**Percutaneous management of acute ischaemic stroke**

Dr Helen C Routledge1, Professor Nick Curzen2

1. Worcestershire Acute Hospitals NHS Trust, Worcester UK
2. University Hospital Southampton NHS Trust, Southampton, UK

*Corresponding Author – Helen Routledge: h.routledge@nhs.net*

Educational objectives

To understand both the rationale and principles behind percutaneous management of stroke

To be aware of the evidence base for this treatment

To appreciate the current logistical challenges and how they might be overcome

**Introduction**

In principle, the similarity between opening an occluded cerebral artery and an occluded coronary artery, when the perfusion to that organ is acutely compromised, is inescapable: to re-establish antegrade flow as quickly as possible to minimise downstream damage. There are, of course, important differences between an acute myocardial infarction (MI) and an acute ischaemic stroke in terms of pathophysiology, diagnosis, procedural technique and ongoing care. However, the similarities are important: the need for a sophisticated emergency network that facilitates rapid diagnosis, transportation to an appropriate facility, a team of highly trained staff capable of delivering the procedure to restore vessel flow, and appropriate in-patient and rehabilitation services. Both procedures are highly effective at improving outcomes, but successful mechanical thrombectomy (MT) for stroke is particularly beneficial: the number needed to treat is just 2.6 to prevent death or major disability, the latter defined as the difference between living independently or remaining reliant on carers long-term [1]. The majority of stroke patients who would benefit from MT do not yet have access to this procedure.

In this article we examine the rationale behind emergency percutaneous intervention in ischemic stroke, the techniques involved and the evidence behind the recommendation that this treatment should now be considered in all adults presenting within 24 hours of symptoms consistent with a large vessel occlusion (LVO) [2]. In the second part of this overview, we discuss the patient pathway and, in particular, the barriers that remain to suitable patients having universal access to effective treatment. Some solutions may lie in utilisation of existing sophisticated networks for primary angioplasty for acute ST elevation MI, and in lessons learned from the development of interventional stroke programs in other countries. What is clear is the urgent need to provide MT to as many suitable patients as possible to minimise avoidable disability and death associated with this condition.

**The size of the problem: estimated numbers of patients suitable for mechanical thrombectomy**

Stroke is one of the leading causes of death and the leading cause of permanent complex disability in the western world. A third of survivors lose their independence. In 2019-20 the UK Sentinel Stroke National Audit Programme (SSNAP)[3] reported 89,280 strokes, of which 77,735 were due to cerebral infarction. Somewhere between 10-25% of stroke presentations can be attributed to a LVO (occlusion of the carotid, proximal middle cerebral, vertebral or basilar arteries) [4]: thus, an estimated 10,000 UK patients per year would potentially benefit from an intervention involving mechanical thrombectomy. Furthermore, considering changing demographics, the problem will grow, with an anticipated 50% increase in the total number of strokes by 2035. Improvements in the procedural technique, logistics and expansion of the indications, in terms of time and salvageable brain tissue, will contribute to a predicted exponential rise in demand for MT in the coming decade.

**Interventional stroke treatment - How does it work?**

While acute MI is caused by plaque rupture in an atheromatous epicardial coronary artery in the vast majority of cases, the vessel occlusion in acute ischemic stroke has a less predictable, more disparate, aetiology. Many ischaemic strokes (30-50%) are caused by embolization of intracardiac thrombus in patients with atrial fibrillation. In such cases, fragments of thrombus lodge most often in the middle cerebral artery causing vessel occlusion and reduced perfusion to the cerebral cortex and basal ganglia. In 25% strokes the cerebral vessel occlusion is caused by atherosclerosis/thrombosis in the internal carotid or vertebrobasilar artery. In the remainder of patients, the aetiology is presumed to be intracranial small vessel disease, a lacunar infarct or cryptogenic.

Just as with coronary occlusion, the use of timely intravenous thrombolysis (IVT) to restore perfusion predated interventional treatment by several years and led to a step change in stroke management. When a large vessel is proximally occluded however, not only is the area of brain at risk largest but IVT alone is effective in fewer than one in ten patients treated, [5] leaving the majority of such patients without reperfusion, but at high bleeding risk. The ability to recanalise the vessel by mechanical means is vastly more effective at restoring perfusion, preventing permanent and disabling brain death. Recanalisation may be achieved by the extraction of embolised thrombus from the occluded vessel at one or more levels above the carotid.

