Endovascular intervention for acute thromboembolic stroke in young patients: an ideal population for aggressive intervention?

Clinical article


Stroke is the third leading cause of death and the leading cause of long-term disability in the US. To date, a dearth of treatment options has existed for acute thromboembolic stroke. A promising therapeutic alternative is acute revascularization via endovascular intervention. Currently, there is much to learn regarding this method of treatment, but a burgeoning body of literature suggests significant potential for benefit.

Administration of intraarterial thrombolitics and/or a glycoprotein IIb/IIIa receptor antagonist, as well as mechanical intervention with microcatheter or microwire manipulation, snare devices, balloon angioplasty, intraarterial ultrasonography, and intracranial stent placement, have all been reported as alternative methods of revascularization associated with successful recanalization of occluded cerebral arteries. There are data to support the suggestion that acute endovascular-mediated recanalization of thromboembolic cerebral vessel occlusion translates into improved clinical outcomes, even be-
Endovascular treatment of young patients who suffer strokes

Beyond 3 hours. To evaluate further the potential role of endovascular intervention in acute thromboembolic stroke, we reviewed our experience with the use of endovascular techniques to treat young patients (ages 18–35 years) who suffer a thromboembolic stroke.

Methods

We retrospectively reviewed a prospective institutional endovascular intervention registry to identify patients between 18 and 35 years of age who presented with acute thromboembolic stroke and who were treated at a single, large-volume primary stroke center (Millard Fillmore Gates Hospital/Kaleida Health) between December 2000 and June 2007. All patients who underwent endovascular stroke intervention were enrolled in the registry. Intervention exclusion criteria included eligibility for and administration of intravenous tPA, intracerebral hemorrhage before the procedure, lack of occlusive clot on initial angiography, > 2 × 3–cm black hole on CT perfusion imaging, or ICA clot burden > 8 cm. Intervention inclusion criteria included new onset (< 8 hours) of stroke symptomatology, presence of a clot in the vascular tree on initial angiography, and decreased cerebral blood flow on CT perfusion imaging. Registry data included demographic factors (age, sex, and time of presentation); clinical features (admission and discharge NIHSS scores, lesion location, and length of hospital stay); procedures performed (type of interventions attempted, and initial and final TIMI scores [0 for absent perfusion, 1 for minimal distal perfusion, 2 for partial perfusion, and 3 for complete perfusion]); and outcomes (duration of follow-up, and mRS score at discharge and at last follow-up). Data are presented as the mean ± standard deviation unless otherwise noted. This study was approved by our Institutional Review Board.

Results

Between December 2000 and June 2007, 8 endovascular interventions for thromboembolic stroke were identified in 7 patients (26 ± 6 years of age; 5 women) (Table 1). For purposes of analysis, the patient who presented twice is hereafter considered to have experienced 2 distinct and separate events (the patient’s strokes occurred 3 years apart, were secondary to a cardiac abnormality, and involved different vascular territories). Presenting mean NIHSS score was 13 ± 4.3 (median 13, range 8–20). All patients presented within 6 hours of symptom onset (0–3 hours for 4 events; 3–6 hours for 4 events).

All events were found to be thromboembolic; no dissections were present, nor was there any indication of baseline atherosclerosis (Table 1). Two events in 1 patient were confirmed to be cardioembolic. Three events occurred in women who were active smokers while taking oral contraceptives. Two events occurred in women smokers, 1 immediately after an intense aerobic workout (with presumed dehydration). Finally, 1 event occurred in a nonsmoking man in whom no likely source could be identified.

Revascularization attempts were accomplished with mechanical thrombectomy/disruption, intraarterial thrombolysis, and/or angioplasty, with or without stent placement (Table 1). Particular interventions (thrombolysis, thrombectomy, angioplasty, and stent insertion) were chosen based on availability (the Merci retrieval device [Concentric Medical] was not available for 3 patients) as well as the physician’s impression of the most beneficial option during the procedure (weighing concerns including intracranial hemorrhage, prolonged antiplatelet therapy, clot response to each successive intervention, and perceived reperfusion risk). All patients were given a loading dose of 650 mg aspirin (or 325 mg if they had already taken aspirin) immediately following the determination that they were not a candidate for tPA and did not have hemorrhage. Heparin was intravenously administered in all patients to achieve the goal of an activated coagulation time of 250–300 seconds. Patients receiving stents were given a loading dose of 600 mg clopidogrel as soon as the decision was made to use the device. Aspirin and clopidogrel were given orally if the patient could tolerate it or otherwise via a nasogastric tube.

