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Complications of Endovascular Treatment for Acute Ischemic Stroke: Prevention and Management

Balami JS[1], White PM[2], McMeekin P[3], Ford GA[4], Buchan AM[5]
832463734
[1]Centre for Evidence Based Medicine, University of Oxford. United Kingdom. Norfolk and Norwich University Teaching Hospital NHS Trust, Norwich, United Kingdom
[2]Stroke Research Group, Institute of Neuroscience, Newcastle University, United Kingdom
[3]School of Health, Community and Education Studies, Northumbria University, United Kingdom
[4]Oxford University Hospitals NHS Trust, John Radcliffe Oxford. Clinical Pharmacology, University of Oxford, United Kingdom
[5] Acute Stroke Programme, Radcliffe Department of Medicine, University of Oxford, Oxford, United Kingdom. Acute Vascular Imaging Centre, University of Oxford, John Radcliffe Hospital, Oxford.

Correspondence to: Prof. Alastair M Buchan
Dean of Medicine
Professor of Stroke Medicine
University of Oxford
John Radcliffe Hospital
Oxford, OX3 9DU
United Kingdom

Telephone: (44) 01865 220346

Email: alastair.buchan@medsci.ox.ac.uk

Tables:
Table 1. Complications of EVT from the RCTs
Table 2. Complications of EVT from the non-RCTS.

Supplementary
Search strategy

Abstract

Endovascular mechanical thrombectomy (MT) for the treatment of acute stroke due to large vessel occlusion has evolved significantly with the publication of multiple positive thrombectomy trials. EVT is now a recommended treatment for acute ischemic stroke (AIS).

MT is associated with a number of intra-procedural or post-operative complications, which need to be minimized and effectively managed to maximize the benefits of thrombectomy. Procedural complications include: access site problems; device-related complications; symptomatic intracerebral hemorrhage; subarachnoid hemorrhage; embolization to new or target vessel territory. Other complications include: anaesthetic/ contrast media related, post-operative hemorrhage, extra-cranial hemorrhage.

Some complications are life threatening and many lead to increased length of stay in intensive care and stroke units. Complications increase costs and delay commencement of rehabilitation. Some may be preventable, the impact of others can be minimized with early detection and appropriate management. Both neurointerventionists and stroke specialists need to be aware of the risk factors, strategies for prevention and management of these complications. With the increasing use of MT for the treatment of AIS, incidence and outcome of complications will need to be carefully monitored by stroke teams.

In this narrative review, we examine the frequency of complications of EVT in the treatment of AIS with an emphasis on peri-procedural complications. Overall from recent RCTs the risk of complications with sequelae for patient from MT is ~ 15%. We discuss the management of complications and identify areas with limited evidence, which need further research.

Introduction

Endovascular mechanical thrombectomy (MT) has evolved as the standard of care for the management of emergent large vessel occlusive (LVO) strokes based on the evidence from the positive randomized controlled trials (RCTs),[1-7] which demonstrated both safety and efficacy. Several registries and non-RCTs have mirrored the findings from RCTs.[8-13] With EVT recommended by multiple national and international guidelines,[14-17] it is being increasingly provided in comprehensive stroke centres.

Endovascular mechanical thrombectomy involves mechanically retrieving a clot in a proximal intracranial artery using aspiration and/or stent-retriever devices. The range of specialties performing MT includes neurointerventional practitioners from backgrounds in neuroradiology/neurosurgery/neurology and, in a few places MT is undertaken by interventional radiologists, vascular surgeons and cardiologists. It is worth noting that the evidence base in the nine recent RCTs involved delivery of MT by neurointerventionists in comprehensive stroke canters and in most centres & operators had to demonstrate high volumes, good process times and acceptable technical/clinical results before they could participate in a RCT. MR CLEAN[1] was the only real exception. PISTE[7] allowed smaller MT volume centres to enroll but all centres (& operators) were high volume [Neurointerventional units]. In the recent endovascular trials, not all patients were treated with mechanical thrombectomy despite being in the intervention arm. For example, in MR CLEAN, 38 (16%) of patients in the endovascular arm were not treated with mechanical thrombectomy. The reasons ranged from neurological deterioration before treatment to functional recovery or lack of treatable occlusion in the intervention-suite.

