Mechanical Thrombectomy and the Collateral Circulation: Expanding Time to Treatment to 24 Hours

Alejandro Enriquez-Marulanda, MD, Kimberly Kicielinski, MD, MPH, Ajith J. Thomas, MD, Christopher S. Ogilvy, MD

Acute ischemic stroke is a cerebrovascular disease in which a thrombus or embolus occludes a cerebral artery, in a specific area of the brain, generating a corresponding sudden loss of neurologic function. The brain is particularly vulnerable to low perfusion with subsequent infarction, because it is one of the most metabolically active organs of the body, requiring almost 20% of the total cardiac output to sustain its energy needs. It is estimated that approximately 1.9 million neurons are lost per minute and 120 million per hour in a region affected by a stroke. Given this fact, the quote “TIME IS BRAIN” has been introduced and emphasis on timely and effective diagnosis and reperfusion therapy have been pursued.

The goal of acute ischemic stroke treatment is to restore blood flow to the penumbra, which is the brain tissue with decreased blood flow that is at risk for but has not yet infarcted. This is accomplished by physically removing or dissolving the blood clot and restoring flow to the occluded vessel. Since the 1990’s, intravenous therapy using thrombolytic agents such as tPA has been used in the acute treatment of stroke. Once this treatment was found to be effective in reducing the stroke mortality and improving functional outcomes, the practice became widespread around the world. While effective, this medication must be given early after symptom onset, but most patients present for treatment outside the 4.5 hour treatment window. Therefore, health policies and guidelines focused on reducing the time to treatment for patients, thereby salvaging the most brain tissue possible. As a regional leader in stroke care, the BIDMC has become a comprehensive stroke center and is leading the way on systems of care and techniques to treat acute ischemic stroke.

Reperfusion therapies continue to evolve and now focus is on employing endovascular the catheter-based techniques through the groin to remove clots mechanically from inside the vessel. This technique involves the mechanical extraction of the thrombus with the use of thrombectomy devices (aspiration or stent retrievers). Five major research trials in 2015 (MR CLEAN, REVASCAT, ESCAPE, EXTEND-IA, SWIFT PRIME) showed the efficacy of endovascular therapy + IV tPA when compared to IV tPA alone for up to 6-8 hours after a stroke onset.
Continued efforts have focused on the rapid evaluation and therapy of stroke patients. However, only a minority of patients present within the appropriate time window for treatment. One study showed that by 8 hours, only one-third of all patients had presented for medical treatment.\(^{10}\)

While timely treatment of stroke is critical, different patients have varying time thresholds for infarction depending on the degree of “collateral circulation” available to help perfuse areas of ischemia. Neurovascular imaging in the form of CT perfusion scans can be used to define infarcted tissue and “tissue at risk” with low perfusion but has not yet infarcted. This area defines the “penumbra” and if present, the patient may benefit from thrombectomy. In the SWIFT PRIME and EXTEND-IA trials, thrombectomy candidates were selected based on this advanced imaging techniques demonstrating large vessel occlusions and the presence of salvageable brain tissue, reflecting the adequacy of collateral blood flow.\(^{5,7}\)

The recently published DAWN trial used physiologic data from imaging to select patients for mechanical thrombectomy in ischemic stroke.\(^{11}\) This trial evaluated the use of endovascular mechanical thrombectomy + standard medical care versus standard medical care alone in patients with acute ischemic stroke due to a large intracranial vessel occlusion with a presentation to the hospital from onset between 6 to 24 hours and documentation of a mismatch between clinical deficit and infarct size. A significantly greater improvement in neurological outcomes with adequate reperfusion rates and safety was shown in the thrombectomy group.

Concurrently, the DEFUSE 3 trial was published and confirmed these findings.\(^{12}\) This trial showed that mechanical thrombectomy plus medical treatment in patients presenting at 6-16 hours after stroke led to significantly improved clinical outcomes. A key feature was the appropriate patient selection by identifying stroke patients with large vessel occlusion who had a mismatch between clinical symptoms and core infarct size based on advanced CT perfusion imaging.

