New and Future Endovascular Treatment Strategies for Acute Ischemic Stroke

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Cerebral revascularization strategies for acute ischemic stroke have been developed during the past decade. Many of these strategies are currently being evaluated and gaining in popularity, offering hope to those with an otherwise nihilistic disease. Herein, the authors discuss the current progress toward these goals and the efforts being made to develop a safe and efficacious method of clot removal in the treatment of acute ischemic stroke. Three endovascular treatment strategies are presented: endovascular thrombectomy with suction or snaring devices, mechanical clot disruption with mechanical or photoacoustic devices, and augmented fibrinolysis with mechanical or ultrasonic devices. Most of these devices are currently undergoing phase I or II trial or are approved for other uses.

Abbreviations: PROACT = Prolyse in Acute Cerebral Thromboembolism, TIMI = thrombolysis in myocardial infarction

On the basis of the National Institute for Neurological Disorders and Stroke study in 1995 (1), intravenous recombinant tissue-type plasminogen activator (alteplase) was approved for use in acute stroke with a clinical onset of less than 3 hours and the appropriate findings at head computed tomography and clinical examination. The combination of successful anecdotal case series (2,3) using direct local intraarterial thrombolysis and the completion of the Prolyse in Acute Cerebral Thromboembolism (PROACT) II study (4) using intraarterial prourokinase (Prolyse; Abbott Laboratories, Abbott Park, IL) less than 6 hours after stroke have proved the efficacy of this approach in large-vessel middle cerebral artery occlusions. Even though the study showed positive results ($P < .046$), it did not lead to U.S. Food and Drug Administration approval of Prolyse or the intraarterial technique due to lack of sufficient statistical power in this randomized trial. Even with the availability of these techniques, only a minority of patients receive acute stroke treatment owing to the facts that (a) many patients delay their arrival to appropriate treatment centers and (b) the use of thrombolytic-based thrombolysis comes with a price—namely the risk of potentially lethal intracerebral hemorrhage. The goal of recent technologic improvements has been toward the more rapid removal of the offending thrombus or the reduction or elimination of the need for pharmacologic thrombolysis and their inherent risk of precipitating a symptomatic hemorrhage. These techniques could potentially improve the overall outcome, expanding patient eligibility by increasing the time window for treatment and reducing the contraindications (eg, recent surgery or use of oral anticoagulants).

Herein, we discuss the current progress toward these goals and the efforts being made to develop a safe and efficacious method of clot removal in the treatment of acute ischemic stroke. Three endovascular treatment strategies are presented: endovascular thrombectomy, mechanical clot disruption, and augmented fibrinolysis. These techniques are currently investigational and, therefore, most reports are anecdotal. This report will include an update of our experience.

ENDOVASCULAR THROMBECTOMY

Endovascular thrombectomy involves the extraction of the thrombus through a catheter and should provide rapid recanalization and reduce the risk of distal embolic complications seen with mechanical clot disruption. This method may be used as a standalone technique or in conjunction with a markedly reduced dose of thrombolytic drug. The technical challenges of thrombectomy include intracranial navigation of these devices, capture of occlusive material within the tortuous and dividing cerebral vasculature, and safety issues related to vessel wall damage or perforation.

Suction thrombectomy is a simple approach that has been used in cases of symptomatic acute internal carotid artery occlusion. It involves the use of a guide catheter with syringe suction to remove sufficient occlusive thrombus and restore flow in an appropriately accessible vessel. A large bore, 7 to 8-F guide catheter is navigated over a guide wire into the thrombus within the internal carotid artery, and a 60-mL syringe is used to aspirate. The guide catheter is slowly withdrawn to facilitate more complete removal of...
the thrombus. The goal of suction thrombectomy is to extract as much thrombus as possible to minimize the amount of thrombolytics needed to achieve recanalization or forego their use altogether. The assessment of collateral flow via the circle of Willis and leptomeninges is crucial when selecting patients for such risky procedures. This technique has been used in those cases of acute carotid occlusion in which the patient did not have adequate collateral flow to perfuse the affected hemisphere. Reopening of the internal carotid artery with such a technique may not be necessary in patients with combined carotid and middle cerebral artery occlusions if the collateral flow in the circle of Willis is adequate and may be futile if the distal obstruction cannot be corrected.

The Angiojet (Possis Medical, Minneapolis, MN) and Oasis (Boston Scientific, Natick, MA) are endovascular thrombectomy devices that combine local vortex suction with mechanical disruption for what has been coined rheolytic thrombectomy. These 4- or 5-F catheters use either a single (Oasis) retrograde high-pressure fluid jet or multiple (Angiojet) retrograde high-pressure fluid jets directed into the primary evacuation lumen to create a hydrodynamic vortex that draws in, traps, and fragments adjacent thrombus. The debris is then simultaneously removed via the recovery lumen. Most of the thrombus can be removed without substantial particulate debris, which is of major concern when considering carotid or intracranial thrombus removal.