There are two methods of percutaneous thrombus extraction: thrombo-aspiration and the use of a Stentriever device. While it was the development of the latter which undoubtedly advanced success rates of the intervention in the 2010s, improvements in the former and use of the two techniques in combination have continued to improve outcomes [6,7].

In common with most percutaneous intra-arterial procedures, default access is via a femoral puncture, although radial access is increasingly employed. The initial familiar short haemostatic sheath is quickly exchanged for a longer (85cm, 7/8F) flexible version designed to give stable access to one or other carotid or vertebral artery. Next, in order to access the relevant intracerebral vessel, usually pre-defined by a computed tomography (CT) angiogram, a 5F shaped diagnostic catheter is chosen and advanced over a 0.035” guidewire, through the long sheath into the common carotid or vertebral artery. Familiar catheter shapes used are illustrated in *Figure 1.*

It is over this 5F device that the long support sheath is then further advanced. Angiographic images are obtained with careful injection of radiopaque contrast to define and roadmap the anatomy, delineate carotid or vertebral pathology and locate the target occlusion. Any device inserted now beyond the petrous portion of the carotid or beyond the vertebral artery will be of small calibre and designed specifically for the intracerebral circulation.

*Intracerebral thromboaspiration*

Following removal of the diagnostic catheter an aspiration catheter is prepared on a second flush line. This single lumen, typically 0.07” internal diameter, hydrophilic microcatheter is advanced through the guide, but needs to be steered to reach the occlusion, by use of a 0.014” floppy guidewire supported by a 160 cm neuromicrocatheter. Closer to the occlusion a magnified road map is recorded and then the 0.014” guidewire can be advanced under screening to follow the typical path of the middle cerebral (or basilar) artery. The guidewire of choice is different from those used in the coronary circulation, with a more supportive tip compensating for the fact that the wire cannot be advanced into distal circulation for support as it might be in the heart. The microcatheter approaches the clot, followed by the Aspiration catheter, advanced to the proximal end of the clot and, on retraction of the microcatheter and wire, an attempt at aspiration can be made (*Figure 2*). Differing techniques of aspiration are described, including proximal contact or piercing the clot with the microcatheter, but there is consensus on the importance of ‘first pass aspiration’ to avoid embolization of fragments. [8] Suction is achieved with large volume locking syringes, familiar to anyone undertaking thrombus aspiration in primary coronary intervention, or infrequently using a vacuum pump device. With the ‘mother and child’ system of catheters described it is important to remember to aspirate on all ports when potentially drawing thrombus back into the guides and sheaths and here a carefully trained and familiar assistant, plus good communication, are vital.

*Stentriever technique:*

The 160cm (0.0021 diameter) neuromicrocatheter, advanced over the 0.014” wire (and inside the aspiration catheter), can alternatively (or subsequently) be used to position and deploy a Stentriever device. Only the wire is removed and replaced by this device, effectively a self-expanding thin and flexible stent (on a stiff wire) that embeds itself in the clot and enables it to be pulled out of the vessel in one piece.

The microcatheter is retracted deploying the device in the clot. Allowing this process to occur over 60 seconds effectively allows the Stentriever to ‘absorb’ the clot. Then, while aspirating on both the aspiration catheter and the sheath, with locking syringes, the Stentriever is withdrawn into the aspiration catheter and out of the body.

Repeating the angiogram at this point should reveal reperfusion and a distal vessel roadmap which is examined in orthogonal views to determine flow, residual tandem occlusions and exclude iatrogenic vessel dissection or perforation.

*Concomitant therapy*

Currently, most patients undergoing thrombectomy receive bridging IVT with Alteplase *en route* to an interventional stroke procedure. Trials to date have failed to consistently demonstrate non-inferiority, in terms of clinical outcomes, of omitting IVT [9,10,11], such that bridging remains the recommendation. It is an interesting observation that in these same studies the likelihood of a patent vessel at angiography pre-MT, after IVT, is less than 7% [9] yet there appears to be some benefit. Hypotheses include easier extraction of a lysed clot or that the lytic somehow deals with residual distal fragments despite it’s short half-life. Tenecteplase has been administered as an alternative, with Alteplase in short supply, and rapid-bolus administration rather than infusion enables easier patient transfer. [12] Whether intra-arterial thrombolysis following MT can contribute to microcirculatory reperfusion continues to be investigated [13].

Minimal heparin is used in MT because of the risk of haemorrhagic transformation in areas of infarct. Heparin is added, in variable doses, to the continuous flush lines to which all devices are connected and this may be supplemented where peri-procedural clot is observed. The role of anti-platelet therapy is less established than in coronary intervention. Intravenous aspirin is usually given and a second anti-platelet reserved for cases in which a stent (usually carotid) needs to be deployed.