Endovascular thrombectomy for acute ischemic stroke is the new standard of care. These recent groundbreaking findings have proved the potential benefit of mechanical thrombectomy on patients who currently fall outside the treatment window for standard IV tPA and have already revolutionized daily practice. The 2018 Stroke guidelines have updated mechanical thrombectomy indications according to the findings of these trials, extending the window for treatment up to 24 hours if imaging criteria are met.\(^{13}\) Additionally, they have brought to attention the critical role of adequate collateral circulation in the amount of salvageable tissue. The extended window does not mean that time no longer matters, and strokes can be treated up to 24 hours. All data suggest patients treated earliest have the best outcomes, and there’s no way to predict which collaterals will be overwhelmed and if the penumbra will transform into infarct.

BIDMC works with the network of referring hospitals on the rapid transfer of stroke patients who are candidates for endovascular reperfusion therapies. BIDMC has recently been recognized as an AHA/ASA Comprehensive Stroke Center for the standard of excellence and quality of care provided to stroke patients. In light of the recent trials, case volume has increased, and BIDMC is equipped and excited to offer this life-saving therapy to an expanded number of patients. We hereby present a case treated by our team successfully with mechanical thrombectomy. This patient had a so called “wake up stroke”, where the exact interval between when the patient was last seen well and when the arterial occlusion occurred is not known with certainty.

**Case Vignette:**
A 74-year-old female patient fell out of bed on the morning (9:20 am) and was noted to have severe left-sided arm and leg weakness. Last known well state was the day before at 10:00 pm when she went to sleep. The patient had a past medical history of atrial fibrillation without anticoagulation treatment. She was diagnosed with an acute ischemic stroke and initially treated at an outside hospital where intravenous tPA was given. Then she was brought to BIDMC emergency department at 11:45 am with persistent neurologic symptoms and Code stroke was activated. A brain CTA on admission showed occlusion of the right M1 segment of the middle cerebral artery (Figure 1). Despite treatment with IV alteplase the patient continued with severe neurologic symptoms.
A brain CT perfusion showed decreased blood flow perfusion on the right MCA territory with a salvageable penumbra (Figure 2). The patient was considered a candidate for mechanical thrombectomy which was performed successfully (Figure 3). After the procedure the patient recovered completely the left arm and leg strength were without neurologic sequelae. After appropriate physical therapy, and initiation of anticoagulation medications for her atrial fibrillation, the patient was discharged home with an adequate functional and neurologic status.

**References**


Flow diversion for brain aneurysms using the Pipeline embolization device (PED) has been a major focus of the Brain Aneurysm Institute. Data on posterior circulation aneurysms (vertebral artery, basilar artery, posterior cerebral arteries) has been limited though it has been increasingly used as an off-label indication (Figure 1).

Recently, a publication in *Journal of Neurosurgery* studied the efficacy and safety of using PED for posterior circulation aneurysms in an international multicenter study*. Using data from centers in USA, Canada and Europe, Dr. Ajith Thomas and Dr. Christopher S. Ogilvy led this retrospective study from eight academic institutions collecting data from patients with posterior circulation aneurysms treated in the years 2009-2016. This is currently the largest series to date. One hundred twenty-nine consecutive patients to treat 131 aneurysms were involved in the study. Aneurysms included were divided into dissecting (29), fusiform (53), and saccular (49) lesions. At a median follow-up of 11 months, complete and near-complete occlusion was recorded in 78.1% (Figure 2). Dissecting aneurysms had the highest occlusion rate and fusiform the lowest. Dissecting aneurysms had the best occlusion rates and multiple publications indeed support the strategy of using this as first line of treatment. Since dissecting aneurysms present with subarachnoid hemorrhage, attention has to be paid to the management of antiplatelet therapy and external ventricular drainage (EVD). In our institution, we place an EVD if indicated prior to the actual PED placement. After the PED, the patient is loaded with 180 mg of Ticagrelor (Brilinta). Ticagrelor has a quick onset of action and has a short half-life. If EVD clamp trials fail, it can be stopped for 24 hours before a shunt surgery and reinstated 24 hours later.