Our experience is similar to the anecdotal clinical experience of others (5), in that we have successfully used this device in cases of acute carotid occlusion and for recanalization of symptomatic dural sinus thrombosis; however, the catheter is not yet flexible enough to allow its navigation into the intracranial arteries. The Angiojet or Oasis may have some advantages over suction thrombectomy as their degree of “suction” should be greater; however, removal of more solid organized embolic material that may not be able to enter the action port will be limited, and the occlusion distal to the petrous carotid segment will require an alternative technique.

The Neurojet (Possis Medical) is a single-channel device that is the same size as a micro-guide wire (Fig. 1), is placed through a 3-F catheter, and uses the same method as the Angiojet. It has been designed specifically for intracranial navigation. As with many of these prototypic devices, the challenge of intracranial navigation can be difficult. Although our experience with this device has yielded some dramatic successes angiographically and clinically and some failures of the device—mainly in its ability to navigate through the carotid siphon—to date there have been no complications. This device is currently undergoing a phase II trial and is showing some early success.

In snare or net embolectomy, a device is used to ensnare, incorporate, or interdigitate with an embolus and then extract it via the guide catheter or sheath or deposit it into a safer vascular territory such as the leg. Four devices are currently available that could serve this purpose in the intracranial circulation: the Microsnare (Microvena, Minneapolis, MN), the Neuronet (Guidant, Temecula, CA), the In-Time Retriever (Target, Fremont, CA), and the EnSnare (Medical Device Technologies, Gainesville, FL). The embolus is approached in a different way with each of these devices, and each may offer a solution given a certain position or consistency to the embolus. These devices should be more useful in more organized or solid material such as organized thrombus and may be especially useful with embolic material that is resistant to chemical thrombolysis.

The Microsnare (Fig. 2), a 90° angled loop that comes in 2-, 4-, and 7-mm diameters, can be placed through any standard 0.018-inch microcatheter and is approved for coil retrieval. Although we have found it especially effective for removing organized emboli at the basilar tip, it is not as effective as other devices in the middle cerebral artery. The technique that we have found that works best is to deploy the device, sized slightly larger than the vessel, just proximal to the embolus, advance both to ensnare its midportion, and then partially constrain the loop for capture. When withdrawing the device and catheter, one must carefully maintain a stable relative position under fluoroscopy, as a 1-mm movement of the device with respect to the catheter may either release or cut the embolus. We will usually withdraw the devices into a straight segment such as the midbasilar artery and check for capture with angiography. If there is no filling, then one can simply repeat the procedure.

The Neuronet (Fig. 3) is a laser-cut nitinol basket that is open proximally, with the crisscrossing basket portion tapering to a shapeable platinum-tipped wire. The opening is eccentric with respect to the proximal wire to facilitate capture. The technique for deployment consists of passing the microcatheter approximately 2 cm beyond the occlusion and then advancing the device to the tip, followed by “unsheathing” the device by pulling back the microcatheter. The device is then withdrawn to capture the embolus but requires no re-sheathing. Although a check angiogram may be obtained, it is often difficult to readvance the system the 3 to 4 cm needed to redeploy. Even when no ensnared material is seen, we will usually withdraw both the snare and microcatheter as there is often a small amount of
material in the device’s apex. Although the eccentric aspect is advantageous, that portion may be oriented incorrectly, and we will usually rotate the device 360°–720° after the first pass. As mentioned earlier, we have found this device to be most effective in straighter vessel segments, such as the M1 segment. The angulation and caliber change between the posterior cerebral arteries and basilar tip results in more collapse of the net, thereby potentially reducing its efficacy.

We have not used the other two devices (Fig. 4) that have very recently become available, the InTime Retriever and EnSnare. On the basis of their design, there may be theoretical advantages in using the In-Time Retriever to capture thrombus in a tortuous segment, as it often opens eccentrically. Conversely, the exposed basket and all-in-one catheter and wire design may limit navigation to the occlusion owing to frictional drag against the vessel wall. This device also does not have a specific open region, which may limit capture. The three-loop design of the Ensnare may improve the capture rate of coils and other devices, and its larger version has been well accepted in peripheral device extraction. In embolectomy, this design may prevent capture as it can only engage the proximal face of the embolus. It also requires an 0.027-inch lumen for the delivery system, which limits the user to either the provided catheter or a high-flow type microcatheter, which tends to be stiff and less navigable.