*Post-Procedure*

Reperfusion may be followed by complete recovery of neurological function but as most procedures are still performed with general anaesthesia, it is the angiographic appearance that determines whether an adequate result has been achieved. TICI (Thrombolyisis in Cerebral infarction) 2b or 3 flow (Table 1 [14]) maybe regarded as success but there is increasing evidence that eventual clinical outcomes are vastly superior with TICI 3 flow. [15] When to stop and accept the result is, as always, determined by operator experience.

The benefits of general anaesthesia include controlled haemodynamics and lack of movement of an often-agitated patient. Procedures may proceed under conscious sedation, and this remains a potential area of future change.[16]

After reperfusion, normalisation of the arterial pressure should be the immediate aim, to avoid reperfusion injury, unless there is a contralateral severe stenosis. Until this point a pressure of 160mmHg systolic or above is allowed as an inherent compensatory mechanism to maintain cerebral perfusion.

Following MT, the long sheath is removed and a vascular closure device often used. Immediate post procedural care should be on a high dependency unit with arterial pressure monitoring and observation for improvement or sudden, sometimes subtle, deterioration in neurological function which may prompt immediate re-imaging or emergency re-intervention.

**The Evidence for Efficacy**

*Thrombolytic treatment for stroke*

In the 1990s, IVT was shown to lead to a favorable outcome in more patients than conservative supportive care. The evidence suggested an odds ratio of 0.85 for death or dependance for patients treated within 6 hours. [17] Prompted by publication of the UK’s National Stroke strategy (2007), [18] and National Institute for Health and Care Excellence (NICE) guidance (2008), [19] streamlined emergency pathways had to be developed so ‘FAST positive’ patients could rapidly access CT scans and specialist stroke nurses. The number receiving Altepase increased, but success was constrained by the time window, contraindications to IVT and importantly that in LVO patients, successful reperfusion remained around 10%. [20] The high reperfusion failure rate and associated bleeding helped to drive the development of interventional procedures. With the early-generation MT devices however, investigators struggled to demonstrate a convincing benefit. [21]

*Endovascular Therapy Trials*

In 2015, multiple randomised controlled trials, using the newer Stentriever devices were published, with clear evidence of clinical benefit from a strategy of IVT followed by immediate MT for anterior LVO stroke. A subsequent meta-analysis [1] showed a number needed to treat of just 2.6 to achieve a 1-point improvement in the modified Rankin score (mRS) (where 0 is no disability and 6 is death).

Treatment has further evolved over the last seven years, and in 2019 NICE [22] concluded that thrombolysis and thrombectomy should be offered to all anterior circulation strokes presenting before 6 hours. Advances in catheter technology and smaller Stentriever devices have enabled MT of more distal or medium-sized vessel occlusions, thus potentially expanding the evidence to a further 25% of ischaemic stroke patients. [23] The simpler, less costly aspiration-first approach has been demonstrated to be effective in many patients. [7] Most importantly, the DAWN [24] and DEFUSE III [25] trials have shown benefit to patients presenting between 6 and 24-hours where salvageable brain tissue was demonstrated by advanced imaging techniques. The latter trials recruited "wake up" stroke patients with uncertain symptom duration as well as patients with symptoms definitely over 6 hours old. Imaging was performed using diffusion weighted MRI or CT-perfusion to confirm salvageable brain before randomisation to medical therapy or mechanical treatment. Notably, most patients did not receive a thrombolytic. Benefit remained, with 40-60% achieving good (mRS 0-2) outcomes, compared to 10-20% in the untreated groups. [26] In this cohort, in whom nothing but supportive care was previously available, another step change in stroke outcomes is achievable by MT.

**The Patient Pathway**

Realisation of the enormous benefits demonstrated in the clinical trials depends upon our ability to get every patient with acute LVO and salvageable brain tissue into a thrombectomy-enabled angiography suite in time. This requires a well organised emergency pathway that begins at presentation and achieves rapid imaging, decision-making and then MT where appropriate.

*Awareness and pre-hospital process*

Public awareness campaigns, to help patients and relatives recognise the possibility of stroke and seek help urgently, have been key. Coupled with this is a focus on co-ordinated, streamlined local and regional pathways, integrating ambulance services (land and air), emergency departments and acute medical teams in all receiving hospitals.

