.61 (±0.27, 0.14–1.19)	0.70 (±0.26, 0.39–1.19)	0.57 (±0.26, 0.14–1.13)
rCBV ratio, mean, (SD, min-max)	0.79 (±0.37, 0.02–1.49)	0.93 (±0.29, 0.48–1.49)	0.71 (±0.39, 0.02–1.34)
rCBF mean, mean, (SD, min-max)	59.81 (±46.90, 11.44–254,05)	69.92 (±36.90, 25.39–155.63)	54.91 (±50.87, 11.44–254.05)
rCBV mean, mean, (SD, min-max)	22.94 (±13.95, 1.85–69.11)	31.45 (±15.05, 31.45–69.11)	18.82 (±11.50, 1.85–45.85)

ASPECTS: Alberta Stroke Program Early CT Score; CT-P: computed tomography perfusion; ICA: internal carotid artery; IQR: interquartile range; IVT: intravenous thrombolysis; mRS: modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; rCBF: relative cerebral blood flow; rCBV: relative cerebral blood volume; SD: standard deviation; TICI: thrombolysis in cerebral infarction. [a]Values assessed by two independent examiners and not rounded to nearest integer.

significant correlations with functional outcome. In contrast, rCBF ratio and rCBV ratio did not show significant correlations with functional outcome (Table 2). There were significant group differences between patients with favourable and poor outcome for mean rCBV and rCBV ratio, but not for mean rCBF and rCBF ratio. All collateral scores showed strong or moderate and statistically significant correlations with rCBF ratio and rCBV ratio, where highest correlations were found between mTan and rCBF ratio, and between OISr and rCBF ratio (Table 3). All collateral scores showed moderate correlations with mean rCBF and mean rCBV, whereas significance of these correlations was only reached for mTan, Miteff and Maas score, but not for OISr. Miteff Score showed the highest correlations with mean rCBF and mean rCBV.

In ROC analyses (Table 4, Figure 2) highest AUC among the four collateral scores were found for Miteff Score and lowest AUC for mTan. However, mean rCBF, mean rCBV and rCBV ratio from the CT-P subsample performed even better in ROC analysis than all collateral scores, whereas the highest AUC was found for mean rCBV. Maas score reached a comparable high AUC compared with Miteff and had a very high sensitivity for good clinical outcome of 96% at the cutoff of 1.75, but low specificity. This high sensitivity was even exceeded by rCBF and rCBV ratios with 100% sensitivity.

Binary logistic regression analysis yielded one model for each collateral score (Figure 3). In every model, NIHSS at admission was a significant factor. The models for mTan Score and OISr showed a moderate,

and the models for Miteff Score and Maas Score a high, explanation of variance. Maas Score was the only collateral score in its corresponding model, which was a significant independent predictor for favourable outcome.

Discussion

The aim of this study was to evaluate the clinical applicability and usefulness of four CT-A collateral scores. Collateral scores can be of high value in management and treatment decision making in AIS, especially when CT-P is not available or is considered unfeasible. In the following sections, we will discuss the inter-rater reliability and potential of predicting a favourable outcome for each score, as well as the score value compared with CT-P features.

Reliability of CT-A collateral scores

Related to their inter-rater reliability, basically all collateral scores are useable and achieve convincing results. Other investigators have shown comparable results in inter-rater reliability for mTan Score.[14,15] Minor differences may be caused by a greater experience of the readers in Yeo et al.'s study.[15] Slightly lower inter-rater reliability of Miteff Score and Maas Score compared with mTan Score and OISr are probably reasoned by the more complex survey of Miteff Score and Maas Score. Best inter-rater reliability was found for OISr, which may be reasoned by the more objective assessment based on counting opacified vessels, compared with the other three scoring systems.

Predictivity of functional outcome

We could show, that mTan Score only weakly correlates with functional outcome and could not discriminate between favourable and poor outcome on the group level. The reason for this may be found in the relatively coarse classification of collateralization into only two classes, which cannot capture gradations of collateralization at the border between full and missing collaterals and, hence, may have limited ability to predict functional outcome by design. Yeo et al.[15] showed that mTan Score is able to distinguish between favourable and poor outcome in AIS patients treated with the intravenous tissue plasminogen activator (t-PA). The divergent results between this trial and our results regarding differentiation of both outcome groups may be caused by the larger population size and the different treatment. A more recent study by Nordmeyer et al.[21] took use of the unmodified Tan Score, which uses more

Table 2. Group comparisons and correlations with modified Rankin Scale (mRS) for collateral scores and computed tomography perfusion (CT-P) values.

	Group comparison (favourable vs poor outcome)	Correlation with mRS
mTan Score	$p = 0.08$	$r_s = -0.14$, $p = 0.12$
Miteff Score	$p = 0.01$[a]	$r_s = -0.14$, $p = 0.12$
Maas Score	$p = 0.03$[a]	$r_s = -0.15$, $p = 0.11$
OISr	$p = 0.05$[a]	$r_s = 0.14$, $p = 0.13$
Mean rCBF	$p = 0.16$	$r_s = -0.332$, $p = 0.01$[a]
Mean rCBV	$p = 0.001$[b]	$r_s = -0.436$, $p = 0.01$[a]
rCBF ratio	$p = 0.06$	$r_s = -0.223$, $p = 0.07$[a]
rCBV ratio	$p = 0.03$[a]	$r_s = -0.183$, $p = 0.11$

OISr: Opercular Index Score ratio; rCBF: relative cerebral blood flow; rCBV: relative cerebral blood volume. Values of p of group comparisons (Mann–Whitney U-test for collateral scores, Student t-test for CT-P parameters) between patients with favourable and poor outcome as well as Spearmans's rho (r_s) and respective p-values for correlations with mRS after three months are given for collateral scores and CT-P parameters. [a]$p < 0.05$, [b]$p < 0.01$.

Table 4. Receiver operating characteristics analyses for collateral scores and computed tomography perfusion (CT-P) parameters.

	AUC (95% CI)	J (Cut-off)	Sensitivity	Specificity
mTan Score	0.59 (0.45–0.78)	0.17 (1.25)	69%	48%
Miteff Score	0.64 (0.51–0.82)	0.23 (2.75)	50%	73%
Maas Score	0.61 (0.48–0.75)	0.19 (1.75)	96%	23%
OISr	0.60 (0.46–0.73)	0.19 (1.25)	48%	71%
rCBF ratio	0.61 (0.44–0.78)	0.29 (0.38)	100%	29%
rCBV ratio	0.67 (0.51–0.82)	0.36 (0.48)	100%	35%
Mean rCBF	0.70 (0.54–0.86)	0.47 (57.15)	67%	81%
Mean rCBV	0.76 (0.62–0.90)	0.48 (22.05)	80%	68%

AUC: area under the curve; CI: confidence interval; J: Youden's Index; mTan: Modified Tan; OISr: Opercular Index Score ratio; rCBF: relative cerebral blood flow; rCBV: relative cerebral blood volume.

Table 3. Correlations between computed tomography perfusion (CT-P) parameters and collateral scores.

	mTan Score	Miteff Score	Maas Score	OISr
Mean rCBF	$r_s = 0.33$, $p = 0.01$[a]	$r_s = 0.42$, $p = 0.002$[b]	$r_s = 0.38$, $p = 0.005$[b]	$r_{s=} -0.35$, $p = 0.009$[b]
Mean rCBV	$r_s = 0.35$, $p = 0.01$[a]	$r_s = 0.42$, $p = 0.002$[b]	$r_s = 0.40$, $p = 0.003$[b]	$r_s = -0.37$, $p = 0.007$[b]
rCBF ratio	$r_s = 0.59$, $p < 0.001$[b]	$r_s = 0.45$, $p < 0.001$[b]	$r_s = 0.44$, $p = 0.001$[b]	$r_s = -0.58$, $p < 0.001$[b]
rCBV ratio	$r_s = 0.48$, $p < 0.001$[b]	$r_s = 0.43$, $p = 0.002$[b]	$r_s = 0.53$, $p < 0.001$[b]	$r_s = -0.49$, $p < 0.001$[b]

r_s: Spearman's rho; OISr: Opercular Index Score ratio; rCBF: relative cerebral blood flow; rCBV: relative cerebral blood volume. [a]$p < 0.05$, [b]$p < 0.01$.