Once the embolus is captured, the next step is safe extraction without embolization to the same or another vascular territory. A femoral sheath is
used in all these cases, and if there is capture we remove the device and guide catheter as one unit. As the embolus approaches the tip of the sheath, we apply suction with a 20 to 60-mL syringe to capture it. If the sheath becomes occluded, we maintain access with an 0.014-inch wire and place a new sheath. Although it is preferable to extract the embolus, it is better to lose the material in the leg vasculature than in other vital organs. Another option may be balloon-tipped guide catheters; however, even with suction one may lose the embolus back into the cerebral circulation if it is too solid and too large to enter the lumen.

We have applied snares and nets to treat acute stroke in 11 patients, six with the Microsnare and five with the Neuronet. Seven of the occlusions were in the anterior circulation and four were in the posterior circulation. We achieved a thrombolysis in myocardial infarction (TIMI) score of 2 or 3 inches six of the 11 (54%) patients, with similar success rates for both devices. No complications, perforations, or even vasospasm has been demonstrated in this early experience. This experience complements that of Kerber et al (6) in that endovascular thrombectomy should be considered as a viable alternative in appropriately selected cases.

The Merci retriever (Concentric Medical, Mountain View, CA) has been specifically designed for intracranial thrombectomy and is currently undergoing phase I and II trial. This device consists of a platinum-tipped nitinol wire with a moderately stiff, gradually enlarging helix (Fig. 5) that is deployed via a microcatheter. In addition, a 9-F balloon-tipped guide catheter is used for flow arrest during retrieval. The basic approach is to navigate the microcatheter distal to the embolus and deploy the first two to three loops of the device. Then, the device is withdrawn to engage the embolus and deploy the remaining loops. To help incorporate the embolus, the device is torqued three to five times clockwise. The balloon in the internal or common carotid artery is inflated and suction applied as the distal device is withdrawn through the carotid artery and into the guide catheter. The initial Merci I trial (7), in which 50 patients with intracranial occlusion were treated with this device, yielded
a recanalization rate of 48% for patients with a TIMI score of 2 or 3, with clot retrieval in 52%. Modified Rankin scores of 0 or 1 were obtained in 32% of those with recanalization and only 6% of those without. Overall mortality in this trial was 36%, but one must remember that this study, unlike PROACT II, included internal carotid and basilar occlusions and had a mean initial National Institutes of Health Stroke Scale score of 21. Investigators for the Merci II trial, which is in progress, plan on enrolling 125 patients at 20 sites.

MECHANICAL CLOT DISRUPTION

Mechanical clot disruption includes any technique by which the interventionalist mechanically fragments or completely destroys the thrombus within the artery. This may be accomplished simply by using guide wire manipulation or in a more complex fashion such as laser shock-wave devices. The goal of mechanical clot disruption is to rapidly establish blood flow and cerebral perfusion. As the thrombus is disrupted and flow reestablished, small emboli are created and carried into distal branches. If these emboli are small enough, they will pass through the distal circulation; if not, further reperfusion may require endogenous or exogenous enzymatic thrombolysis. The potential for distal embolization and worsening cortical perfusion exists and must be considered in each technique and for each patient. For example, if there is a thrombus in the M1 branch of the middle cerebral artery and the patient has good distal middle cerebral artery distribution perfusion via retrograde flow through leptomeningeal collateral vessels, the creation of multiple distal branch occlusions may actually decrease brain perfusion despite the establishment of proximal antegrade flow. Conversely, poor collateral flow disrupting the thrombus may substantially improve perfusion. In addition, clot disruption increases the exposed surface area, which may facilitate clot dissolution by the inherent endogenous fibrinolytic system. Because smaller emboli may also facilitate exogenous thrombolysis, mechanical clot disruption may also be applied as an augmented thrombolysis technique.

A number of devices have been used for this purpose. The most basic of these devices, and the easiest to apply, is the simple micro-guide wire. In intraarterial thrombolysis, a microcatheter is navigated over a micro-guide wire up to the proximal portion of the thrombus. The micro-guide wire can usually be easily advanced through the thrombus into the distal vessel. Multiple passes through the clot with the wire and microcatheter is one form of mechanical disruption that may fragment the thrombus if it is not organized. As a stand-alone technique, it is only marginally effective; however, in combination with chemical thrombolysis, this disruption aids in the process by increasing the surface area of the thrombus exposed to the thrombolytic. In our experience, mechanical manipulation incrementally improves the recanalization rate. In our series (2,3), the recanalization rate for patients with a TIMI score of 2 or 3 was 75%; the recanalization rate obtained in PROACT II (4), in which no mechanical manipulation was performed, was 65%.