The newer generation devices such as stent retriever and aspiration thrombectomy have demonstrated superiority, safety and reduced complications compared to older generation thrombectomy apparatus. There are further technological and methodological developments aimed at reducing complications such as distal embolization such as claimed improvements to stent retriever designs, large bore distal access catheters (DAC) and more flexible balloon guide catheters. Despite the advances in improved design of the new generation devices and the demonstrated safety and clinical benefits of MT, the procedure is not free from significant complications.

Complications of MT may occur during or after the procedure and range in their severity, but some may be fatal and others can result in long-term disability or prolonged length of stay. Other complications may not result in significant or permanent harm. Each step of the MT procedure carries a risk of potential complications. Referring and treating physicians require an appropriate understanding of potential complications and how to prevent and manage them to optimize the safety and benefits of MT. Similarly, clinicians who manage patients after thrombectomy need to be aware of these complications and their management. The involvement of other specialists in delivering MT for the treatment of AIS may be associated with an increased risk of MT-related complications. There is good literature evidence on aneurysm practice in neurointervention linking volumes to outcomes [18,19] and it would be unwise to anticipate that MT in stroke would differ; particularly bearing in mind the acute time pressure the operator is under in stroke MT. Indeed there is robust evidence from USA linking higher centre volumes to significantly lower mortality in 8533 patients undergoing MT October 2012-June 2016.[REF Rinaldo L et al STROKE 2017 **DOI: 10.1161/STROKEAHA.116.016360**]

Most of the published literature on MT for the treatment of AIS has focused on the evidence for safety, efficacy and clinical benefits of the therapy. There are limited recent publications on the complications and their management.[20-24] This review examines complications from the recent RCTs and non-RCTs with an exclusive focus on the new-generation thrombectomy devices from studies published in the last four years, with the aim of increasing awareness of complications and highlighting approaches to reduce their incidence and improve their prevention and management; NB. obsolete devices/techniques are not considered in this review. Furthermore, this review will focus mainly on the procedural-related complications of endovascular therapy as beyond the immediate periprocedural period the complications might be those relating to stroke not thrombectomy or a mixture of both.

Procedural-related complications

Procedural-related complications (PRCs) can be divided into extracranial and intracranial complications and patients can experience more than one complication. Reported PRC rates in the trials vary between 4% and 29%[1-5, 7] and in prospective studies and registries between 7% to 31%.[10,8,13,22,23,25] There was limited published information on procedure-related complications in THERAPY trial.[26] Definitions and reporting of complications differed between studies, which probably accounts for much of the wide range reported.

Complications reported in individual RCTs and non-RCTs include: access site haematoma, failure to recanalises well/at all, device related failure/fracture/mis or displacement, parent artery occlusion, embolization to new arterial territory (ENT)/distal embolization in target territory, vessel dissection, vessel perforation, arterial access site hematoma, asymptomatic and symptomatic intracerebral hemorrhage (sICH), subarachnoid hemorrhage (SAH), cranial nerve palsy, cerebral vasospasm, access site bleeding, infection & pseudoaneurysm (Tables 1 & 2).

Complications such as embolisation to a different territory, dissection of the arteries, ICH and SAH can occur during or immediately after EVT.

Access-site complications

Access-site complications range from vessel/nerve injury and infection. They can result in: access-site hematoma, distal arterial embolization, critical limb ischemia, increased infection risk, dissection, pseudoaneurysm formation and specifically at the groin, retroperitoneal hemorrhage. In the arm, compartment syndrome is also possible. Acute airway obstruction can occur with direct carotid puncture and safely achieving hemostasis afterwards is more problematic with direct carotid approach with risk of airway obstruction and/or arrhythmias.[27] Generically a puncture site complication can result in anemia and its' complications.

Although access site difficulty is not considered as a peri-procedural complication, problems with gaining access could prolong procedural time and lead to other complications, which in turn could impact negatively on clinical outcomes. Access problems can occur at all locations and along the entire catheter delivery route including aorta (branches arising) extracranial and intracranial arteries. The trans-femoral approach via a common femoral artery is the usual route due to the size and length of endovascular equipment required, but gaining access to the carotid or vertebral circulation through the femoral artery in the circumstances of acute stroke is sometimes difficult and on occasion unsuccessful. Technical difficulties most commonly arise from vascular changes associated with ageing and hypertension such as arterial tortuosity and severe atherosclerosis of the femoral/iliac and aortic arch.[28] These, of course, are common in LVO stroke patients. Access difficulty can on occasion arise from a variety of vessel anomalies or anatomic variants such as aortic arch elongation variants.[29] and obstruction from large retrosternal goitre.[30.] The brachial,[31, 32] radial,[33] transcervical [34] and direct carotid artery[2, 31, ,35] vessels have been utilised, mostly where it was impossible to gain access through either common femoral artery.