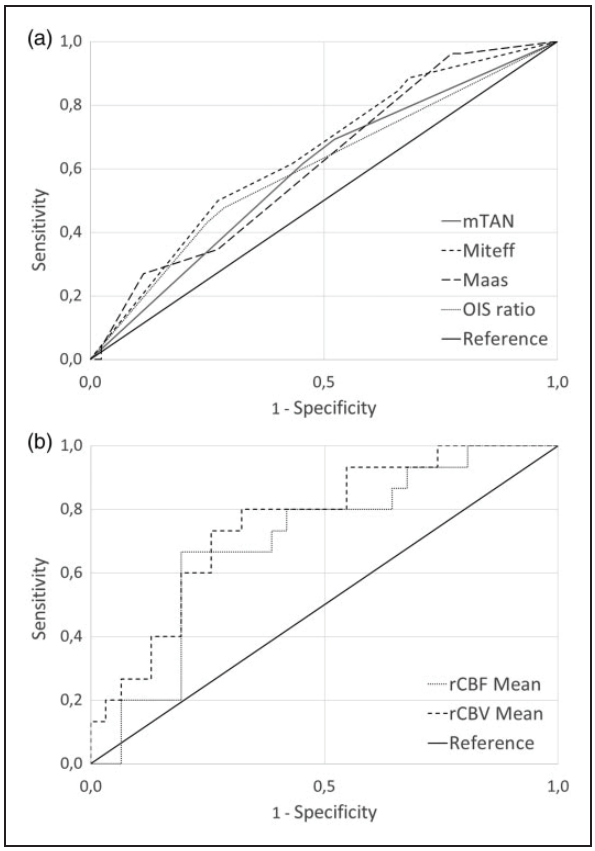


Figure 2. Receiver operating characteristic analyses. Receiver operating characteristic curves for (a) Modified Tan (mTan) Score, Miteff Score, Maas Score and Opercular Index Score (OIS) ratio and for (b) relative cerebral blood flow (rCBF) mean and relative cerebral blood volume (rCBV) mean to estimate long term functional outcome by means of three-months modified Rankin Scale (mRS). For illustration purposes, receiver operating characteristic analysis for OIS ratio was referred to poor outcome prediction to facilitate visual comparability.

classes than the mTan Score. They found that the score is an independent predictor of death in follow-up after discharge, but, similarly to our results, could not find a significant effect in dichotomised mRS.

The Miteff Score showed the highest correlation coefficient with functional outcome among the tested collateral scores, significant differences between favourable and poor outcomes and reached the highest AUC in ROC analysis. A study examining the functional outcome of patients receiving systemic intravenous t-PA in AIS showed a better prediction of outcome using the Miteff Score compared with the Maas Score and the mTan Score.[15] This is in line with our results regarding the higher correlation of Miteff with three-months mRS and its higher AUC in ROC analysis compared with both scores. However, after adjustment in binary logistic regression analysis, the Maas Score achieved better results than the Miteff Score.

The Maas Score revealed significant differences between patients with favourable and poor outcome and showed moderate, but not significant, correlation with three-months mRS, that was higher than that for the mTan and the OISr but lower compared with Miteff. Previous investigators showed that favourable collateral state measured with Maas Score is associated with favourable outcome.[14,15] It obtained the best results in binary logistic regression analyses compared with the other collateral scores. Furthermore, the Maas Score reached by far the highest sensitivity for the prediction of favourable outcome in ROC analysis.

We only found a weak correlation between the OISr and functional outcome, but significant differences between patients with favourable and poor outcome. Compared with the study introducing the OISr, our findings indicate a much lower sensitivity and specificity for the prediction of functional outcome in the entire patient sample.[16] A reason for these differences may be the substantially lower number of patients in the original study or differences in study design between the two studies.

The results of binary logistic regression models of Miteff and Maas Scores emphasise the relevance of collateral status for patient outcome in AIS and indicate that collateralization is even more important than the factor time, which is commonly focused on when contemplating AIS management and treatment. This appraisal is underpinned by recent large randomised trials as the Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo (DAWN) study[5] or the Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3 (DEFUSE 3) study,[6] which show that the factor time is not that restrictive for indication of ET and patients could benefit from endovascular therapy even 24 h after stroke-onset depending on their collateral status in cerebral perfusion.[5] Several other studies show similar results regarding the relationship between collaterals, time and functional outcome.[7,22]

Overall, the more complex scores, Maas and Miteff, perform best for the prediction of functional outcome. Given the high predictive value and high sensitivity of 96% at the cutoff of 1.75 for the Maas Score, this score seems to be most favourable for decision-making in endovascular treatment planning in AIS. In this regard, patients with a Maas Score of ≥ 2 have the potential to profit from thrombectomy, while patients with a score of one have virtually no potential to achieve good outcome and could be considered to be excluded from endovascular treatment. However, this result should be confirmed in larger study samples.

CT-P and collateral scores

A more direct assessment of brain perfusion and collateralization can be achieved with analysis of CT-P measurements.[22,23] The prognostic value of CT-A and CT-P was emphasised by the results of van Seeters et al.,[12] which showed that CT-A and CT-P parameters could successfully differentiate between favourable and

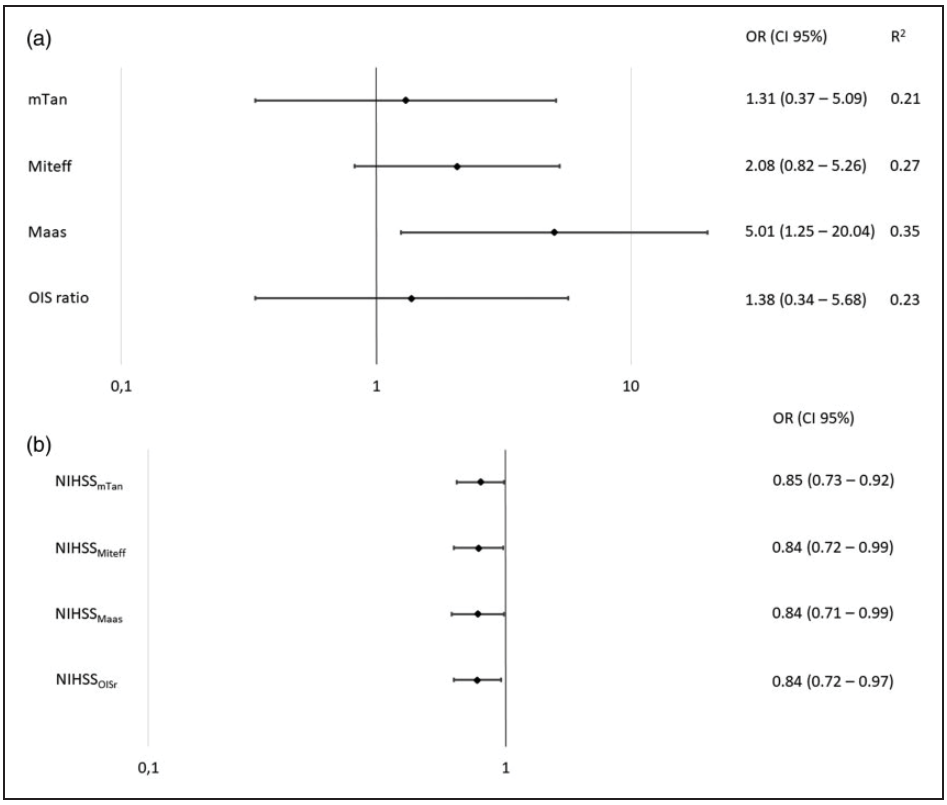


Figure 3. Binary logistic regression analyses. Forest plots indicating odds ratios (ORs) and confidence intervals (CIs) for the binary logistic regression models for each collateral score and corresponding National Institutes of Health Stroke Scale (NIHSS) are shown. For illustration purposes, binary logistic regression for Opercular Index Score ratio (OISr) was referred to poor outcome prediction to facilitate visual comparability. mTan: modified Tan.

poor outcome, which is in line with our results. It has already been shown that there are significant correlations between rCBV and collateral scores in an analysis of the Solitaire™ With the Intention For Thrombectomy as PRIMary Endovascular Treatment (SWIFT PRIME) trial data,[9] which is in line with our results. Furthermore, it was shown that rCBV is able to mark cerebral collaterals and possible survival of tissue-at-risk.[9,24]

In this analysis, mean rCBV showed a high and statistically significant correlation with functional outcome, which was higher than for any collateral score. Furthermore, the differences between patients with favourable and poor outcome were highly significant and it showed a high AUC in ROC analysis compared with the four collateral scores. Miteff Score correlates best with rCBV mean, followed by the Maas Score, which reflects their good applicability for the prediction of functional outcome. While the means of rCBV and rCBF performed better in outcome prediction, corresponding ratios yielded better results for correlation with collateral scores due to their methodical proximity.