Major complications were most frequent in fusiform aneurysms. However fusiform aneurysms in the posterior circulation have a poor natural history and high complication rates with microsurgical and endovascular treatment. Minor complications occurred most commonly in saccular aneurysms. In patients with saccular aneurysms, clopidogrel responders had a lower complication rate than did clopidogrel non-responders. The majority of dissecting aneurysms were treated in the immediate or acute phase following subarachnoid hemorrhage, a circumstance that contributed to the highest mortality rate in those aneurysms.

In a second study from this group, the authors showed that thromboembolic complications were not related to crossing peripheral branches*. When they occurred, the emboli were often in distal branches and most likely a function of inadequate antiplatelet therapy.

A subset of these patients with flow diveters across the basilar bifurcation were analyzed in a separate study and found to be a safe modality of treatment*. While the neurointerventional community has been cautious about the placement of Flow Diverter across perforator rich areas such as the basilar artery and its bifurcation, these papers demonstrate that with adequate antiplatelet therapy it is an efficacious and safe mode of treatment.
References


Trigeminal Neuralgia Treatment Options

Georgios A. Maragkos, MD, Christopher S. Ogilvy, MD, Ajith J. Thomas, MD, Abdulrahman Alturki, MBBS (Hon), MSc (Epi), FRCSC

Trigeminal neuralgia (TN), also called “tic douleureux”, is a chronic pain condition that affects the trigeminal nerve. In patients with TN, even mild stimulation of the face (e.g. brushing teeth or putting on makeup) can trigger excruciating facial pain. Patients may initially experience short, mild pain on the face, but TN is a progressive condition that can eventually cause severe, debilitating pain. Annual incidence is 4/100,000, with a female-to-male ratio of 1.8:1, and a mean age of 63 (usually >50). Multiple treatment modalities are offered to effectively manage TN, including medications, injections or surgery. The Brain Aneurysm Institute provides treatment of this debilitating disease using a multimodality approach.

The most common pathophysiology is a structurally normal blood vessel (artery or vein) impinging on the trigeminal nerve close to its origin from the brainstem. However, nerve compression without TN is possible and is seen in up to 50% of autopsies. Alternatively, the myelin sheath of the trigeminal nerve can be disrupted because of aging or due to demyelinating conditions like multiple sclerosis (MS). Two percent of patients with MS have TN, whereas about 18% of patients with TN have MS. Rarely, a tumor can compress the trigeminal nerve. Lastly, brain lesions (e.g. stroke) or facial trauma can be causing the trigeminal nerve’s relay to be perceived by the brain as actual pain, and present as TN.

Patients with TN may present with episodes of brief, sudden electric shock – like pain. They are unilateral in nature. Common pain triggers include: shaving, touching your face, eating, drinking, brushing your teeth, talking, putting on makeup, encountering a breeze, smiling or washing your face. The episode may last seconds to minutes. These episodes may be interspersed with quiescent periods lasting months to years. Attacks may become more severe and frequent and the pain can transform into a burning neuropathic pain.

Treatment Modalities

Medication: The first-line treatment for TN is the anticonvulsant carbamazepine (Tegretol®) and gabapentin (Neurontin®). These drugs are associated with a 69% chance for acceptable or complete relief, and relief after carbamazepine is a strong clue supporting the diagnosis of TN. The mechanism of action has been suggested to be lessening or blocking of the afferent pain relay from the trigeminal nerve to the brain. Other similar drugs that can be used instead of carbamazepine are oxcarbazepine (Trileptal®), lamotrigine (Lamictal®), clonazepam (Klonopin®), and phenytoin (Dilantin®). Medications are used as long as the pain is controlled, and the side effects do not interfere with a patient’s activities. When medication is no longer effective, surgical procedures are usually considered.