Arterial Closure Devices (ACD) are often used after MT; but they are themselves associated with a range of risks/problems (including infection & critical limb ischaemia) and careful patient selection, experience in their use and attention to detail are all important to use them safely.[36]

The reported rate for access site haematoma for the trials ranged from 2%-10.7% [2,3,5,6] and 1%–2% for the non-RCTs.[9-11] However, determination of what constitutes groin hematoma varies and was not uniform across trials. ESCAPE reported two cases of significant puncture site hematoma: the first, a neck hematoma from undertaking a direct carotid artery approach due to failed femoral artery approach; the second, a groin hematoma at the site of the puncture. In EXTEND-IA, one patient developed groin /retroperitoneal hematoma that required blood transfusion.

Clinical management

The management will vary depending on the status of the individual patient condition and can range from emergency vascular surgery (establishing hemostasis/re-establishing arterial flow) to semi-urgent vascular repair (open or endovascular) to initiating blood transfusion to conservative management for the least severe complications (watchful waiting). Conservative management for groin hematomas is usually the main stay of treatment as even some pseudoaneurysms (1% incidence overall) can be managed non-surgically and only rarely is surgery required for groin haematoma.

Radiation risks

Radiation risks: CT/CTA and then MT are likely to result in a combined dose of around 10-12 mSv. This carries a risk of radiation-induced cancer of approximately 1 in 3000 for over 60y (but a somewhat higher risk for younger patients).[37] This is modest compared with the risk of LAO stroke but should not be forgotten as strategies/practices still need to be optimized to minimize radiation exposure.

Device-related complications

Device-related complications can occur with the primary thrombectomy device itself or can be related to ancillary devices such as guide catheter, distal access catheter, balloon guide, microcatheter and support/exchange wire or other guidewire including microguidewire. Allergic reactions to contrast, latex or components of devices (especially nickel) are not uncommon but are rarely severe and life threatening.

Arterial perforation

Arterial perforation (AP) is one of the most serious and feared complications during thrombectomy that may result in poor functional outcomes and higher mortality. It is especially dangerous with recent/ongoing thrombolysis infusion.

The type of AP was not uniformly defined in RCTs but occurred in 0.9 %-4.9 % for the recent RCTs and 0.7%-4.9% of non-RCTs.[8, 25, 9,38,39, 13] The harder one looks, the more likely it is that a small localized perforation or SAH will be recognized. That can relate to a) quality of digital subtraction angiographic equipment (neuro-optimized biplane flat detector systems providing optimal image quality), b) how still the patient keeps and c) operator awareness/experience.

In seven of the RCTs, perforations were recognized and reported- 12/868 patients (1.4%), there were a total of two (0.9%) perforations in MR CLEAN; one (0.6%) in ESCAPE; one (2.9%) in EXTEND-1A; one (1%) in SWIFT PRIME; five (4.9%) in REVASCAT; one (1.8%) in THERAPY and one (0.7%) in THRACE. In EXTEND IA, the procedure was abandoned in one patient following a guidewire perforation that led to parenchymal hematoma with associated clinical deterioration prior to the deployment of the stent retriever. Arterial perforation is usually identified by extravasation of contrast material.[12, 20, 40]

The risk of AP is increased during a) "blind maneuvering" while trying to gain access to/beyond occluded intracranial vessels with a microguide wire/microcatheter and b) while withdrawing a stent retriever.[20, 38, 39] In the case series reported by Mokin et al., 2016, 16 perforations occurred in1599 patients (1%) mainly due to either difficulty navigating the intracranial arterial occlusion or in the process of stent retriever removal. Additionally, the perforations involved more distal vessel segments in 63% of cases.[38] Among the 16 patients with perforations there was 56% (9/16)) in-hospital deaths, 63% (10/16) 90-day mortality and 25% (4/16) good functional outcome at 90 days**.**