It was shown that collaterals assessed with dynamic CT-A showed a stronger association with radiological outcome than with single-phase CT-A.[25] Nevertheless, dynamic CT-A comes along with the major limitation of high radiation dose and that comprehensive availability is not given for initial diagnostics at all institutions. Regarding minor institutions or patient cases in which a higher radiation exposure should be avoided, single-phase CT-A collateral scores may be more applicable. This also concerns cases where patients are too agitated to provide a valid CT-P or when total volume of contrast agent should be limited.

Limitations

We have several limitations to admit. First, this study is limited by the total number of patients. The imaging protocols are not uniform across the sample, as some patients were referred to the local department from external hospitals. Intentionally, CT-A protocols in this study differ to reflect a realistic setting of a major institution for stroke treatment, treating internal as well as externally referred patients. Additionally, the external validity is raised by this approach and results are more generalisable. We ensured that neuroimaging of all included patients reached a minimum standard which allowed sufficient analysis. Additionally, two different CT scanner types (64 and 128 detector rows) were used for local image acquisition. Again, the use of different scanners should raise generalisability of results and represents a realistic setting in medical

care. Means of rCBV and rCBF are limited in their usability due to their missing standardization across analysis software and missing global thresholds. Due to this issue, interpretation of ratios of rCBV and rCBF is preferable and decisions on absolute mean values only reliably applicable at the same institution with standardised processes. Another point that might be raised is the low level of experience of one of the two raters. We indeed chose the design with one experienced and one unexperienced rater by intention, as a valuable collateral score should be reliably reproducible for readers, independent of their level of experience.

Conclusions

CT-A collateral scores are valuable tools for estimation of collateralization, as they are highly reliable and potent to predict functional outcome after ET in AIS, although to a different degree. The more complex scores, Miteff Score and Maas Score, are preferable because of their better performance in outcome prediction. Especially the Maas Score can be particularly useful for selecting patients for endovascular treatment. However, if available, CT-P should be favoured over using single-phase CT-A collateral scores.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

ORCID iD

Daniel Weiss https://orcid.org/0000-0002-3118-7627

References

1. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med* 2015; 372: 11–20.
2. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med* 2015; 372: 1019–1030.
3. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med* 2015; 372: 2296–2306.
4. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med* 2015; 372: 1009–1018.
5. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med* 2018; 378: 11–21.
6. Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med* 2018; 378: 708–718.
7. Sharma R, Llinas RH, Urrutia V, et al. Collaterals predict outcome regardless of time last known normal. *J Stroke Cerebrovasc Dis* 2017; 27: 971–977.
8. Christoforidis GA, Vakil P, Ansari SA, et al. Impact of pial collaterals on infarct growth rate in experimental acute ischemic stroke. *AJNR Am J Neuroradiol* 2017; 38: 270–275.
9. Arenillas JF, Cortijo E, Garcia-Bermejo P, et al. Relative cerebral blood volume is associated with collateral status and infarct growth in stroke patients in SWIFT PRIME. *J Cereb Blood Flow Metab* 2017; 38: 1839–1847.
10. Miteff F, Levi CR, Bateman GA, et al. The independent predictive utility of computed tomography angiographic collateral status in acute ischaemic stroke. *Brain* 2009; 132: 2231–2238.
11. Tan IY, Demchuk AM, Hopyan J, et al. CT angiography clot burden score and collateral score: Correlation with clinical and radiologic outcomes in acute middle cerebral artery infarct. *AJNR Am J Neuroradiol* 2009; 30: 525–531.
12. van Seeters T, Biessels GJ, Kappelle LJ, et al. The prognostic value of CT angiography and CT perfusion in acute ischemic stroke. *Cerebrovasc Dis* 2015; 40: 258–269.
13. Maas MB, Lev MH, Ay H, et al. Collateral vessels on CT angiography predict outcome in acute ischemic stroke. *Stroke* 2009; 40: 3001–3005.
14. Tan BY, Wan-Yee K, Paliwal P, et al. Good intracranial collaterals trump poor ASPECTS (Alberta Stroke Program Early CT Score) for intravenous thrombolysis in anterior circulation acute ischemic stroke. *Stroke* 2016; 47: 2292–2298.
15. Yeo LL, Paliwal P, Teoh HL, et al. Assessment of intracranial collaterals on CT angiography in anterior circulation acute ischemic stroke. *AJNR Am J Neuroradiol* 2015; 36: 289–294.
16. Copelan A, Chehab M, Brinjikji W, et al. Opercular Index Score: A CT angiography-based predictor of capillary robustness and neurological outcomes in the endovascular management of acute ischemic stroke. *J Neurointerv Surg* 2017; 9: 1179–1186.
17. Kaschner MG, Caspers J, Rubbert C, et al. Mechanical thrombectomy in MCA-mainstem occlusion in patients with low NIHSS scores. *Interv Neuroradiol* 2018; 24: 398–404.
18. Gliem M, Lee JI, Barckhan A, et al. Outcome and treatment effects in stroke associated with acute cervical ICA occlusion. *PLoS One* 2017; 12: e0170247.
19. Wahlgren N, Moreira T, Michel P, et al. Mechanical thrombectomy in acute ischemic stroke: Consensus statement by ESO-Karolinska Stroke Update 2014/2015, supported by ESO, ESMINT, ESNR and EAN. *Int J Stroke* 2016; 11: 134–147.
20. Turowski B, Haenggi D, Wittsack HJ, et al. [Computerized analysis of brain perfusion parameter images]. *Rofo* 2007; 179: 525–529.
21. Nordmeyer H, Webering N, Chapot R, et al. The association between collateral status, recanalization and long term outcome in stroke patients treated with stent retrievers – are there indications not to perform thrombectomy based on CT angiography? *J Neuroradiol* 2017; 44: 217–222.
22. Campbell BC, Christensen S, Levi CR, et al. Cerebral blood flow is the optimal CT perfusion parameter for assessing infarct core. *Stroke* 2011; 42: 3435–3440.

23. Schaefer PW, Barak ER, Kamalian S, et al. Quantitative assessment of core/penumbra mismatch in acute stroke: CT and MR perfusion imaging are strongly correlated when sufficient brain volume is imaged. *Stroke* 2008; 39: 2986–2992.
24. Cortijo E, Calleja AI, Garcia-Bermejo P, et al. Relative cerebral blood volume as a marker of durable tissue-at-risk viability in hyperacute ischemic stroke. *Stroke* 2014; 45: 113–118.
25. van den Wijngaard IR, Holswilder G, Wermer MJ, et al. Assessment of collateral status by dynamic CT angiography in acute MCA Stroke: Timing of acquisition and relationship with final infarct volume. *AJNR Am J Neuroradiol* 2016; 37: 1231–1236.

Clinical Imaging 57 (2019) 1–6

Contents lists available at ScienceDirect

Clinical Imaging

journal homepage: www.elsevier.com/locate/clinimag

Neuroradiology

Predictors for basal ganglia viability after mechanical thrombectomy in proximal middle cerebral artery occlusion

Marius Georg Kaschner[a,*], Raul Lande[a], Christian Rubbert[a], Julian Caspers[a,b], John-Ih Lee[c], Michael Gliem[c], Sebastian Jander[c], Bernd Turowski[a]

[a] Department of Diagnostic and Interventional Radiology, Heinrich Heine University Duesseldorf, Medical Faculty, Germany
[b] Institute of Neuroscience and Medicine (INM-1), Research Centre Jülich, Germany
[c] Department of Neurology, Heinrich Heine University Duesseldorf, Medical Faculty, Germany

ARTICLE INFO

Keywords:
Basal ganglia infarction
Thrombectomy
Predictors for basal ganglia viability
Computed tomography perfusion imaging
Ct angiography
Collateral score

ABSTRACT

Background/purpose: In acute proximal middle cerebral artery (MCA) occlusion covering the lenticulostriate arteries (LSA), ischemic tolerance of basal ganglia is limited due to supposed lack of collateral supply. However, in several patients, basal ganglia (BG) infarction was absent after successful mechanical thrombectomy (MTE). Purpose of our study was to evaluate predictors for BG viability in stroke patients despite prolonged MCA mainstem occlusion.

Material/methods: We retrospectively reviewed all stroke patients from our local registry with MCA mainstem occlusion after mechanical thrombectomy between November 2009 and October 2016. All patients underwent non-enhanced post-interventional cranial CT imaging (NCCT) and were classified according to 6 patterns of BG viability: complete: putamen (P) and globus pallidus (GP); partial: P or GP, and combination of complete or partial BG and/or adjacent white matter/cortical (WMC) viability. We compared viability patterns with respect to pre-interventional stroke imaging including NCCT, CT-angiography (CTA), CT perfusion (CTP); demographics, pre- and intra-procedural data and occurrence of post-procedural intracerebral hematoma (ICH). CTP imaging of the affected and contralateral BG-territories were obtained separately and CTA-collateral score (CS) was assessed.