Microvascular decompression (MVD): This procedure involves the relocation or removal of blood vessels that are in contact with the trigeminal nerve root. During MVD a skin incision is made over the mastoid process and a craniectomy is performed. The trigeminal nerve is accessed (Figure 1) and insulating material (Ivalon®) is placed between the compressing artery (most commonly the superior cerebellar artery) and the nerve. Partial sensory rhizotomy may also be performed at this stage, if no arterial compression is identified. MVD has a 75-80% success rate in completely eliminating pain, and an additional 10% of patients experience subtotal pain relief. Recurrence of the pain is possible. About 70% of patients can be expected to be either pain-free or have minor pain recurrence 8.5 years postoperatively. Similarly, the annual risk for major pain recurrence is 3.5%. Patients with an identified arterial nerve compression have the lowest recurrence rates, indicating that MVD is usually therapeutic for these patients. MVD has a mortality rate of 0.2-2%, when done by experienced teams (>900 operations), and a 1-10% chance for neurologic morbidity, including deafness, vestibular or facial nerve dysfunction.

Percutaneous trigeminal rhizotomy (PTR): This includes procedures targeted at lesioning the trigeminal (Gasserian) ganglion. The objective is to destroy the Aδ and C nociceptive fibers, while leaving the Aα and Aβ tactile fibers intact.
Ideally the procedure should cause a retrogasserian lesion, instead of lesioning the ganglion itself. These techniques are recommended for patients who are poor candidates for major surgery (e.g. elderly) or multiple sclerosis. Initial success rate is 91-99%, while recurrence rate varies from 20-54% at 4 years. Recurrences are easily treated by repeat procedures. All PTR techniques involve high risk for facial numbness, ranging from 60-98%. There are three techniques to achieve PTR:

- **Radiofrequency thermal lesioning.** (Figure 2) The objective of this procedure is to selectively destroy pain nerve fibers. Under sedation, a needle is inserted through the face and into the foramen ovale under fluoroscopic guidance. Subsequently, the patient is allowed to wake up and is stimulated through the electrode to identify an area reproducing the patient’s symptoms. When the area is identified, it is lesioned with short-acting anesthesia.

- **Balloon compression.** A needle is inserted through the face and into the foramen ovale under fluoroscopic guidance. Then a No. 4 Fogarty catheter balloon is inflated to lesion the pain fibers.

- **Glycerol injection.** During this procedure, a needle is inserted through the face and into Meckel’s cave. Then, sterile glycerol is injected inside the trigeminal cistern, which damages the nerve fibers and disrupts pain relay.

**Brain stereotactic radiosurgery:** In this procedure, a focused 70-80 Gy radiation beam is used, centered on the trigeminal root entry zone, as identified on MRI. This procedure is generally useful for patients with comorbidities, high-risk medical illness or on anticoagulation (which need not be reversed for Gamma knife). Significant pain reduction is expected in 80-90% of patients, but complete pain relief is less common. Relief occurs gradually and is evident after a median of 3 months after the intervention (range 1 day to 13 months). Pain may recur in about 10-25% of cases, and retreatment is possible at least 3 months after the initial intervention.

**References**

**Percutaneous Transverse Sinus Cannulation for Coiling of Dural Arteriovenous Fistula**

Georgios A. Maragkos, MD, Abdulrahman Alturki, MBBS (Hon), MSc (Epi), FRCSC, Alejandro Enriquez-Marulanda, MD, Christopher S. Ogilvy, MD, Ajith J. Thomas, MD

Intracranial dural arteriovenous fistulas (DAVFs) consist of anomalous connections between branches of dural arteries to dural venous sinuses, dural veins, meningeal veins or cortical veins. These lesions account for approximately 15% of intracranial arteriovenous malformations and usually involve the transverse and sigmoid sinuses. DAVFs can be asymptomatic, however, in high-risk lesions, they can be associated with either intracranial hemorrhage, venous hypertension and non-hemorrhagic deficits such as seizures which make them eligible for treatment. Currently, endovascular embolization is the mainstay treatment for DAVFs,
however, other treatment options such as observation, microsurgery, stereotactic radiosurgery or a combination of these modalities are acceptable alternatives in selected cases.¹

Endovascular embolization by a transvenous approach is very challenging in cases of an occluded sigmoid sinus proximally, especially in cases with isolated transverse sinus. In these cases, a craniotomy for sinus packing or surgical excision was the preferred approach.³ Here we describe a case in which a combination of endovascular and open approach was performed to access an isolated transverse sinus.

