Mechanical Thrombectomy in Acute Stroke: Prospective Pilot Trial of the Solitaire FR Device while Under Conscious Sedation

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AJNR Am J Neuroradiol published online 19 July 2012
http://www.ajnr.org/content/early/2012/07/19/ajnr.A3200
Patients presenting with acute ischemic stroke can be treated medically by lysing the clot via intravenous fibrinolysis or endovascularly by removing the clot through an intra-arterial method to re-establish vascularization in the blocked territory. The therapeutic reference for acute ischemic stroke is intravenous thrombolysis with rtPA within 4.5 hours of stroke onset. When the occluded artery is proximal or blocked territory, the therapeutic reference for acute ischemic stroke is intravenous thrombolysis with rtPA within 4.5 hours of symptom onset for the anterior circulation, and within 24 hours for the posterior circulation. After intravenous thrombolysis (when no contraindications), thrombectomy was performed with the Solitaire device in patients under conscious sedation. Primary efficacy and safety end points were good functional outcome (mRS ≤2) at 3 months and mortality at 3 months. Secondary end points were recanalization (TICI ≥2) and failure rate.

RESULTS: From May 2010 to July 2011, 36 patients were treated. Median baseline NIHSS score was 17.5. The occlusion site was MCA in 21 patients (58.4%), ICA-MCA tandem occlusion in 9 patients (25.0%), terminal ICA in 2 patients (5.5%), and basilar artery in 4 patients (11.1%). Twenty-three patients (63.9%) received intravenous thrombolysis. Superselective catheterization of the occluded vessel was not feasible in 3/36 cases (13.9%). Successful revascularization was achieved in 28/36 patients (77.8%). After 3 months, 22 patients (61.1%) showed good functional outcome (mRS ≤2) and the median NIHSS score was 8.5. Overall mortality rate at 3 months was 22.2% (8/36).

CONCLUSIONS: In acute ischemic stroke, mechanical thrombectomy while under conscious sedation is feasible in a large percentage of cases (86.1%) and is associated with a short procedure delay and a high percentage of good functional outcomes at 3 months (61.1%).

ABBREVIATIONS: ASPECT = Alberta Stroke Program Early CT; IQR = interquartile range; mRS = modified Rankin Scale; TICI = Thrombolysis in Cerebral Infarction.
Materials and Methods

The goal of this pilot study was to prospectively evaluate the feasibility, safety, and efficacy of mechanical thrombectomy using the Solitaire FR device in patients with acute ischemic stroke treated under conscious sedation. We compared our results with the other Solitaire series of patients under general anesthesia.

The protocol for this study received institutional review board approval. Informed consent was obtained from the patients or their relatives.

This was a prospective single-center, single-arm, intention-to-treat study. All patients with acute stroke with relevant neurologic symptoms, as defined by an NIHSS score ≥8, presenting within 6 hours of symptom onset for the anterior circulation and within 24 hours for the posterior circulation, with occlusion of a large intracranial vessel (ICA and/or MCA; basilar artery) depicted on MR imaging (or CT angiography when contraindication) and confirmed by angiography (TICI grade 0 or 1), and without initial spontaneous intracranial hemorrhage were consecutively included. The exclusion criteria were spontaneous NIHSS improvement, recanalization before endovascular treatment viewed on the first angiographic run, and contraindication to endovascular treatment (vascular blush, fistula) determined on the first-run angiogram.

Upon admission, each patient with suspected acute ischemic stroke was examined by an experienced stroke unit neurologist. An acute MR imaging was then performed. Blood pressure, pulse, and respiration rate were monitored continuously and watched by the stroke unit neurologists. The NIHSS score was calculated to determine a clinical severity score. The stroke unit neurologist administered IV tPA (alteplase [Actilyse]; Boehringer, Ingelheim, France) at an effective dose (0.9 mg/kg) within a 4.5-hour window, if no contraindication. The interventional radiologist on call was notified, and when the diagnosis was confirmed, the patient was transferred to the angiography suite (immediately for patients who did not receive intravenous thrombolysis, or after 30–60 minutes with no clinical improvement for those who received it). Because we did not have an anesthesia team dedicated to this procedure, the stroke neurologist provided conscious sedation. All patients received 1 mg of IV midazolam before the arterial puncture. Then, in case of agitation or pain, an IV bolus of 1 mg of midazolam was administered and repeated, if necessary. Standby intubation was not available during the procedures, as anesthesiologists were involved only in severe cases. Blood pressure was lowered with nicardipine in case of uncompensated hypertension, defined as systolic blood pressure exceeding 180 mm Hg or diastolic blood pressure exceeding 110 mm Hg. After the endovascular treatment, the patient was transferred to the stroke intensive care unit.