Results: A significant correlation between higher collateral score and viability of GP (OR = 1.949; p = .011), P (OR = 2.039, p = .011), and the combination of GP, P and WMC (OR = 2.767, p = .007) was revealed. Higher relative CBV ratio (rCBVR) was significantly associated with viability of the pattern GP + WMC (univariate: OR = 3.160, p = .014; multivariate: OR = 6.058; p = .021).

Conclusion: CTA collateral score and rCBVR were predictive for BG viability in stroke patients after successful MTE in prolonged complete MCA-mainstem and LSA occlusion.

1. Introduction

Prolonged occlusion of the pre-bifurcation M1 segment of the middle cerebral artery (MCA) and lenticulostriate artery (LSA) ostia commonly results in basal ganglia (BG) infarction. Occasionally sparing of adjacent deep white matter can be observed in MCA infarction with occlusion of the MCA mainstem, because collaterals may sustain tissue in the peripheral MCA territory. Since BG are supposed not to possess a significant collateral blood supply, ischemic tolerance should be lower than that of the hemispheric cortex and the white matter. In contrast, we found in preliminary observations absent BG infarction after successful mechanical thrombectomy (MTE) in many patients with M1 segment occlusion, that covered the anatomic region of LSA ostia.

Infarction of basal nuclei is associated with higher rates of hemorrhagic transformation, worse dysfunction and disability at discharge, and longer hospitalization [1].

Therefore risk assessment of intracerebral hemorrhage (ICH) due to BG infarction is necessary for neurointerventionalists to adapt endovascular procedures, in order to retain clinical effectiveness in relation to the risk of significant intracerebral hemorrhage (ICH). We investigated imaging parameters, in particular computed tomography angiography (CTA) collateralization, CT perfusion (CTP), procedural,

* Corresponding author at: Department of Diagnostic and Interventional Radiology, Heinrich Heine University Duesseldorf, Medical Faculty, Moorenstr.5, 40225 Duesseldorf, Germany.
E-mail address: marius.kaschner@med.uni-duesseldorf.de (M.G. Kaschner).

https://doi.org/10.1016/j.clinimag.2019.04.013
Received 11 August 2018; Received in revised form 30 March 2019; Accepted 23 April 2019

and clinical and demographic data to indicate predictors for survival of BG in acute stroke patients with M1 segment and LSA occlusion.

2. Material and methods

We retrospectively reviewed all patients undergoing MTE treated in our hospital between November 2009 and October 2016 according to protocol approved by our local Ethics Committee. The acute stroke imaging protocol at our institution includes non-enhanced cranial CT (NCCT) and segmental brain CTP followed by craniocervical CTA for all patients with suspected acute ischemic stroke clinically evaluated by a neurologist. Only patients with proximal MCA M1 segment occlusion or tandem ICA and M1 segment obturation, that covered the LSA ostia documented on CTA were included, to ensure that no blood supply to the LSA existed and if integrity of the BG in NCCT and CTP before MTE was preserved. Subsequent digital subtraction angiography (DSA) in patients treated with MTE confirmed proximal M1 occlusion prior to MTE and reperfusion of LSA immediately after recanalization. Furthermore, DSA allowed detecting anatomical variants of BG collateralization retrospectively. BG viability was evaluated at routinely post-interventional follow-up NCCT after 24 h.

For all included patients, the following data were collected (Table 1): demographics (gender, age, cerebrovascular risk factors), admission NIHSS (National Institutes of Health Stroke Scale Score), time from symptom onset to stroke imaging, treatment details (use of intravenous recombinant tissue plasminogen activator (rt-PA) in the emergency room, time from stroke imaging to opened stent retriever and to recanalization, intraarterial local rt-PA, antiaggregation in permanent stent implantation). We recorded the final revascularization result of the primary arterial occlusive lesion from the angiogram by TICI score (Thrombolysis in cerebral infarction). Clinical outcome data included discharge NIHSS, discharge modified Rankin Scale (mRS), duration of hospitalization. ICH was defined as hemorrhagic infarction (HI) or parenchymal hematoma (PH) according to the European Cooperative Acute Stroke Study classification (ECASS) and was assessed by post-interventional NCCT after 6–24 h [2].

Table 1
Baseline characteristic and treatment outcome.

Subject sample n = 92	
Socialdemographic characteristics	
Age (years), mean ± SD	72 ± 13.4
Female	n = 53 (57.6%)
Pre-existing conditions:	
Coronary artery disease	n = 26 (29.5%)
Myocardial infarction	n = 7 (7.6%)
Atrial fibrillation	n = 45 (51.1%)
Arterial hypertension	n = 69 (78.4%)
Peripheral arterial occlusive disease (PAOD)	n = 7 (8%)
Diabetes mellitus	n = 22 (23.9%)
Dyslipidaemia	n = 37 (42%)
COPD	n = 15 (17%)
Glucose level (mmol/L) (mean ± SD)	123.5 ± 31.5
Coumarin treatment	n = 10 (11.5%)
Previous stroke	n = 0 (0%)
Treatment details	
Admission NIHSS median (mean ± SD)	14 (13.4 ± 5.5)
Collateral status (0–3) median	2
IV rtPA	n = 69 (77.5%)
IA rtPA	n = 47 (52.2%)
Mean time (min) (mean ± SD)	
- From symptom onset to imaging	99.9 ± 78.7
- First flow M1	220.8 ± 91.5
- To final recanalization M1	232.6 ± 101.4
Treatment and clinical outcome	
TICI 2b-3	n = 80 (86.9%)
TICI 2a	n = 12 (13.0%)
TICI 2b	n = 37 (40.2%)
TICI 3	n = 43 (46.7%)
Discharge NIHSS median (mean ± SD)	7 (7.9 ± 6.1)
Symptomatic intracranial hemorrhage (ECASS:PH2)	n = 11 (11.9%)

2.1. Imaging protocol

2.1.1. CT stroke protocol

The CT stroke protocol, performed on different multisection scanners (Somatom Definition Flash, 128 detector rows; Somatom Definition AS, 64 detector rows; both Siemens Erlangen, Germany). Standard CT protocol included pre- and post-contrast CT head scans with the following parameters:

2.1.2. Non-contrast CT (NCCT)

120 kV (peak) (kVp), 250 mAs, 0.6 mm collimation, 1 s/rotation, and table speed of 1 mm/rotation.

2.1.3. CT-perfusion (CTP)

Sectional CTP was acquired at level of the cella media, angled parallel to the orbitomeatal plane CTP scan parameters were 80 kVp, 180 mAs (Somatom-FLASH) or 80 kVp, 120 mAs (Somatom Definition AS), 1 second rotation and iodinated contrast medium infusion of 30 ml iomeprol 400 mg J/ml (Imeron®, Bracco, Milan, Italy) at Somatom-FLASH, and 40 ml iohexol 300 mg J/ml (Accupaque GE Healthcare Buchler GmbH &Co, Munich, Germany) at Somatom Definition AS, via automated antecubital injection at 5 ml/s with a 3 second delay, followed by 30 ml saline solution, collimation of 1 × 10 mm (Definition FLASH) or 64 × 0.6 mm (Definition AS). Reconstructions covered 2 × 1 cm representative slices of the MCA territory.

Calculation of perfusion maps including time to maximum (Tmax), mean transit time (MTT), relative cerebral blood volume (rCBV), and relative cerebral blood flow (rCBF) were performed with manufactured in-house software (STROKETOOL-CT) (Version 2.0, H.-J. Wittsack, http://www.digitalimagesolutions.de).

Quantitative analysis of DICOM-data from parameter images (MTT, Tmax, rCBF, rCBV) was performed semiautomatically using the imaging processing software Angiotux CT 2D (ECCET 2006/Beck A., Aurich V.)

2.1.4. CT-angiography (CTA)

CTA covered the aortic arch to the vertex with continuous axial sections parallel to the orbitomeatal line; with collimation 128 × 0.6 mm, 120 kVp, 100 mAs, 1 s/rotation, and table feed of 1 mm/rotation (Somatom Definiton FLASH) or with collimation 64 × 0.6 mm, 120 kVp, 175 mAs, 1 s/rotation, and table feed of 1 mm/rotation (Somatom Definition AS).

After a single bolus of intravenous contrast injection (70–80 ml iomeprol 400 mg J/ml) at 4 ml/s flow rate, acquisitions were started auto-triggered by appearance of contrast in a region of interest manually placed in the ascending aorta.