As with STEMI, optimal organisation will vary between rural and urban networks, particularly regarding the best first port of call for a ‘FAST’ positive patient. The need to get the suitable minority of stroke patients to an MT-enabled angiography suite quickly must be balanced against the potential for overwhelming centralised units with non-LVO patients and stroke mimics, who need repatriation for appropriate treatment locally and in order to maintain the service. This issue is exacerbated by the ever-worsening hospital bed crises. While studies suggest that ‘drip and ship’ can work as well as a ‘direct to mothership’ pathway, [27] it’s clear that outside of a trial setting, the factors influencing whether a patient gets this intervention rarely favour the patient presenting to a local hospital. The ideal of pre-hospital triage is limited by a lack of *pre*-hospital imaging (outside of the mobile stroke unit model) and the complexity of scan interpretation, in stark contrast to the relative simplicity of recognising ST elevation on an electrocardiogram in the STEMI pathway.

Thus, the National Stroke Service model [28] describes the much needed and ongoing work to facilitate pathways that allow for rapid recognition and referral of *all* suitable patients for MT, wherever they present.

*Receiving the patient*

When a potential MT patient is recognised in the community, the teams involved in arranging, interpreting and reporting the CT/CT angiogram should be pre-alerted to avoid delay. Investment has been made into software solutions equipped with artificial intelligence (AI)-mediated scan interpretation, which can be set up to alert the entire stroke team right from the ambulance, thereby introducing highly streamlined processes.

The receiving clinician in the first hospital is key to ensuring that the correct patients have timely access. In many units this will be a specifically trained ‘thrombolysis nurse’ / advanced care practitioner. Their role is to establish that the patient is presenting as a likely LVO stroke, to determine the pre-stroke mRS and National Institute of Health Stroke Scale (NIHSS) scores on arrival, to verify the history and timings of the events surrounding presentation and to determine contra-indications to thrombolysis, anti-coagulants and anti-platelet therapy. All of this ideally undertaken while accompanying the patient without delay to the CT scanner.

*Imaging*

A plain CT-scan excludes intracerebral haemorrhage or stroke mimic such as tumour. If normal or demonstrating early infarct then the protocol should mandate an immediate CT-angiogram. Whether further advanced imaging is appropriate in the receiving hospital or only in the neuroscience unit, and who is responsible for image interpretation and or transfer has been the subject of intense discussion since thrombectomy recommendations were written. This has now helpfully been standardised with the national optimal stroke imaging pathway (NOSIP, Figure 3). [28]

*Secondary transfer*

Similar to door-to-balloon times, by which cardiology teams are judged in STEMI, the door-to-groin puncture is used as a metric in MT centres. Of equal, perhaps greater, importance for the patient population is the ‘door in door out’ time: that is, the delay between presenting at a non-neuroscience centre and leaving that hospital for transfer to the thrombectomy centre, having been scanned, referred and accepted by the MT team. One pertinent time-saving recommendation is that the patient remains on the original ambulance trolley with the paramedics, direct to the CT-scanner and until accepted for secondary transfer, which can then occur immediately.

*Mobilising the team*

Most interventional stroke teams are employing automated alerting systems linked to a single point of contact, so that anaesthetists, interventional nurses, stroke unit and ITU co-ordinators, radiographers and interventionalists can have sight of the data for an incoming patient as soon as it is available, or it is the intention to do so. Via this mechanism, the entire team should be primed to make the door to groin/reperfusion time as short as possible.

**How are we doing in the UK?**

Access to timely emergency intervention for stroke has increased across the world since 2015, but not at the pace which was intended. Currently, in the UK, around 3% of all strokes or, at best, 20% of those who might benefit, gain access to MT. While this is more than double the number in early 2020, few of the 27 neuroscience centres provide a service 24 hours a day 7 days to their own patients and access remains harder for referring hospitals. Thus, the majority of our patients with LVO stroke still do not access MT. Strategies to rapidly increase capacity at each stage of the pathway are still needed. Aside from the life and disability saving at the patient level, the cost saving for each hospital and the wider healthcare economy is large. [29]

On top of the logistical and workforce issues concerning (a) access to imaging and reporting, (b) networked pathways for coordinated recognition, referral and transfer all suitable patients, a central issue is the number of trained MT operators. Approximately 100 operators in the UK are now regularly performing MT. All but 5 are career neurointerventional radiologists. To cover the same population, 647 interventional cardiologists provide full 24/7, 365 rota cover for PCI for STEMI patients (on average 1:7). To provide an equivalent emergency stroke intervention service across the UK, there are 28 neuroscience centres, compared to a network of 68 sites on-call 24/7 for STEMI. Further, (and as stated by the Royal College of Radiology [30]) *the plans to expand the neuro-interventional workforce will not facilitate sustainable 24/7 coverage for the UK within the next decade*. This inevitably means that it is essential to train other specialists to perform MT.