Akpinar and colleagues (2016)[20] reported one case of AP that was caused by microguidewire while trying to gain access through an occluded MCA. Leishangthem et al., 2014 reported a case of AP that occurred during withdrawal of the stentriever.[39] Among the eight cases (3.3%) of perforations reported by Soderqvist and colleagues, one of the perforations occurred in the common iliac artery.[25] Potential predisposing factors for AP include vessel tortuosity & athersoclerosis, which is frequently found in older people. In a case report, the patient had moderate tortuosity of the supraclinoid ICA and Intracranial atherosclerosis, both of which might have been contributing factors.[39]

Clinical management of AP

Intra-procedural perforation requires immediate action as patients are at very high risk of sICH and further deterioration. Similar to any procedural vessel rupture, the perforating device should not be pulled back immediately as it may be partially occluding the site of the perforation. Leaving the catheter in situ initially could also reduce the occurrence of SAH that could be increased by prior use of IV rt-PA.[20,40]

General measures include the immediate verification of the perforation by careful, controlled guide catheter angiogram. Initial measures include careful BP management and reversal of anticoagulation (if systemic anticoagulation has been used) using appropriate measures.[20, 39] Even the simple expedient of hypotension is not without major risk though as it may cause any collateral circulation to fail and a major infarct to result. Inflation of an intracranial balloon can also be considered.[38] If the bleeding persists after a period of balloon inflation (5-10 minutes), injection of liquid embolic agents (NBCA or Onyx) or insertion of detachable coils can be used to occlude the damaged arterial segment.[20, 38] There will be the need for subsequent radiological imaging to monitor for potential development of pseudoaneurysm at the site of perforation and thromboembolic complications.[40] Clearly parent artery occlusion in these circumstances will often result in major stroke with attendant risks of severe disability, requirement for hemicraniectomy or perioperative death (with potential medicolegal consequences - in the UK at least).

Arterial dissection

Arterial dissection (AD) is often asymptomatic if localized and recognized early. However, it increases the risk of occlusive or thromboembolic complications and may lead to severe neurological deficits.[41] This is particularly a risk if the dissection is not recognized promptly- so that the MT approach is not modified accordingly. The rates of AD range between 0.6%-3.9% for the RCTs [2,1,6,5] and 1%-6.7% for the non-RCTs.[8,11, 13, 20, 25, 23,22, 42]

Arterial dissection can occur during any catheter or guidewire manipulation.[20,21] Among the three cases (5.4%) of ADs reported by Akpinar and colleagues, one was attributed to intimal vessel injury caused by balloon-guiding catheter inflation during the intervention. The second was due to the stiff guide-wire that was required to guide the catheter in tortuous vessels.[20] In another case series, two of 92 (2.2%) cases with ADs occurred during guidewire manipulations.[42]

Dissection can involve any vessel, either extracranial, at the puncture site or intracranial vessels. In the case series by Akinar et al., intracranial dissection was noted in two patients (7%) and extracranial dissection in one patient (3.5%).[21] In the RCTs, ESCAPE had one and REVASCAT had two of the three reported cases of carotid artery dissection, A review of the SWIFT database for peri-procedural complications identified vessel dissection in five of 144 patients (3.5%). In four of the patients, the site of the dissection was the cervical carotid artery and in one case both the cervical and petrous portions of the ICA were dissected.[43] Arterial dissection with associated adventitia penetration may be diagnosed as contrast extravasation during thrombectomy.[42] It more often appears as a localized contrast pocket or a double lumen or an intimal flap on DSA images. Other indirect indications of dissection may be arterial occlusion, stenosis, string sign, aneurysm, or pseudoaneurysm.[41]

Clinical management of dissection

Treatment options include the use of anticoagulant or [dual] antiplatelet therapy for non-flow-limiting dissections or asymptomatic cases. In severe cases, particularly in flow-limiting dissections, balloon angioplasty or stenting may be necessary to align the intimal flap to the vessel wall and secure the access site.[21, 32, 41,] Of course with acute stent placement the use of dual antiplatelet therapy is usually required and this is recognized to increase the risks of ICH/HTI.