An acute 3T MR imaging (Achieva 2.1; Philips Healthcare, Best, the Netherlands) was performed to confirm the diagnosis of stroke, locate the occluded vessel, and search for exclusion criteria. DWI was used to assess the extent of the ischemic lesion. A time-of-flight sequence focused on the circle of Willis was used to locate the site of vessel occlusion. T2 gradient-echo imaging was performed to screen for intracranial hemorrhage. Flair-weighted imaging completed the protocol. No perfusion-weighted imaging was acquired. We calculated the ASPECT score on DWI to assess the ischemic severity score for the anterior circulation and pc-ASPECT for posterior circulation. In case of MR imaging contraindication, a head CT and CT angiography were performed to confirm the vessel occlusion. The occlusion location was divided into 4 categories: MCA including M1, M1-M2, and M2; ICA; basilar artery; and ICA-MCA tandem occlusion (occlusion of the proximal ICA and MCA).

Three neurointerventionalists performed the mechanical thrombectomy on a biplanar system (Axiom Artis dBA; Siemens, Erlangen, Germany). All patients were treated via a femoral arterial approach while under conscious sedation. In either the anterior or posterior circulation, we used a 6F guide catheter (Chaperon 6F; MicroVention, Aliso Viejo, California) or a 6F long sheath (Flexor Tuohy-Borst; Cook, Bloomington, Indiana) to reach the target artery. No intravenous heparin was administered if an intravenous thrombolysis was performed before the mechanical thrombectomy. If not, 2500 IU of heparin was delivered at this time. Occlusion of the target vessel was verified angiographically and rated on the TICI scale. Using a coaxial system, we advanced a 0.21-inch internal diameter microcatheter (Prowler Select Plus; Cordis, Miami Lakes, Florida, or Rebar –027; ev3) over a guidewire (Tracker Excel 14; Boston Scientific, Natick, Massachusetts) placed through the thrombus. After removal of the guidewire, a microcatheter angiographic run was performed to confirm the correct positioning and visualize the vascular lumen distal to the thrombus. All patients were treated using the Solitaire FR device (ev3). Under fluoroscopic control, the Solitaire was advanced through the microcatheter across the vessel occlusion and deployed completely by pulling back the microcatheter. An angiographic run was performed to evaluate the correct placement and expansion of the device and control for flow restoration. The stent was kept deployed for 3–5 minutes before retrieval. We did not use a balloon guide catheter to achieve flow arrest, nor did we work with a special aspiration catheter. The unsheathed Solitaire stent and microcatheter were then removed (as a single unit) into the guide catheter, while applying suction through the guide catheter using a 20–50 mL syringe (Vac-Lok Syringe; Merit Medical, South Jordan, Utah). An angiographic run was performed to evaluate flow restoration. If necessary, the entire process was repeated until the end of the therapeutic window. Groin punctures were routinely closed with an Angio-Seal (St. Jude Medical, Minnetonka, Minnesota). In cases of tandem occlusion, the choice of whether to treat the ICA or MCA occlusion first was decided by the neurointerventionalist, considering technical conditions (tortuous vessel), remaining time to treat, and extent of the lesions. The interruption of the procedure before complete recanalization was decided on a case-by-case basis by the interventional neuroradiologist and the neurologist, according to remaining time to treat, the clinical status of the patient (growing agitation), and vascular anatomy (very atheromatous vessels), avoiding any technical complications or clinical worsening.

Clinical data were recorded for every patient upon admission, at the end of the endovascular procedure, at day 1, at discharge by the neurologists in the stroke unit, and at the 3-month consultation conducted by an independent neurologist. When a face-to-face visit was impossible, the independent neurologist performed the Rankin assessment by phone.

The following time points were collected for every patient: time from symptom onset to the beginning of the endovascular procedure (defined as the first angiographic run); duration of the procedure (from the first to the last angiographic run); and time from symptom onset to recanalization (last angiographic run). Revascularization was assessed on a final angiographic run performed immediately after the end of the procedure. Flow restoration was evaluated by the neurointerventionalist using the TICI flow classification. Symptomatic hemorrhagic events were evaluated using a 24-hour CT. A symptomatic


hemorrhagic event was defined as any intracerebral bleeding causing neurologic deterioration (NIHSS increase ≥4).