An 84-year-old woman presented with new-onset of staring spells and episodic word finding difficulty with aphasia. Continuous electroencephalographic monitoring captured a left temporal epileptic focus and a brain MRI demonstrated abnormal blood vessels in the left temporal lobe. Digital subtraction angiography demonstrated venous congestion and multiple corkscrew vessels in the left temporal lobe draining into the region of the left transverse sinus confirming a diagnosis of a transverse sinus DAVF (Figure 1). The transverse sinus was isolated from all venous circulation and its arterial feeders originated from the occipital artery, precluding both arterial and venous access for effective obliteration of the fistula.

Therefore, the patient underwent a combined open surgical/endovascular approach, where the sinus was percutaneously cannulated through a single burr hole, allowing access for effective coiling of the fistula (Figure 2).

A catheter was placed in the left common carotid artery and a direct injection was performed to obtain a road map of the transverse-sigmoid junction. Then, a microcatheter was advanced through the cannula into the left transverse sinus. Under roadmap guidance, Target Excel 360 coils were placed into the left transverse sinus, until the transverse sinus and the beginning of the sigmoid sinus were completely obliterated. At this point there was no flow into the sinus. Angiography demonstrated complete cure of the DAVF (Figure 3).

Postoperatively, the patient complained of headaches, and therefore a head CT scan was performed demonstrating no bleeding or new infarcts (Figure 4). The patient was discharged to rehab on postoperative day 5, after her headaches had resolved. At the time of discharge, she had no seizures, though remained on her anticonvulsant medication. She had mild residual anomia, but her language was fluent.

References:


HELP MAKE SEPTEMBER NATIONAL BRAIN ANEURYSM AWARENESS MONTH

Friday, September 7, 2018
Please join us in Boston at the State House for a special Awareness Event
Please go to bafound.org for more details closer to the date

Every year over 30,000 families in the U.S. experience the unspeakable tragedy caused by a ruptured brain aneurysm. About 40% of those experiencing a ruptured brain aneurysm will die. Those that survive often face significant challenges, greatly impacting their lives and the lives of their families.

1 in 50 people will develop a brain aneurysm. If a brain aneurysm is diagnosed early with proper screening, it can be treated before it ruptures.

Lives can be saved if people know the risks, the signs, and when to get help.

Franciele Cristina Kipper, PhD
Research Fellow in Neurosurgery

Franciele was born and raised in Brazil. She received her Bachelor’s degree in Biomedical Science at Federal University of Health Science of Porto Alegre (UFSCPA) in 2010. In 2013, she received a Master’s degree and PhD degree in 2017, in both Cellular and Molecular Biology at Federal University of Rio Grande do Sul (UFRGS).

She has experience in cancer signaling pathways (apoptosis, autophagy, senescence, cell cycle) and cancer stem cell research. Early on in her studies, she worked with purinergic signaling and during her PhD; she established patient-derived glioblastoma cell culture, to investigate changes in gene expression in response to pharmacological agents.

Her work is targeting and understanding intracellular signaling in glioma cell lines; also with other tumoral e normal lineages. She has experience with cloning and expression of recombinant proteins carried by lentiviral vectors to promote gene/protein overexpression or knockdown. Currently at BIDMC, she is working with an in vitro model of blood-brain barrier and starting a project to study tumor vasculature in glioblastoma specimens. The focus now is to expand the understanding of the cross talk between tumor and endothelium, in order to find better therapeutic targets.