The various microsnares and nets described earlier can also be used to more aggressively fragment thrombus. One must be careful to avoid dissections and perforations when using these devices as a mechanical disruption device. These devices will result in variable-sized fragments and, as an isolated technique, may result in multiple distal branch occlusions. As an adjunctive technique, the use of snares should result in more fragmentation and, theoretically, more rapid recanalization than does the use of micro-guide wires (8).

Intracranial angioplasty in the setting of acute stroke can be used as a primary technique to mechanically fragment the thromboembolus or for treating an underlying atherosclerotic lesion when chemical thrombolysis is
ineffective. In a recent review of his experience, Chaloupka (9) described the use of primary angioplasty in patients with acute stroke who had a contraindication to thrombolitics. His overall experience using low-pressure silicone balloons such as the Hyperform (Microtherapeutics, Irvine, CA) or Sentry (Boston Scientific, Target) was quite positive, with most patients achieving recanalization and substantially improved outcomes. He described one perforation with this technique that responded to occlusion with a long balloon inflation time.

Our experience is more variable, although we have not used angioplasty as a primary technique. In the setting of underlying atheromatous disease, we have had good success similar to that seen with other anecdotal reports (10–12), with persistent recanalization in five of seven patients. In patients with thromboembolic disease in whom laser or chemical thrombolysis had failed, only partial recanalization was seen in one of four patients. The fact that our results are less optimistic than those obtained by Chaloupka (9) is most likely due to our use of balloons in failed thrombolysis and selection of more solid organized thrombus or plaque embolus. Although we have not had a perforation in this setting, it was quite difficult to remove the balloon in one patient with an embolus after cardiac catheterization, most likely due to the plaque embolus acting like a cam to lock the device within the vessel. With catheter advancement and wire manipulation, we were able to extract this device without sequelae. In another report, Spreer et al (13) reported success in primary angioplasty and stent placement in basilar occlusion resistant to thrombolitics with recanalization in all three patients reported. Two of the three patients also had an excellent clinical outcome (13).

Laser thrombolysis is another method of mechanical thrombolysis that is currently under investigation. The goal in laser thrombolysis is to safely obliterate the embolus into microscopic fragments small enough to pass through the capillary circulation. The approach with direct laser thrombolysis is different than that with the more completely studied laser angioplasty and laser thrombo-endarterectomy, in which higher-power argon ion and neodymium-yttrium-aluminum-garnet lasers designed to destroy atheromatous plaque are used (14,15).

Laser thrombolysis for acute stroke uses a lower-power pulse-dye or diode laser tuned to the hemoglobin absorption peak or facilitated by an exogenous administered chromophore. The absorbed energy vaporizes the hemoglobin molecule and adjacent water molecules to create a vapor bubble that expands and contracts to create shock waves that focally shatter the embolus.

To minimize damage to the adjacent vessel wall, the two devices currently under investigation apply this energy differently. The LaTis device (LaTIS, Minneapolis, MN) uses the slow injection of contrast material (arrow) as a “light pipe” to carry the laser energy to the thrombus and away from the catheter tip (arrowhead).
vessel wall, this allows vaporization and photoacoustic mechanical disruption of the thrombus while minimizing the risk to the vessel wall and perforation. These devices are currently undergoing phase II clinical trials. Although our initial clinical experience with these two trial devices has found them to be effective in a modest percentage of patients, there remain substantial hurdles with device and laser modulis designed to maximize efficacy and minimize risk.

AUGMENTED FIBRINOLYSIS

In a broad sense, augmented fibrinolysis can use any method with a fibrinolytic to more rapidly recanalize and reperfuse the brain. Microcatheters, guide wires, or any of the embolectomy or mechanical devices mentioned earlier, when used in addition to fibrinolytics, should, in some sense, help accomplish this goal. The use of snares, nets, balloons, or other mechanical devices to fragment or disrupt a thrombolytic-laden embolus may greatly increase the rapidity of reperfusion. In a recent review of the use of the Microsnares in combination with thrombolytics, Qureshi et al (8) described an increase in recanalization rates. The MicroLysUS catheter (EKOS, Bothell, WA) is specifically designed for augmented fibrinolysis and is currently undergoing a phase I/II trial for acute stroke. With this device, a cylindrical ultrasonic transducer at the tip of the microcatheter is used to microfracture the embolic material and create microstreaming of the thrombolytic agent into the thrombus (Fig. 8). In the initial feasibility trial of 14 patients (16), this device was used without complications. The time to recanalization was somewhat earlier than that obtained with other thrombolytic trials and reports. This device is currently being evaluated with recombinant tissue-type plasminogen activator in the Interventional Management of Stroke II trial.

CONCLUSION

At the present time, the mainstay of treatment for acute ischemic stroke is intravenous or intraarterial fibrinolysis. Other endovascular treatment strategies that can be applied in the treatment of acute stroke are now undergoing feasibility and safety studies.

References

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