All 7 patients (8 cases) had TIMI Grade 0 flow on initial angiography. At the conclusion of the interventions, TIMI 3 was achieved in 5 cases, TIMI 2 in 1 case, and in 2 cases the TIMI grade remained 0.

One intraoperative complication occurred (vessel perforation with the wire while navigating the clot), and therefore the procedure was aborted without achieving reperfusion (TIMI 0). The second case in which recanalization was not achieved (TIMI 0) occurred early in our experience, before approved mechanical thrombectomy devices were available. This patient received intraprocedural reteplase without evidence of recanalization. Both patients experiencing no recanalization presented within 0–3 hours of symptom onset, suggesting little correlation, within this cohort, between time from symptom onset and success of attempted recanalization. No deaths occurred in our series.

The mean discharge mRS score was 2.2 ± 1.5 (median 1.5), with 5 patients (62.5%) having achieved independence on discharge (mRS Score 0–2). The mean length of hospital stay was 6.5 ± 3.7 days (4.4 ± 1.5 days for patients with mRS scores of 0–2; 10 ± 3.6 days for patients with an mRS score of 4). At last follow-up (29 ± 25 months), all patients were independent and had achieved an mRS score of ≤ 2.

Discussion

Stroke is the leading cause of long-term disability in the US. Among all stroke survivors, 50–70% regain functional independence, 15–30% are permanently disabled, and 20% require institutional care at 3 months after onset. According to Walker et al., 3.7% of all strokes occur in patients between the ages of 15 and 45 years; of these, a relatively small proportion of the episodes are thromboembolic. Still, the avoidance of major deficits in young patients has the potential for significant societal benefit; because of their long life expectancy, young patients account for as much as 20% of potential life-years lost due to stroke.

Currently, acute ischemic stroke represents a major therapeutic challenge, with only 5% of patients meeting the strict inclusion criteria for intravenous recombinant tPA.
therapy. For patients who do not meet intravenous tPA criteria, endovascular attempts at revascularization with thrombolysis or mechanical devices have been reported to be beneficial. Since the publication of the Prolyse in Acute Cerebral Thromboembolism II study in 1999, there have been several reports of the use of various pharmacological and mechanical methods to achieve recanalization with improved clinical outcomes. Among patients with M1 or M2 MCA occlusion enrolled in the Prolyse in Acute Cerebral Thromboembolism II study, TIMI 2 or 3 recanalization was achieved in 66% of the prourokinase treatment group, and occurred spontaneously in 18% of the control group. The MERCI trial considered a heterogeneous group of arteries, including ICA terminus lesions that were occluded, and revealed an overall rate of TIMI 2 or 3 flow in 64% of patients. Flint et al. presented single-institution, pooled MERCI and Multi-MERCI data wherein they achieved a recanalization rate of 63%, whereas Kim et al. presented single-institution data of all MERCI and trials demonstrated good recovery in 40% of patients who undergo recanalization, compared with 6% of patients who do not receive recanalization. Although all patients eventually achieved independence (mRS Score 0–2), the early discharge and excellent discharge status of patients experiencing recanalization suggests a potential benefit to revascularization. That said, the eventual good outcome in all patients forces one to consider whether, in the long term, the advantages of youth may supersede the short-term benefit of recanalization. Further studies with larger numbers of patients, are needed for an appropriate determination of the actual value of recanalization.

Young patients may be particularly suited to benefit from endovascular acute stroke therapy as a result of having, typically, more favorable vascular anatomy with less tortuous vessels, atherosclerosis, and calcification, as well as maintaining a baseline quality of health that facilitates their ability to tolerate procedural stresses. The avoidance of major deficits in young patients has potential for major societal benefit. Because of their long life expectancy, young patients account for as much as 20% of potential life-years lost due to stroke. In our series, patient outcomes compare favorably with those in previously published, similarly injured populations. In a community-based study, only 53% of patients who experienced their first-ever cerebral ischemic event when younger than 45