CTA data were processed to reconstruct 2D-multiplanar 9-mm maximum intensity projections (MIP) in axial, coronal and sagittal plane, 1-mm coronal and sagittal multiplanar reconstructions (MPR) and 0.75- and 4-mm axial CTA source images.

2.1.5. Endovascular treatment

MTE of the anterior circulation was performed under local anesthesia of the groin, intra-venous application of 5000 IU heparin (after intraarterial 8F, 80 cm sheath placement) and 1 g metamizol. The occluded vessel was probed by a microcatheter through a 5F or 6F intermediate catheter (e.g., Navien, Medtronic, Irvine, California, USA; Neurobridge, Acandis, Pforzheim, Germany; SOFIA®, MicroVention, Düsseldorf, Germany) and in elongated vessel anatomy an additional 8F guiding-catheter was used. MTE was subsequently performed after passage of the clot using a stent-retriever system (e.g., Aperio®, Acandis, Pforzheim, Germany). In cases of incomplete recanalization after MTE additional procedures, such as intra-arterial thrombolysis,

angioplasty or wire fragmentation of the clot were used. Internal carotid stenting (Carotid WALLSTENT™, Boston Scientific, Marlborough, MA, USA) of high-grade stenosis was performed to establish access to intracranial vessel occlusions if required.

2.2. Imaging analysis

2.2.1. CTP

Relative CBV (rCBV), relative CBF (rCBF), Tmax and MTT values of BG were recorded using region of interest (ROIs) in anatomic structures that are exclusively supplied from M1-perforators (globus pallidus and putamen). Relative CBV ratio (rCBVR) and relative CBF ratio (rCBFR) were defined as quotient of ipsi- and contralateral rCBV, and rCBF, respectively [3].

2.2.2. Angiography

Post-treatment recanalization was graded according to the Thrombolysis in Cerebral Infarction (TICI) classification on final DSA images subsequent to recanalization [4]. TICI grade 0 and 1 were considered non-recanalized, grade 2a with incomplete distal branch filling of < 50% of the expected territory as inadequate reperfusion. TICI grade 2b (incomplete distal branch filling > 50%) to 3 (complete distal branch filling) were defined as successful recanalization of the occluded MCA territory.

2.2.3. CTA collateral score

Collateral supply of the occluded MCA territory from pre- interventional CTA scans was scored on the basis of the CTA collateral grading system by Tan et al. on a scale of 0–3 [5]. A score of 0 corresponds to absent collateral supply, a score of 1 to collateral supply filling < 50% but > 0%, and a score of 2 corresponds to collateral supply filling > 50% but < 100% of the occluded MCA territory. One hundred percent collateral supply of the occluded MCA territory was scored as 3.

2.2.4. Basal ganglion infarction and hemorrhagic transformation (HT)

BG regions, that were exclusively supplied by the M1-perforators (globus pallidus and putamen = nucleus lentiformis) were selected for assessment on NCCT.

Six patterns of non-infarcted (viable) basal ganglia were identified on NCCT:

- putamen (P),
- globus pallidus (GP),
- both, globus pallidus and putamen (GP + P),
- putamen and adjacent white matter/cortical region (P + WMC) of the middle cerebral artery (MCA) territory,
- globus pallidus and adjacent white matter/cortical region (GP + WMC) of the MCA territory,
- both, globus pallidus and putamen and adjacent white matter/cortical region (GP + P + WMC) of the MCA territory.

Any hemorrhagic transformation (HT), including hemorrhagic infarction (HI) and HT with parenchymal hematoma (PH) was evaluated according to ECASS classification.

Representative cases of basal ganglia infarction patterns are given in Figs. 1–3.

2.2.5. Imaging reading

Imaging reading was performed by three readers (R.L., M.G.K., and B.T.). R.L. is a final-year medical student extensively instructed and trained in the evaluation of CTP images, of the Tan CTA collateral score, in TICI scoring on cerebral angiograms, and in the evaluation of infarct patterns on NCCT. M.G.K. and B.T. are senior interventional neuroradiologists with 10 and 20 years' experience in (neuro-) radiology, respectively.

Retrospective assessment of CTP values, assessment of collateralization (Tan score), revascularization success (TICI) and infarct pattern (NCCT) were performed by R.L., M.G.K. and B.T. by consensus reading. To avoid recall bias, CTP images, CTA collateral scores, angiograms and post-interventional NCCT images were evaluated independently of each other and personal patient data were anonymized, so that readers were blinded to the results of the other image modalities of the respective case.

2.3. Statistical analysis

Statistical analysis was conducted in SPSS version 21.0.0 (IBM, Armonk, New York). Odds ratios (OR) were calculated by binary univariate logistic regression analysis to quantify association between BG/WMC region viability with respect to the above mentioned viability patterns and the following baseline characteristics and treatment outcome data, summarized in Table 1: socialdemographic characteristics, pre-existing conditions including cardiovascular risk factors; treatment details, and treatment- and clinical outcome. OR to determine correlation between BG/WMC viability and pre-interventional perfusion parameters (CBV, Tmax, CBF, MTT) was calculated by binary uni- and multivariate logistic regression analysis. To determine correlation between prementioned factors and percental viability of WMC region a linear logistic regression analysis was performed. For BG/WMC viability Fisher's exact ratio test was used as significance test for the OR. Results were considered significant at a level of $p < .05$.

3. Results

3.1. Baseline characteristics

A total of 92 patients meeting the inclusion criteria were enrolled.

Demographic data, pre-existing cardio-vascular diseases and risk factors of included patients are shown in Table 1. There was no significant correlation between demographic parameters and basal ganglia viability.

A significantly negative correlation was observed between elevated blood glucose level and basal ganglia viability in all basal ganglia and white matter patterns summarized in Table 2 (OR = 0.938–0.975; p = .012–0.043). The remaining pre-existing cardio-vascular diseases and risk factors had no influence on viability of BG/WMC region.

3.1.1. CTA collateral score

Univariate regression analysis revealed a significant correlation between higher CTA collateral score (CS) and integrity of BG for all predefined parts of BG and white matter/cortical region patterns of the middle cerebral artery (MCA) territory (Table 3). The strongest positive correlation between BG viability and high CS values was observed for the unit of globus pallidus and white matter/cortical-MCA region (GP + WMC) (OR 3.006, p = .003) and for the unit of P + WMC or GP + Putamen + WMC (GP + P + WMC, OR: 2.767; p = .007). Linear logistic regression analysis revealed a highly significant influence of CS on percental viability of the WMC region (regression coefficient: 0.247, R^2: 0.385, p = .000).

3.1.2. Procedural data

TICI 2b and 3 recanalization was achieved in 86.9%. Mean time from symptom onset to initial CT perfusion imaging was 99.9 min (SD ± 78.7) and to first flow in the M1 segment 220.8 min (SD ± 91.5). In 3 cases a Penumbra system was used for recanalization of the M1 segment (1 case in 2009, 2 cases in 2012). In all three patients TICI 2b final recanalization grade was achieved. Stent retriever thrombectomy was performed with a Solitaire stent retriever (Medtronic) in 6 cases and in one case with a TREVO stent retriever system (Stryker). The other cases in that stent retriever thrombectomy was performed the Aperio system was used. There was no significant

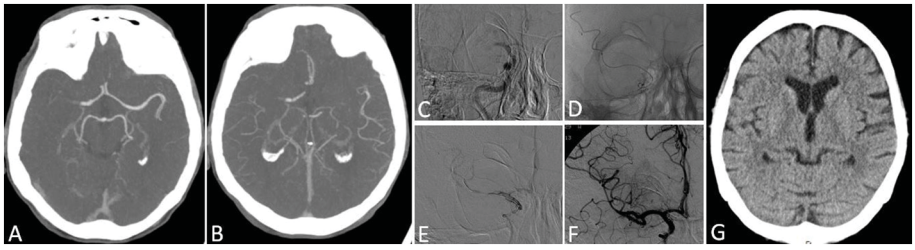


Fig. 1. Exemplary axial CTA maximum intensity projection (MIP) demonstrate proximal occlusion of the right-sided M1 segment (A) with good collaterals. Tan Score was 2 (> 50% of affected MCA territory opacified in comparison to non-affected MCA territory) (B). The combination of both angiographic images via guiding-catheter proximal the occlusion site (C) and via microcatheter after thrombus passage (D) demonstrates thrombus extension. Angiographic control run with opened stent retriever (Aperio) covering the thrombus (E). TICI 3 final recanalization was achieved (F). Basal ganglia without signs of infarction on postinterventional control NCCT (G).

correlation between BG viability and pre-treatment factors (admission NIHSS, i.v. rt-PA), procedural factors (i.a. rt-PA, duration from onset to recanalization), and recanalization rate (TICI) (Table 1). Hemorrhagic transformation (PH1, PH2) of white matter and cortical region of the MCA territory correlated significantly with decreased BG viability (Table 4). We identified no anatomical variants of BG collateralization in any patient in final DSA scan after successful MTE.