Vasospasm

Vasospasm usually results from “irritation” of the vessels by catheter manipulation during thrombectomy,[20] it can also involve the vessels at the access site.[23] Behme and colleagues reported vasospasm of access vessels in five of 176 patients (3%).[23] Although usually asymptomatic, it can lead to decreased blood flow and potentially poor recanalization in the event of the vasospasm being severe enough to cause significant arterial occlusion.[44] Arterial vasospasm was not uniformly defined in RCTs but occurred in 3.9%-23%[5,4,6] and 3%-20% of non-RCTs.[23, 25,20] Arterial vasospasm was the commonest procedural complication in THRACE trial, reported in 33 of 200 patients (23%).[6] A review of the SWIFT database detected angiographic vasospasm in 29 of 144 patients (20%), but it is important to note that none had any resulting permanent adverse effects or clinical deterioration.[43]

Clinical management

For catheter or guidewire-induced vasospasm, the device should be immediately retracted to minimize irritation of the vessel wall and control imaging performed to ensure flow is not occluded. In most cases, vasospasm will diminish within minutes without further treatment. If vasospasm persists, BP may be increased and intra-arterial nimodipine can be injected slowly – typically 0.5mg-1mg over several minutes.[20] (NB Nimodipine is not licensed for this use). Whilst calcium channel blockers are effective, their propensity for lowering BP necessitates close monitoring of MT stroke patients.[20] Prophylaxis against vasospasm in neurointerventional procedures may be effected by use of Glyceryltrinitrate (GTN) patch or addition of nimodipine to catheter flush bags. However, in AIS neither maneuver can be routinely recommended due to the risks posed by hypotension in LVO stroke patients.

Intracerebral hemorrhage

Intracerebral hemorrhage (ICH) is one of the commoner and potentially more serious complications of MT, with consequent increase in morbidity and mortality. It can occur during thrombectomy or postoperatively within 72 hours. Like ICH following IVT it may be symptomatic or asymptomatic.[32, 45] Most patients treated with MT receive IV thrombolysis, which is probably the main risk factor for sICH in MT patients, but there is no evidence to suggest an increase in the rate of sICH in patients treated with combined IVT and MT compared with IVT-alone, particularly from the RCTs.

Randomised trials and other studies do not all report the incidence of ICH using the same definition. The different definitions include those in: The European Cooperative Acute Stroke Study (ECASS) II, The National Institute of Neurological Disorders and Stroke (NINDS) and The Safe Implementation of Thrombolysis in Stroke: A Multinational Multicentre Monitoring Study of Safety and Efficacy of Thrombolysis in Stroke (SITS-MOST). Allowing for different definitions, reported frequency of sICH for the RCTs range from 3.6%-9.3%.[1, 2, 5, 26, 6]. In the pooled analysis of five of the trials, the overall risk of sICH was 4.4% (28/634) in the combined IVT and MT group and 4.3% (28/653) in the IVT/control group.[46] The rate of sICH in the MT-alone group was not reported by the trials. While

THERAPY reported the highest rate of 9.3%, EXTEND-IA, SWIFT PRIME and PISTE did not report any sICH. In ESCAPE, the one patient with sICH had hemicraniectomy. The unmonitored reported rates of sICH for the non-RCTs ranged from 1.9%-15.8%.[13, 47, 9-12, 8] Minnerup et al. 2016, reported the highest rate of sICH among the non-RCTs.[8]

Imaging parameters such as low ASPECTS score, large ischemic core, very low cerebral blood flow and thrombus length >14 mm as well as clinical factors including baseline stroke severity and diabetes have all been shown to be associated with increased risk of sICH.[48-50] Prolonged thrombectomy procedural time has also been found to be associated with increased risk of sICH.[48, 49] Other potential risk factors include: reperfusion injury and device-related vessel injury or perforation.[32, 39, 41] In the case series by Nikoubashman et al., 2016, the reported four cases of ICH were caused by vessel perforation.[9] Likewise in the case series by McCuster et al., 2015, two of the 14 patients who developed sICH were caused by rupture and perforation of the right MCA, presumably by a microguide wire.[12]

Symptomatic ICH can be suspected clinically through deteriorating neurological status and confirmed radiologically with an emergency brain imaging.[32] Alternatively, compression of the major cerebral arteries (anterior or middle cerebral arteries) on angiogram could aid with the detection of significant bleed in the basal ganglia region.[41] Bleeding secondary to a perforated vessel can be diagnosed on fluoroscopy/fluorography during thrombectomy.[51] Intraprocedural Cone Beam CT on angio machine may also be obtained if procedural SP/ICH/SAH is suspected and can be helpful in immediate management.