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age at Tx (yrs), Sex</th>
<th>Vascular Territory</th>
<th>Cause</th>
<th>TIMI Pre/Post-Tx</th>
<th>NIHSS at Admission</th>
<th>mRS at Discharge (days)</th>
<th>LOS (days)</th>
<th>FU (mos)</th>
<th>mRS at Last FU</th>
<th>Intervention†</th>
<th>Pre-Tx</th>
<th>Post-Tx</th>
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<tr>
<td>1</td>
<td>33, M</td>
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<td>4</td>
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* FU = follow-up; IA = intraarterial; LOS = length of stay; LSA = lenticulostriate artery.
† Performed during a single session, with maneuvers listed in sequence. Devices and manufacturers were as follows: EKOS microinfusion catheter, EKOS Corp; Merci retriever, Concentric Medical; Neuroform stent, Boston Scientific; and Vision stent, Guidant Corp.
‡ This patient had a stroke 3 years later, which was analyzed as a separate event.
§ Perforation; therefore procedure was aborted.

TABLE 1: Data for young patients undergoing endovascular interventions for acute thromboembolic stroke*
years of age achieved mRS scores of 0–2 at last follow-up (mean follow-up duration ~ 50 months, although not directly determinable from the presented data).19 Additionally, a second study reported that in a population of patients younger than 45 years old who suffered stroke and who had the same median NIHSS score as this cohort (NIHSS Score 13), only 28% of patients achieved mRS scores of 0–1 at 3 months and 7% had died.18 In contrast, we experienced a 0% mortality rate and observed that 50 and 62% of patients had achieved mRS scores of 0–1 and 0–2, respectively, by discharge and that 100% had achieved an mRS score of 0–2 at last follow-up evaluation (29 ± 25 months).

Although direct comparison between the populations from the aforementioned studies and our patient cohort is not reasonable (substantial selection bias exists in our population; our patients were somewhat younger; and there were different source populations), some suggestion that a potential benefit exists for endovascular revascularization in young patients with acute stroke may be cautiously inferred. The natural history of stroke in this young age group is not fully understood; nevertheless, without vascular recanalization, the risk of disability, particularly in the short term, is substantial.18,19 That said, it should be noted that all patients in the present series achieved mRS scores of ≤ 2 at last follow-up, regardless of whether recanalization was achieved. Nevertheless, revascularization was strongly associated with a much more favorable short-term outcome.

Significant limitations are present in this series. As previously stated, the patients herein are subject to selection bias, because they represent only those patients who presented to our endovascular service with a clinical picture sufficiently dire (NIHSS ≥ 8), within an appropriate time window, and with a demonstrable lesion amenable to attempted intervention. Because these patients were not part of a randomized trial, there is no true control group, which would be necessary to make any verifiable statements regarding efficacy or benefit, and without which all such comments are only supposition. Additionally, because thromboembolic stroke in young patients is rare, there is an insufficient number of patients to generate widely applicable data. Finally, the heterogeneous nature of the endovascular revascularization techniques that were attempted make interpretation of any intervention modality impossible. Instead, we hope only to provide a case series highlighting the excellent outcomes observed when endovascular intervention, no matter the modality, is embraced as an option in young patients with thromboembolic stroke.

Conclusions

We present a series of endovascularly treated young patients with thromboembolic stroke. This series reports the outcomes in these patients, which demonstrate the relative safety of endovascular intervention in young patients with thromboembolic cerebral ischemia as well as suggesting a potential benefit in outcome. Further investigation, with larger numbers of patients and an appropriate control population, is indicated.

Disclosure

For Dr. Hopkins: industry grant support from Boston Scientific, Cordis, and Micrus; honoraria from Bard, Boston Scientific, and Cordis; has an ownership interest in AccessClosure, Boston Scientific, Micrus, and Square One, Inc.; and serves as a consultant to member of the advisory board for Abbott, Bard, Boston Scientific, Cordis, and Micrus.

For Dr. Levy: industry grant support, other research support (devices), and honoraria from Boston Scientific; stockholder in Micrus Endovascular; receives grant support from ev3; serves as a consultant to Cordis Neurovascular and Micrus Endovascular; receives fees for carotid stent training from Abbott Vascular and ev3.

For Dr. Mocco: research grant from the Brain Aneurysm Foundation.

For Dr. Siddiqui: research grant from the University at Buffalo; and honoraria from Genentech, and the American Association of Neurological Surgeons’ course and Emergency Medicine conference.

References