3.1.3. Perfusion analysis

There is a significant correlation between rCBV ratio (rCBVR) values and integrity of globus pallidus (GP) in conjunction with white matter/cortical (WMC) region of the MCA territory (OR = 3.160; p = .014). There was a positive correlation between viability of GP and WMC and higher rCBVR values but without significance for the remaining BG/WMC patterns. The multivariate analysis including rCBVR, rCBFR, Tmax and MTT revealed an increased OR 6.058 for rCBVR as a predictor for GP + WMC viability (p = .021, Table 5). rCBF, Tmax and MTT were not significantly correlated with BG/WMC viability.

4. Discussion

BG infarction is associated with an increased risk of parenchymal hematoma (PH) and hemorrhagic infarction (HI). In most cases MCA occlusion with complete LSA blockade results in broad BG infarction in the dependent LSA territories, even after rapid and technically successful recanalization [6]. However, in our own study population there were several cases with predominantly none infarcted BG after successful recanalization, where no anatomical vascular variants explain these findings. Hence, the intention was to identify predictors for BG viability in MCA-mainstem occlusion covering LSA.

In the present study high rCBVR values significantly correlated with viability of the BG in combination with white matter and cortical region of the MCA territory. Mokin et al. separately analyzed BG and cortical CTP abnormalities to predict hemorrhagic transformation and clinical outcomes in patients with MCA occlusion undergoing endovascular therapy. Decreased rCBV correlated significantly with parenchymal hematoma and hemorrhagic infarction [7]. Loh et al. classified terminal ICA and M1 occlusions according to diffusion MRI patterns ranging from complete BG infarct to relative sparing of the BG in patients with terminal ICA and M1 occlusion before MTE. Patients with completed BG infarction had a higher rate of parenchymal hemorrhagic transformation than the other groups (OR 6.7, 95% CI 1.02 to 183.3). PH was associated with higher rates of death and dependency at discharge. Patients with complete BG infarction had also worse pre- and post-thrombectomy NIHSS, longer hospital length of stay, and higher rates of discharge mRS [1].

As a further predictor for BG integrity in the current study the CTA based collateralization score correlated significantly with all pre-defined BG and WMC viability patterns of the MCA-territory. Patients with a good collateralization of the MCA territory showed a significant higher rate of BG integrity. Patients with high collateral score values might not only have a better leptomeningeal collateral blood supply, but also increased blood flow in general, including the recurrent artery of Heubner, the anterior choroidal artery and perforators arising from the P1segment and the posterior communicating artery. Accordingly, viability of globus pallidus could be explained in this way.

Interestingly also putamen, seems to profit from high collateral scores, although no collaterals of the putamen, with the exception of its anterior part, could be detected in angiographic examinations [8]. Infarcted and viable lateral BG showed no significantly different rCBVR values. This discrepancy might be caused by low sensitivity of rCBVR to detect perfusion differences between intact and infarcted lateral BG. A sufficient collateral circulation protects the brain against ischemic injury and can potentially mitigate the effect of an occluded artery, thereby the time window for clinical effective mechanical recanalization can be extended based on additional information on collateral flow und local perfusion. Several studies showed an excellent correlation between collateralization, infarct volume and clinical outcome [5,9–13]. Although in CT based collateral score systems the ASPECT- and regional leptomeningeal collateral score offer scoring of regional collateralization separately for BG [10,11] to our knowledge there are no studies available that evaluated the impact of CT based collateral scores as a predictor for BG infarction in particular. Kim et al. tested a modified regional angiographic collateral score, in that collateral flow was recorded for 15 anatomic areas based on vascular territories. Angiographic collateral score correlated with infarct volume on follow-up CTs and follow-up NIHSS. A high accuracy was obtained for the MCA territory (AUC: 0.76–0.92) and the lowest accuracy was observed for the BG (AUC: 0.87). The authors assumed that BG are supplied by end arteries and are least affected by collaterals. Angiographic

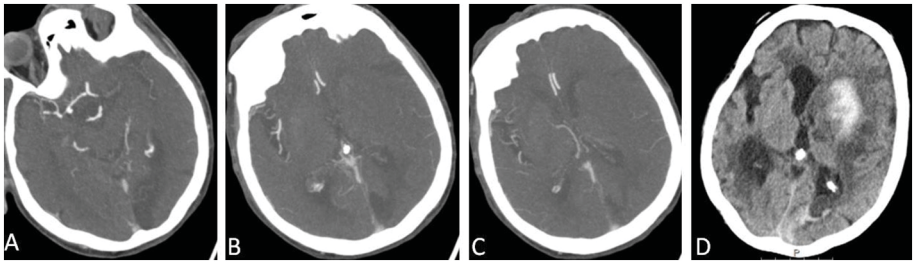


Fig. 2. Exemplary representative axial CTA maximum MIPs demonstrate proximal occlusion of the left-sided M1 segment (A) with poor collaterals. Tan Score was 1 (< 50% of affected MCA territory opacified in comparison to non-affected MCA territory) (B + C). Infarction pattern with lesions of the entire basal ganglia, white matter, and associated cortex. Hyperattenuation due to parenchymal hematoma and contrast media extravasation within the infarct is shown (D).

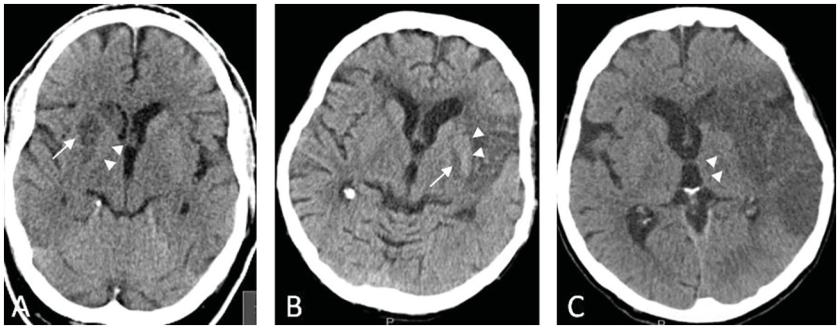


Fig. 3. Representative examples for incomplete basal ganglia infarction on control NCCT after MTE: Hypoattenuation of the putamen (arrow) and caudate nucleus as sign of infarction, while the pallidum is not affected (arrowheads) (A). Hypoattenuation of the pallidum (arrow) and supraganglionic MCA territory indicates infarction, while the putamen (arrowheads) has a normal appearance on post-interventional NCCT (B). Caudate nucleus, putamen and broad areas of the MCA territory are infarcted. Medial part of the BG representing the pallidum (arrowheads) shows no signs of infarction (C).

Table 2
Negative correlation between elevated glucose level, and viability of basal ganglia and WMC region.

Cerebral region	Glucose (mg/dl)	
	OR (95% CI), intact BG	p
GP	0.971 (0.949–0.994)	.015
P	0.975 (0.952–0.998)	.037
GP + P	0.958 (0.926–0.990)	.012
GP + WMC	0.968 (0.938–0.999)	.043
P + WMC	0.938 (0.888–0.991)	.022
GP + P + WMC	0.971 (0.949–0.994)	.015

GP, globus pallidus; P, putamen; WMC, white matter/cortical region.

Table 3
Correlation between CTA collateral score and basal ganglia and WMC region viability.

Cerebral region	CTA collateral score (0–3)	
	OR (95% CI), intact BG	p
GP	1.949 (1.169–3.252)	.011
P	2.039 (1.179–3.526)	.011
GP + P	2.260 (1.276–4.003)	.005
GP + WMC	3.006 (1.457–6.205)	.003
P + WMC	2.767 (1.314–5.828)	.007
GP + P + WMC	2.767 (1.314–5.828)	.007

GP, globus pallidus; P, putamen; WMC, white matter/cortical region.

Table 4
Correlation between hemorrhagic transformation of the WMC region of the MCA territory and basal ganglia viability.

Cerebral region	Hemorrhagic transformation (PH1-PH2) of WMC region	
	OR (95% CI), intact BG	p
GP	0.198 (0.053–0.731)	.015
P	0.265 (0.074–0.944)	.040
GP + P	0.275 (0.078–0.975)	.046
GP or P	0.190 (0.051–0.708)	.013

Table 5
Correlation between rCBVratio (rCBVR) and viability of Globus pallidus + WMC unit; uni- and multivariate regression analysis.