Small areas of contrast extravasation caused by the disrupted blood brain barrier following stroke plus MT might be mistaken for ICH. An MRI brain scan can differentiate ICH from contrast extravasation but usually CT or serial CT demonstrating clearing suffices.[41, 51,52] Some of the imaging signs suggestive of contrast extravasation over a procedural bleed include absence of mass effect and hyperdensity in exact area of infarct seen on baseline non-contrast CT.

Clinical management

The risk of ICH might be minimized through appropriate selection of suitable patients for MT and improved outcomes might be achieved with surveillance for detection of early neurological deterioration, both peri-procedural and post-operatively.[45, 49] This is in addition to optimizing blood pressure management, particularly post-operatively. However, the evidence for any effect of BP management in this clinical scenario is weak.[32, 41, 45]

Subsequent management will depend on the cause and severity of the bleed.
In cases of sICH resulting from vessel perforation or dissection all measures should be taken to stop and prevent further bleed using appropriate interventions for management of perforation and dissection. Adherence to guidelines for the management of spontaneous ICH is recommended.[53] As yet there are no proven therapeutic options in post stroke/MT related ICH.

Subarachnoid hemorrhage

Subarachnoid hemorrhage is a common complication that is not infrequently benign, but extensive or severe SAH can lead to neurological deterioration with consequent poor outcomes. The reported rate of SAH in the RCTs was 0.6%-4.9%[2,1,4, 5] and 1%-5.5% for the non-RCTs.[9, 11, 47, 54]

The proposed mechanisms for SAH include: intra-procedural vessel perforation or dissections, occult rupture resulting from stretching of the arterioles and venules in the subarachnoid spaces during the process of withdrawing the stent retriever and disruption of the cerebral microvascular barriers.[12, 35, 55] McCuster and colleagues reported a case of SAH due to rupture of the MCA with resultant diffuse SAH.[12] In the case series by Yoon and colleagues, the reported 16% of SAH was claimed not to relate to vessel dissection or perforation but to occult bleed detected angiographically.[55]

Clinical management
Careful surveillance is appropriate in asymptomatic cases of SAH as there are still risks of delayed hydrocephalus and/or vasospasm with delayed cerebral ischemia (DCI) may occur. In cases resulting from procedural vessel perforation or dissection then the bleeding has to be stopped if possible using appropriate interventions.

Stent detachment

Unexpected/inadvertent stent detachment during mechanical thrombectomy is a well-recognized complication. Stent detachment has been reported to be associated with higher rates of ICH, poorer clinical outcomes and increased mortality.[56,57] It occurred in 0.66%-3.9% of patients treated in the non-RCTs.[59, 20-22, 58,] None of the recent major trials reported stent deployment as a complication – whether this is because it never occurred or just it was not recorded/reported is uncertain. Unsurprisingly it is a problem occurring predominantly with detachable stents (Solitaire AB™). Masoud et al., 2016 found all stent detachments were related to first-generation stroke thrombectomy devices.[59] Although usually asymptomatic itself, further procedural complications, such as vasospasm, arterial perforation or parent artery occlusion and ICH, may arise – particularly if retrieval of the detached stent is attempted.

Kim and colleagues reported unexpected stent detachment among nine of 232 (3.9%) cases during thrombectomy using Solitaire.[58] Similarly, Castano et al., 2016 reported unwanted detachment in six of 262 patients (2.3%).[56] In a review of the Manufacturer and User Facility Device Experience (MAUDE) database, among the 85 patients with adverse events related to the use of the Solitaire FR stent, 80 patients had an inadvertent detachment of the device.[57] The majority of the stent detachments occurred with the first-generation and not the second-generation Solitaire FR device. This was redesigned to reduce the risk of unwanted detachment (There is no information on SOLITAIRE AB/FR versus FR2 use from the trials).

The potential causes or predisposing factors for stent detachment include: the structural features of the stent; the number of stent passes during the procedure; the nature and length of the thrombus or plaque; tortuous anatomy, arterial wall calcifications and arterial stenosis [57, 58,60] Among the other causes of stent detachment are device fatigue, which may occur following more passes; pusher wire fatigue and device retrieval through a proximally stented artery.[59] Patients with tandem artery occlusions requiring deployment of a proximal carotid stent before retrieving the distal clot are at appreciable risk of device detachment due to entanglement in the proximal carotid stent.[59, 61]