Schematically, we had 3 categories of results: “recanalized” if TICI score ≥2a, “treatment failure” if we were unable to attempt a recanalization (the stent was not opened), and “no recanalization before exceeded deadline.” The efficacy and safety criteria were evaluated in the whole series and defined according to the trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke suggested by Higashida et al.19 The main efficacy judgment criterion was functional outcome at 3 months, defined by an mRS of 2, 5, or 6. As a consequence, only 31 patients were treated. 28 were recanalized and 3 were not recanalized in the time remaining (despite 1 or 2 openings of the stent).

Regarding the 3 agitated patients for whom the treatment failed, the remaining time was too short to have them under general anesthesia and continue the treatment by mechanical thrombectomy. In the 2 patients untreated due to vessel tortuosity, 1 had a good (mRS = 2) and 1 had a moderate (mRS = 3) functional outcome at 3 months.

Seven patients were agitated and needed addition of midazolam during the procedure (from 2–13 mg). After 3 months, 3 of these 7 patients presented with a good functional outcome (mRS ≤2), 2 had a moderate or bad functional outcome (mRS = 4 and 5), and 2 patients died of symptomatic intracranial hemorrhage. The 3 patients with failed treatment had an mRS of 2, an mRS of 5, and 1 was deceased at 3 months.

Time from symptom onset to endovascular treatment was 115–360 minutes (mean = 269 ± 60 minutes; median = 275 minutes [IQR = 225–320]). The duration of the procedure was 12–81 minutes (mean = 33 ± 20 minutes; median = 27.5 minutes [IQR = 20–46]). The time from symptom onset to recanalization was 122–405 minutes (mean = 302 ± 65 minutes; median = 320 minutes [IQR = 256–481]). Successful recanalization was achieved in 28 of 36 (77.8%) patients (TICI ≥2A) (Table 2). TICI 3 was achieved in 14 patients (38.9%) and TICI 2b occurred in 6 patients (16.7%). The median number of stent deployments was 1.5 (IQR = 1–2). In 2 patients (5.5%), ICA stent placement (Wallstent; Boston Scientific) was necessary to access the target vessel because of acute occlusion of the cervical ICA.

At 3 months, 22 patients (61.1%) showed good functional outcome (mRS ≤2), 4 patients (11.1%) had a moderate outcome (mRS = 3 or 4), and 10 patients (27.8%) had a poor outcome (mRS = 5) or died. At 3 months, median NIHSS score (calculated on the 28 living patients) was 8.5 (IQR = 1–14), with a mean (±SD) of 9.0 (8.8). Eighteen patients (50%) presented with a NIHSS score of ≤1 or an improvement of at least 8 points from baseline.

Hemorrhagic complications were depicted on 24-hour CT in 10 patients (27.7%)—7 were asymptomatic (19.4%) and 3 were symptomatic (8.3%). Symptomatic hemorrhage was observed in 1 patient with tandem occlusion and agitation during the treatment, 1 patient with tandem occlusion previously treated with IV thrombolysis and no agitation, and 1 patient presenting with an acute ischemic stroke with a large vessel occlusion were treated at our institution with the Solitaire FR stent.
with MCA occlusion. Seven of 10 patients (70%) had combined treatment with intravenous thrombolysis. Symptomatic hemorrhagic complications at 3 months concerned 6 patients (16.7%), 3 already diagnosed at 24 hours and 3 occurring, respectively, at day 3, day 8, and day 8.

The overall mortality rate at 3 months was 22.2% (8/36) (Table 3). There were 5 fatal outcomes (13.9%) due to symptomatic intracranial hemorrhage, and 3 patients died of extensive brain infarction with intracranial hypertension (their recanalization status was, respectively, TICI 0, 1, and 2a).

We observed 1 (2.7%) arterial dissection of segment M1 of the MCA in a nonagitated patient with extravasation of contrast media during the procedure, and hematoma on the post-operative CT. No functional improvement was observed at 3 months.

Discussion

Various types of sedation are used in acute ischemic stroke interventions. The operator’s habits and the institution’s opportunity to have an anesthetic support team are the main factors for the decision to treat while under general anesthesia or conscious sedation. Three recent reports of retrospective data suggest that general anesthesia may negatively impact the outcome of acute ischemic stroke interventions. Two series recently demonstrated that chemical (intra-arterial urokinase) and mechanical thrombectomy (using Merci and Penumbra devices) under conscious sedation were as safe as under general anesthesia and provided a better clinical outcome after 3 months (mRS ≤2). Abou-Chebl et al also noticed a lower mortality rate with conscious sedation. However, these 2 large studies had several limitations, including their retrospective nature, selection bias, and inclusion of some occlusion locations only.