Parameter	OR (95% CI), viability of globus pallidus + WMC unit			
	Univariate	p	Multivariate	p
rCBVR BG	3.160 (1.260–7.923)	0.014	6.058 (1.317–27.869)	.021
rCBFR BG	1.058 (0.886–1.264)	0.532	1.041 (0.853–1.272)	.691
MTT BG	1.018 (0.969–1.070)	0.475	0.952 (0.879–1.031)	.223
Tmax BG	0.944 (0.828–1.076)	0.390	1.052 (0.902–1.226)	.521

BG, basal ganglia; WMC, white matter/cortical region.

hypervascularization of BG, indicating “luxury perfusion” was only an imprecise predictor for infarction [12]. Although the CTA score assesses collateralization in general and does not allow a separate assessment of BG collateralization, our study shows that collateral status is a strong and independent predictor of BG viability. Based on these results, we hypothesize, contrarily to the prementioned studies, that variable unspecific deep parenchymal collaterals of the striatum might exist, so that a sufficient collateralization in general also supplies the BG that way [14]. A further indication of deep parenchymal collateralization of BG might be our observation of significant negative correlation between hematoma of white matter and cortical regions and increased rate of basal ganglia infarction. Regional scores take in consideration that neurological outcome depends on lesion localization. Previous studies confirm that the volume of abnormality on CTA source images at baseline is a very close accordance to the volume of final infarct on follow-up scanning in case of contemporary recanalization. Future studies have to approve if CTA score parameters are predictive for irreversible extensive BG infarction to estimate risk of symptomatic BG reperfusion hematoma. In our own study CTA collateral score was more predictive for BG infarction than CTP but the impact of these findings are limited by the retrospective nature of this study.

Kleine et al. evaluated in an angiographic study the effect of MTE to prevent striatal infarction in patients with acute isolated M1 occlusion. In seven of the 22 patients, that did not develop the expected infarction pattern there were no variants of vascular supply detectable as explanation for the false positive results [6]. These findings support our own observations, that in exceptional cases BG might have an increased ischemic tolerance. Further trials have to focus on these special cases to evaluate determinants that allow to identify salvageable tissue and to predict infarct expansion of BG. Preexisting hyperglycemia worsens the clinical outcome of acute stroke [15]. However, elevated blood glucose had only a minor influence to BG viability in this study. A major limitation of this study is the use of a consensus reading design that might include restrictions like absent of recorded variability in the readers' interpretations and bias due to possible influence of junior readers from senior readers. One limitation might be evaluation of BG infarction on NCCT instead of MRI that is more sensitive for early signs of infarction. However, reliability of NCCT in the determination of early phase basal ganglia infarction has been demonstrated as a sensitive imaging modality, too. Hypoattenuation specifically in the basal ganglia as an early ischemic stroke sign can be observed within 6 h after onset [16]. Decreased attenuation of the lentiform nucleus (obscuration of the lentiform nucleus), leading to a less clear delineation between white and grey matter, indicates cytotoxic edema and can be observed within 2 h after stroke onset on NCCT already [17]. To reduce bias by different imaging modalities, we included only patients with NCCT follow-up into this study. At last, future prospective studies involving a large number of patients will be needed to get more detailed information about blood supply of the BG in the setting of ischemic stroke due to MCA mainstem occlusion.

5. Conclusion

Extended MCA mainstem occlusion generally causes broad BG infarction. Yet, BG integrity after technically effective MTE in complete MCA occlusion was observed in several patients. CT collateralization score and rCBV ratio values were predictive for postinterventional BG condition, and may help guiding endovascular treatment decisions.

The authors declare that they have no conflict of interest.

References

[1] Loh Y, Towfighi A, Liebeskind DS, MacArthur DL, Vespa P, Gonzalez NR, et al. Basal ganglionic infarction before mechanical thrombectomy predicts poor outcome. Stroke 2009;40:3315–20.

[2] Fiorelli M, Bastianello S, von Kummer R, et al. Hemorrhagic transformation within 36 hours of a cerebral infarct: relationships with early clinical deterioration and 3-month outcome in the European Cooperative Acute Stroke Study I (ECASS I) cohort. Stroke 1999;30:2280–4.

[3] Turowski B, Haenggi D, Wittsack HJ, Beck A, Aurich V. Computerized analysis of brain perfusion images. Rofo 2007;179:525–9.

[4] Higashida RT, Furlan AJ, Roberts H, et al. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. Stroke 2003;34:e109–37.

[5] Tan IYL, Demchuk AM, Hopyan J, Zhang L, Gladstone D, Wong K, et al. CT angiography clot burden score and collateral score: correlation with clinical and radiologic outcomes in acute middle cerebral artery infarct. AJNR Am J Neuroradiol 2009;30:525–31.

[6] Kleine JF, Beller E, Zimmer C, et al. Lenticulostriate infarctions after successful mechanical thrombectomy in middle cerebral artery occlusion. J NeuroIntervent Surg 2016;0:1–6.

[7] Mokin M, Morr S, Fanous AA, Shallwani H, Natarajan SK, Levy EI, et al. Correlation between cerebral blood volume values and outcomes in endovascular therapy for acute ischemic stroke. J NeuroIntervent Surg 2014;0:1–4.

[8] Bozzao L, Fantozzi LM, Bastianello S, Bozzao A, Fieschi C. Early collateral blood supply and late parenchymal brain damage in patients with middle cerebral artery occlusion. Stroke 1989;20:735–40.

[9] Wildermuth S, Knauth M, Brandt T, Winter R, Sartor K, Hacke W. Role of CT angiography in patient selection for thrombolytic therapy in acute hemispheric stroke. Stroke 1998;29:935–8.

[10] Coutts Shelagh B, Lev Michael H, Eliasziw Michael, et al. ASPECTS on CTA source images versus unenhanced CT added value in predicting final infarct extent and clinical outcome. Stroke 2004;35:2472–6.

[11] Menon BK, Smith EE, Modi J, et al. Regional leptomeningeal score on CT angiography predicts clinical and imaging outcomes in patients with acute anterior circulation occlusions. AJNR Am J Neuroradiol 2011;32:1640–5.

[12] Kim JJ, Fischbein NJ, Lu Y, Pham D, Dillon WP. Regional angiographic grading system for collateral flow correlation with cerebral infarction in patients with middle cerebral artery occlusion. Stroke 2004;35:1340–4.

[13] Hwang YH, Kang DH, Kim YW, et al. Impact of time-to-perfusionon outcome in patients with poor collaterals. AJNR Am J Neuroradiol 2015;36:495–500.

[14] Liebeskind D. Collateral circulation. Stroke 2003;34:2279–84.

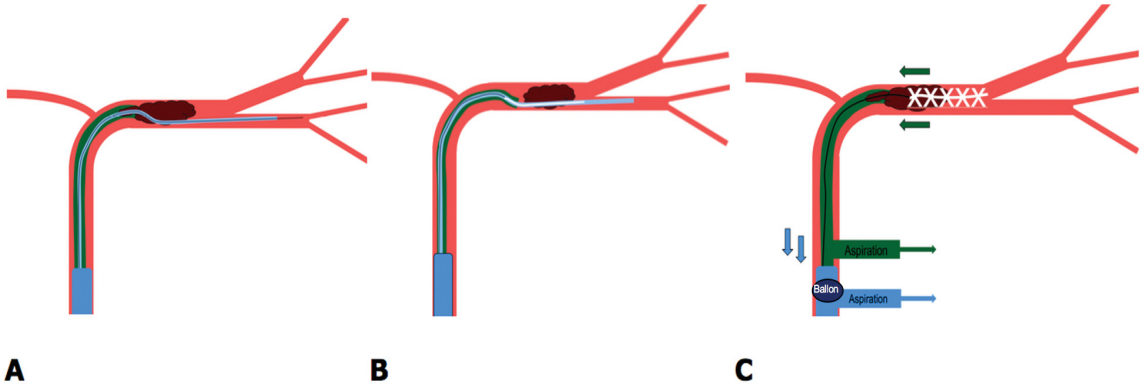
[15] Havelli H, Barreto AD, Liebeskind D, et al. Identifying patients at high risk for poor outcome after intraarterial therapy for acute ischemic stroke. Stroke 2009;40:1780–5.

[16] Wardlaw JM, Mielke O. Early signs of brain infarction at CT: observer reliability and outcome after thrombolytic treatment—systematic review. Radiology 2005;235:444–53.