From the MAUDE database, the identified causes for stent detachment included: device resistance during retrieval of device among 12 of 34 cases (35%); stent snagged on a previously inserted carotid stent for eight of 34 cases (24%); cases of devices relatively larger in diameter to the target vessel occurred in one case (3%) and in another case (3%) during the exchange of a second micro catheter with the first micro catheter after engagement of the stent retrievers. This is in addition to the following: tortuous anatomy in five of 34 cases (14.7%), a hard or lengthy thrombus in three of 34 cases (8.8%) and a calcified or large-burden plaque in five of 34 cases (14.7%).[57] A recent multiple regression analysis of the North American Solitaire Stent Retriever Acute Stroke registry identified three or more thrombectomy passes among other factors as a predictor of poor functional outcome despite high recanalization rates.[62] However, this is a correlate of poor/failed recanalization not of device failure per se.
Adhering to the manufacturer’s instructions for use (IFU), particularly as to the maximum number of passes for each of the different devices may reduce the frequency of stent detachment.[63]

Clinical Management
The treatment option will depend on an evaluation of the risks and benefits of recovering the detached stent. Nonetheless, the treatment options include: to leave the stent in place if the target vessel is open[59, 60] the use of a second device to attempt to capture & retrieve the detached device and lastly surgical extraction of the detached stent [60] – intracranially this is an heroic and high risk proposition and unlikely to be considered post IVT. Balloon angioplasty of the stent might be considered in cases of tandem artery occlusions with a situation where an intracranial retriever stent becomes caught in a carotid stent (more likely if recently implanted).[57,59]

Embolisation to new vascular territory

Embolisation is a major issue, occurring in 1%-8.6% in most trials[1-3, 5,6] and 1%-12.5% in the non-RCTs.[11, 13, 10, 22] While MR CLEAN had the highest rate of embolisation among 20 of 233 patients (8.6%),[1] SWIFT PRIME & PISTE trials had no reported embolisation.[4, 7]
A recent post-hoc analysis of ESCAPE found infarct in a new previously unaffected territory (INT) in a total 14 (4.5% overall), 5.0% (n=8) in the MT group and 4.0% (n=6) in the control group on post-operative imaging. [64] Gascou et al., 2014 reported the highest rate of embolisation among the non-RCTs at 12.5%.[22]

Infarctions in a new territory are more related to an interaction between where the thrombus is and the procedure.
A clot during retrieval can migrate to a proximal previously unaffected territory (thence distal migration may occur) or distally within the target artery. In distal embolization, the migrated clot can remain in the same vessel or break up and dissipate into many multiple tiny branches and possibly affect other surrounding vessel territories.[32] The risk of embolisation occurring, particularly distal embolisation, is increased during the retrieval of a proximal clot.[65] Similarly, variation in the guide catheter used and the clot type have been attributed as potential contributing factors.[65] It has been reported to occur less often with the use of balloon guide catheters.[66]

Clinical management
The treatment option will be determined by the location of the emboli. In proximal embolisation, the displaced clot can be removed using a stent retriever or any of the other devices[32] for distal embolization, intra-arterial thrombolytics could be used if appropriate and in the absence of any contraindication- (NB Alteplase is not licensed for this intra-arterial use).[51]

Strategies for Preventing Complications

The key strategy to minimise complications associated with MT, particularly the peri-procedural ones, is obvious and simple – it is for thrombectomy to be only performed by trained physicians competent in intracranial endovascular procedures and undertaking them regularly to maintain skills; as recommended by the various multi-disciplinary guidelines.[15, 67-69] MT should be performed by a multidisciplinary team operating within comprehensive stroke centres with adequate (high) volumes, and undertaking regular assessment/audit of technical and clinical results, process times and complications.

The frequency of device-related complications could also be minimised by careful adherence to manufacturers' IFUs. Clinical guidelines have recommended the use of the stent retrievers as first-choice devices and the older generation devices should not be used.[67] There is limited evidence for the identification of which of the new-generation devices cause fewer side effects. The role of direct aspiration versus stent-retrievers in particular remains unclear and is also the subject of ongoing trials. Although in the ASTER trial there were no statistically significant differences, in procedural complications like sICH and embolisation in a new territory between stent retriever and ADAPT (a direct aspiration first pass technique) (Lapergue B,2017).[70] Similarly, two observational studies found no differences in the rates of sICH or procedural complications between the two procedures (Stapleton CJ et al. 2017, Lapergue B et al. 2016).[71,72] We can anticipate many more head to head device trials in the future.