Potential disadvantages of general anesthesia are increased delay in time to recanalization due to intubation and ventilation, hypotension with administration of induction agents, uncontrolled hypertension during intubation, and prolonged intubation after the procedure leading to longer intensive care unit stays. These disadvantages are overcome by conscious sedation, which also allows clinical evaluations of the patient during the procedure. On the other hand, conscious sedation can be associated with the lack of patient cooperation, potentially leading to intraprocedural complications.

At our center, the decision to treat under conscious sedation was initially due to the lack of an anesthesia team available for mechanical thrombectomy procedures. Our series was prospective, and the analyses were conducted in an intention-to-treat population. Therefore, precise knowledge of the feasibility, efficacy, and safety of mechanical thrombectomy using the Solitaire device under conscious sedation can be obtained.

In our series, mechanical thrombectomy under conscious sedation was feasible in a high percentage of cases (86.1%). Treatment failed in 5 cases (13.9%) due to anesthetic conditions (patient agitation) in 3 cases (8.3%), and significant vessel tortuosity in 2 cases (5.6%). In addition, in 1 case, rapid worsening of the clinical condition led to intubation and general anesthesia at the beginning of the endovascular procedure. Because our analysis was conducted on an intention-to-treat basis, these patients were included in the recanalization rate determination and safety and functional outcomes at 3 months.

The recanalization rate parameter is not as easy to handle because it can be evaluated in different ways from 1 series to another. The recanalization rate is certainly improved if a final angiographic run is performed with some delay after the end
of the procedure. In addition, the differentiation between TICI 2a and 2b is not always easy to assess. In our series, the final angiographic run was performed immediately after the last Solitaire pass and a strict TICI score grading was used.

Because of the failed procedures, the recanalization rate (77.8%) was lower compared with other Solitaire series (89% and 90.9% in the 2 largest series).\textsuperscript{10,11} Excluding patients with failed treatment, the recanalization rate would be very similar to those observed in other series (28/31 patients; 90.3%). In addition, the recanalization rate in our series compares favorably with those in the MERCI and Penumbra trials (69.5% and 81.6%, respectively).\textsuperscript{7,8}

Despite the relatively low recanalization rate observed in our series, a higher percentage of patients were functionally independent after 3 months (61.1%) compared with the Solitaire series (50%).\textsuperscript{10} One potential explanation was a shorter time to recanalization compared with other Solitaire series (Table 4).

Overall mortality at 3 months was 22.2%, which was in agreement with rates reported from other series, ranging from 7.1% (evaluation at discharge) for Machi et al\textsuperscript{11} to 33% for Stampf et al.\textsuperscript{12} Symptomatic hemorrhagic complications at 24 hours occurred in 3/36 (8.3%), which equals other series, ranging from 1.7% for the Machi et al series to 16.6% for Stampf et al.\textsuperscript{9,11,12} One case of arterial dissection of the M1 part of the MCA (2.7%) was observed in our series, leading to symptomatic intracranial hemorrhage with a poor 3-month clinical outcome (mRS = 5). This complication was not previously reported in Solitaire series. It was probably related to inappropriate manipulations of the guidewire to pass through the clot in a patient who was not agitated.

Our study had several limitations. First, the number of patients was relatively small, but the sample size is similar to other previously published Solitaire series. Second, the lack of a control group, which was the main flaw of any of those series (including ours), made it difficult to judge the clinical relevance of this treatment.

Conclusions
In acute ischemic stroke, mechanical thrombectomy while the patient is under conscious sedation is feasible in a high percentage of cases (86.1%). Furthermore, a good functional outcome at 3 months was observed in a high percentage of cases (61.1%). Consequently, in most cases, conscious sedation appears to be a valuable alternative to general anesthesia. Nevertheless, anesthesiologists will have a major place in stroke endovascular therapy by selecting and giving the most appropriate and least deleterious anesthesia to patients with acute stroke treated by mechanical thrombectomy. Further studies are needed to directly compare the outcome of patients treated with mechanical thrombectomy under general anesthesia or conscious sedation.

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Disclosures: Laurent Pierot—UNRELATED: Consultancy: Codman, ev3, MicroVention, Penumbra, Sequent.