[17] Tomandl BF, Klotz E, Handschu R, et al. Comprehensive imaging of ischemic stroke with multisection CT. RadioGraphics 2003;23:565–92.

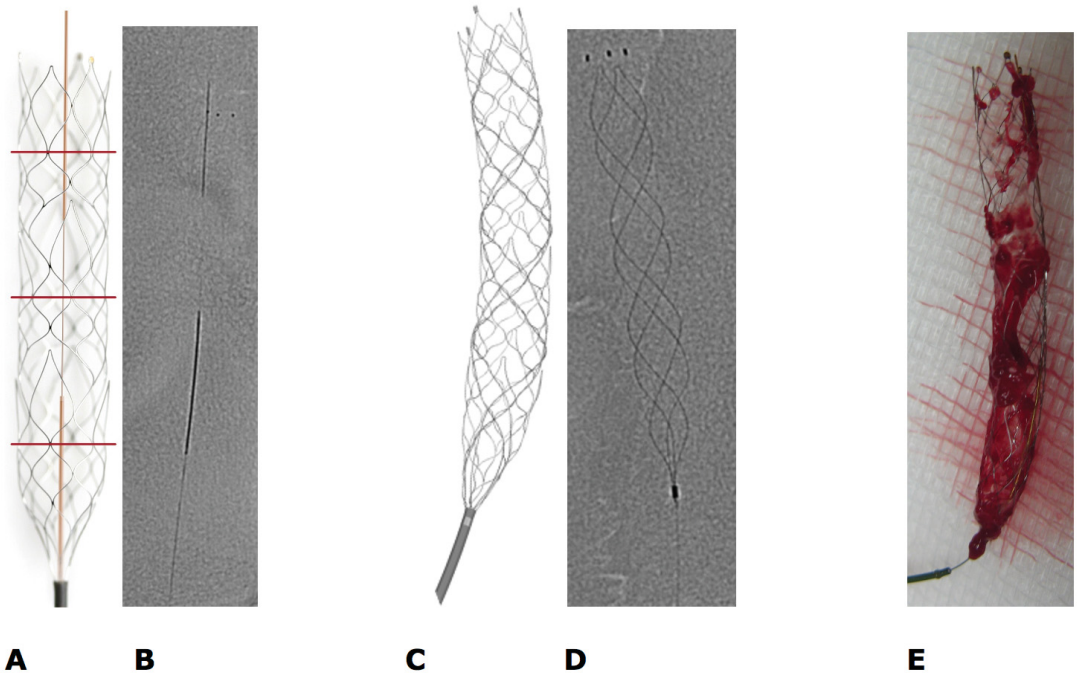
Anhang

Abbildung 1: Prinzip der Stent-Retriever-Thrombektomie



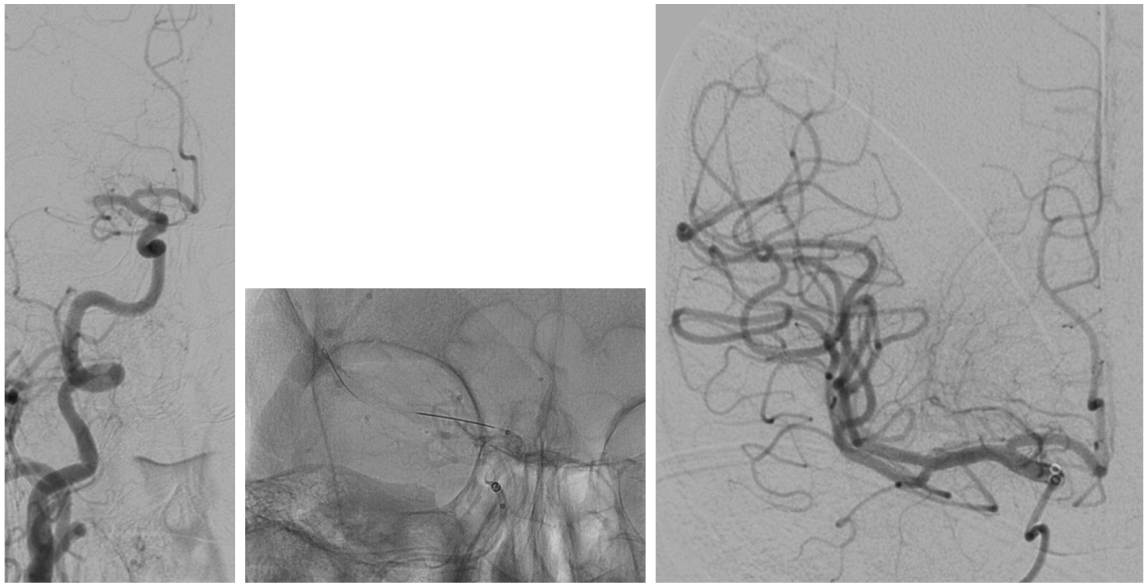
A–C) Schematische Darstellung der Stent-Retriever-Thrombektomie (Quelle: Eigene Darstellungen). A) Verschluss des Hauptstammes der A. cerebri media durch einen Thrombus (braun). Koaxiales Kathetersystem: Großlumige Schleuse oder Führungskatheter (blau) in der ACI, distaler Aspirationskatheter (grün) vor dem Thrombus. B) Passage des Thrombus mit einem Mikrodraht (schwarze Linie) über den der Mikrokatheter (hellblau) geführt wird. Mikrokatheter distal des Thrombus mit innenliegendem zusammengefaltetem Stent-Retriever (weiß). C) Stent-Retriever (weiße X-Symbole) nach distal den Thrombus überlappend. Der Thrombus wird mit dem Stent-Retriever in den distalen Aspirationskatheter unter Sog zurückgezogen. Alternativ: Einklemmen des Thrombus zwischen Stent-Retriever und distalem Aspirationskatheter und Rückzug des gesamten Systems in die Schleuse unter Aspiration an Schleuse (blaue Pfeile) und Aspirationskatheter (grüne Pfeile), optional mit zusätzlicher proximaler Flussblockade durch einen inflatierten Ballon an der Schleuse bzw. dem Führungskatheter.

Abbildung 2: Beispiel für in dieser Arbeit verwendete und untersuchte Stent-Retriever-Systeme



A) Das Aperio-Thrombectomy-Device (Foto aus dem offiziellen Firmenkatalog, mit freundlicher Genehmigung der Fa. Acandis). Funktionelle Segmente (zwischen den roten Linien): kleine geschlossene Zellen, große geöffnete Zellen, die Anordnung der repetitiven funktionellen Segmente ermöglicht die Anpassung des Stent-Retrievers an die Thrombuslänge. B) Das vollständig geöffnete Aperio-Thrombectomy-Device unter Röntgendurchleuchtung (Mit freundlicher Genehmigung der Fa. Acandis). Sichtbare Anteile von proximal nach distal: proximaler und distaler Transportdraht-Marker markieren die Gesamtlänge des Stent-Retrievers, drei distale punktförmige Marker zeigen die vollständige Öffnung an. C) Das Aperio-Hybrid-Thrombectomy-Device (Foto aus dem offiziellen Firmenkatalog, mit freundlicher Genehmigung der Fa. Acandis). Gleicher Aufbau der funktionellen Segmente wie bei dem Aperio-Thrombectomy-Device mit eingeflochtenen röntgendichten Drähten über die gesamte Stent-Retriever-Länge. D) Das vollständig geöffnete Aperio-Hybrid-Thrombectomy-Device unter Röntgendurchleuchtung (Mit freundlicher Genehmigung der Fa. Acandis). Verbesserte Sichtbarkeit durch die zwei integrierten röntgendichten eingeflochtenen Drähte. E) Extrahierter Thrombus in einem Stent-Retriever (Foto mit freundlicher Genehmigung der Firma Acandis).

Abbildung 3: Digitale Substraktionsangiographie: Beispiel für eine Stent-Retriever-Thrombektomie bei Gefäßverschluss im vorderen Hirnkreislauf



A **B** **C**

A–C: Abbildungen aus dem Institut für diagnostische und interventionelle Radiologie des Universitätsklinikums Düsseldorf mit freundlicher Genehmigung von Univ.-Prof. Dr. med. G. Antoch.
A) Proximaler Verschluss der rechten A. cerebri media. B) Entfalteter Stent-Retriever (3 distale Marker, distaler und proximaler Transportmarker). C) Angiogramm nach Stent-Retriever-Rückzug in den distalen Aspirationskatheter (Marker des Katheters in terminaler ACI vor der Bifurkation). Vollständige Rekanalisation des Mediastromgebietes (Rekanalisationsgrad TICI 3).