Likewise whether balloon guide use will reduce complications is uncertain with some evidence favouring it.[73,74]

Tandem occlusions can provide treatment challenges with a potential higher risk of procedural complications. In a recent systematic review of tandem occlusion treated with acute ICA stenting in combination with thrombectomy, the rate of sICH was 7 % and mortality 13% (Sivan-Hoffmann et al., 2017).[75] In a single retrospective data analysis of Tandem occlusion treated with carotid artery stenting and mechanical thrombectomy concurrently the procedural complications included arterial dissection (2 patients), vasospasm (3 patients). There were 2 [4.4%) sICH 24 hours post procedure and 5 (11%) inpatient deaths (Rangel-Castilla et al. 2017).[76] Villwock et al. in their comparison of carotid artery stenting versus angioplasty alone in the setting of ischemic stroke found a higher mortality rate in the angioplasty-alone compared with the carotid stenting group (9.0% vs. 3.8%)[Villwock et al. 2015].[77]

Simple proven safety measures such as use of pre-surgical checklists (e.g. World Health

Organisation one) should not be overlooked in the haste to achieve recanalisation at all costs. In the absence of specific guidelines for the management of complications in the setting of mechanical thrombectomy, adherence to existing management strategies for neuroendovascular interventions and to specific national guidelines for thrombectomy [21, 69] is appropriate whilst further areas of research are pursued - including into the role of GA, direct aspiration, balloon guide use etc. in MT.

The use of general anesthesia in MT is controversial. In a pre-planned subgroup analysis of MR CLEAN, GA was associated with worse outcomes [78] and this tallies with an earlier meta-analysis of predominantly non RCT data.[79] In a recent subgroup analysis of MR CLEAN a decrease in mean arterial pressure (MAP) during EVT under GA was associated with poor outcome. (Treurniet er al 2017).[80] On the contrary, in the recent ANSTROKE study, there was no difference in the 90-day neurological outcome between the GA and CS groups (Löwhagen Hendén P et al., 2017).[81] Similarly, in the preliminary results from the GOLIATH study, MT under GA, did not result in worse outcome (NCT02317237).[82] Likewise, in an earlier small single centre German RCT, GA was not inferior to conscious sedation/LA technique.[83] Larger multicenter pragmatic RCTs are required to clarify this.

Another key strategy to minimise complications is to recognize the fairly select group of patients included in recent trials and not routinely extrapolate the use of MT to other patient groups - where it may be less effective and more hazardous- until appropriate evidence to justify such an extension of practice is available.

Appropriate and judicious use of critical care facilities post-operatively should be considered on a case-by-case basis and must be immediately available (as in NICE guidance).[69] Neurocritical care may help reduce the impact of procedural complications and may minimise the risk of some post-operative ones.

Conclusion

With MT now the established treatment for the management of LVO AIS and recommended by multiple national and international guidelines, the wider use of thrombectomy is likely to provoke a consequential rise in the frequency of the complications associated with the procedure. Many of the complications reviewed are not uncommon such as embolisation to new vascular territory, sICH, vessel dissection and perforation. They are widely reported, including in RCTs, where thrombectomy was generally performed by expert neurointerventionists in high volume units (the probable “best case” scenario). Overall from recent RCTs undertaken in high volume expert centres, the risk of complications with actual/probable sequelae for a patient from MT is ~ 15% (comprised of: ~4% access-site related, ~6% SAH &/or IVH &/or additional sICH, extracranial bleeding/perforation and 5% distal or new arterial territory embolisation).

There are limited evidence-based guidelines for the management of most of the complications. Early recognition of the potential risk factors might help prevent the more likely complications and promote proactive management of affected patients to reduce poor outcomes.

Evidence for the current management of complications associated with MT is based mainly on extrapolation from other related procedures/clinical situations, or restricted to anecdotal or published expert opinions. There is, therefore, a need for research on the prevention and treatment of most of the complications associated with MT. This will help formulate evidence-based guidelines and recommendations for the best patient care.

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JSB searched the literature, reviewed available studies, and wrote the paper. PMW made critical revisions, co-wrote the paper, PM reviewed the paper. GAF reviewed the paper and made critical revisions. AMB reviewed the paper and made critical revisions.

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PMW – educational consultancy work for Codman and Microvention Terumo Inc.;
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AMB –senior medical science advisor of Brainomix.
JSB- declare no conflict of interest.
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