**How could we do better?**

We have fallen short of the NHS long-term plan target for 10% of all stroke patients to access MT by 2022, but important achievements have begun to overcome some of the remaining barriers. Independent stroke delivery networks (ISDN) have been established, whose focus is on learning and planning how to organise and deliver the entire stroke pathway. Publication of the NOSIP, investment in AI secured at a national level, and appointment of digital lead are helping to enable access all regions. [29]

The rate-limiting factor to address now is the training of an adequate workforce to provide geographically equitable emergency treatment. The long-term plan promised that the NHS would work with Health Education England ***“with a focus on cross-specialty accreditation of particular ‘competencies’”* and that**this would include work with the Royal Colleges and specialty societies to develop a credentialing programme for consultants from relevant disciplines to be trained to offer mechanical thrombectomy. Indeed, a credentialling curriculum has eventually been agreed between the neuro-interventional radiologists and the GMC, but the training element, essential for other specialities, is not described and has yet to commence. The case for training existing specialists with transferable catheter skills, including interventional cardiologists and radiologists, is convincing, but willing specialists have yet to access a bespoke training program that takes account of their existing skillset and is feasible alongside delivery of current workloads [31]. The suitability of experienced interventional cardiologists to learn to deliver MT safely with 3-6 months of specialist training has been demonstrated in other countries. In those countries their role on hybrid MT rotas is now well established. [32,33] Such specialist teams are familiar with 24/7 emergency rotas and procedures involving complex decision-making. The British Cardiac Intervention Society has established that over 50% of IC specialists would be prepared to undertake training and contribute to hybrid rotas which are sustainable. NHS leaders will need to facilitate this training pathway, if we are to deliver MT to all suitable stroke victims soon.

Key Points

* Mechanical thrombectomy for acute ischaemic stroke is a highly effective intervention with a number needed to treat of just 2.6 to prevent death or major disability. Only 1 in 5 eligible patients in the UK currently access this treatment.
* The technique and the time sensitive nature of the intervention has many similarities to emergency coronary intervention for myocardial infarction.
* A large body of evidence supports bridging intravenous thromboylsis and mechanical thrombectomy within 6 hours of onset for large vessel occlusion stroke. Work continues on rapidly advancing techniques and expanding indications so that many more patients might benefit.
* Access in the UK is improving with streamlining of emergency pathways and imaging. Sufficient workforce for sustainable 24/7 rotas can be achieved by appropriate training of interventional cardiologists and radiologists.

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Table 1: Thrombolysis in Cerebral Infarction grades: **The extended eTICI scale [14]:**

|  |  |
| --- | --- |
| TICI 0 | No flow past occlusion  |
| TICI 1 | Minimal penetration distal to obstruction with no perfusion of distal territory |
| TICI 2 | Distal perfusion of brain present but either to only a partial territory or with inadequate perfusion  |
| **TICI 2a**  | **Partial filling of < 50% of the territory** |
| **TICI 2b**  | **Partial filling of > 50% of the territory** |
| **TICI 2c** | Near complete perfusion except for slow flow in a few distal cortical vessels or presence of small distal cortical emboli. |
| TICI 3  | Complete and normal distal perfusion |

Figure Legends:

Figure 1: Diagnostic catheter shapes used to access the cerebral circulation with Variations in design according to manufacturer. These 5F devices are familiar to most who undertake percutaneous vascular interventions. A. Bernstein Catheter B. Vertebral Catheter C. Simmons shape catheter for more tortuous anatomy

Figure 2: Thromboaspiration technique in a middle cerebral artery. (A) The guide catheter is positioned in internal carotid artery. Through this an aspiration catheter is advanced over a neuromicrocatheter and guidewire. (B) The guidewire and microcatheter are advanced through and distal to the thrombus and provide support for the aspiration catheter to be advanced to the thrombus. (C) Aspiration is applied and maintained while the aspiration catheter is removed. Image reproduced with permission from Turk AS, Spiotta A, Frei D, et al. Journal of NeuroInterventional Surgery 2014;6:231-237.

Figure 3: National Optimal Stroke Imaging Pathway. The recommended imaging pathway to be made available to all patients presenting with suspected acute stroke as described in the NHS England National Stroke services Model 2021.[28]. CT: Computed Tomography; AI: Artificial Intelligence; IV intravenous; DWI: Diffusion Weighted Imaging.

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