Retrievable stents, "stentrievers," for endovascular acute ischemic stroke therapy

Roberta L. Novakovic, MD
Gabor Toth, MD
Sandra Narayanan, MD
Osama O. Zaidat, MD, MS

Correspondence & reprint requests to Dr. Novakovic: Robin.Novakovic@utsouthwestern.edu

ABSTRACT

Endovascular therapy for acute ischemic stroke continues to evolve to improve both efficacy and safety. In the late 1990s, intra-arterial chemical thrombolysis with prourokinase was shown to be effective in achieving partial recanalization and improving clinical outcome, in comparison with intra-arterial heparin administration. However, this was at the expense of an increase in the rate of symptomatic intracranial hemorrhage to 10%. To improve the rate of recanalization, expand the time window, and reduce the risk of symptomatic intracranial hemorrhage, mechanical thrombectomy was introduced, with initial approval of the Merci clot retriever, a corkscrew-like device, and then more recently with approval of the Penumbra thromboaspiration system. Both devices are associated with a high rate of recanalization (total, partial, and complete). However, time to recanalization was on average 45 minutes, with a low rate of complete clot resolution, given that the majority of patients achieved only partial recanalization. More recently, retrievable stents have shown promise in reducing the time to recanalization, and they achieve a higher rate of complete clot resolution with improved feasibility. The retrievable stent can be opened within the clot to engage it within the stent struts, and subsequently it is retrieved by pulling it under flow arrest. The retrievable stents provide a new tool in the armamentarium of devices that can be used to achieve safe and timely clot removal. This review provides the historical evolution of endovascular therapy to use of stentreivers. ***Neurology*® 2012;79 (Suppl 1):S148–S157**

GLOSSARY

AIS = acute ischemic stroke; **CI** = confidence interval; **ECASS** = European Cooperative Acute Stroke Study; **FDA** = US Food and Drug Administration; **IA** = intra-arterial; **ICA** = internal carotid artery; **ICH** = intracerebral hemorrhage; **IMS** = Interventional Management of Stroke; **MCA** = middle cerebral artery; **mRS** = modified Rankin Scale; **NIHSS** = NIH Stroke Scale; **NINDS** = National Institute of Neurological Disorders and Stroke; **OR** = odds ratio; **PROACT** = Prolyse in Acute Cerebral Thromboembolism; **RSs** = retrievable stents; **rtPA** = recombinant tissue plasminogen activator; **SESs** = self-expanding stents; **SWIFT =** Solitaire FR With the Intention for Thrombectomy; **TICI** = thrombolysis in cerebral ischemia; **TIMI** = thrombolysis in myocardial infarction.

Acute ischemic stroke (AIS) therapy is based on the concept that early recanalization of the occluded artery leads to improved clinical outcome through preservation of the time-sensitive penumbra.[1–3] There has been an evolution in the development of techniques used to achieve faster and safer rates of recanalization. Because of the limited efficacy of pharmacologic thrombolysis, mechanical and multimodality methods have been sought to aid revascularization of the occluded artery. A newer endovascular approach using retrievable stents (RSs) shows promising results for better and faster rates of recanalization with possibly better short-term outcomes.

THE EARLY FOUNDATION OF STROKE THERAPY IV thrombolytic treatment with recombinant tissue plasminogen activator (rtPA), initiated within 3 hours from symptom onset, is the only medical therapy currently approved by the US Food and Drug Administration (FDA) for AIS. This approval was based on the results published in 1995 by the National Institute of Neurological Disorders and Stroke (NINDS) and rtPA Stroke Study Group trial.[4] The NINDS study group reported that compared with the placebo group, administration of rtPA to patients with AIS within 3 hours of symptom onset led to an overall 32% relative (12% absolute) increase in the proportion of patients with minimal or no disability at 3 months.[4]

From the University of Texas Southwestern Medical Center (R.L.N.), Dallas; Cleveland Clinic Foundation (G.T.), Cleveland, OH; Wayne State University (S.N.), Detroit, MI; and Medical College of Wisconsin (O.O.Z.), Milwaukee.

Go to Neurology.org for full disclosures. Disclosures deemed relevant by the authors, if any, are provided at the end of this article.

A subsequent analysis of the NINDS study[5] and a pooled analysis of 6 major randomized placebo-controlled IV rtPA stroke trials[3] showed an association of outcome with early stroke treatment. The combined analysis—Alteplase Thrombolysis for Acute Noninterventional Therapy in Ischemic Stroke (ATLANTIS) I and II, NINDS I and II, and European Cooperative Acute Stroke Study (ECASS) I and II—included 2,775 patients who were treated with IV rtPA or a placebo within 360 minutes of symptom onset.[3] The analysis confirmed the benefit of treatment up to 3 hours and further suggested a potential benefit beyond 3 hours for a certain subgroup of patients. In a narrower subgroup of patients, the benefit of IV rtPA 3 to 4.5 hours from onset of symptoms was later confirmed by the ECASS-III trial.[6]

A Cochrane Database review analyzed 18 trials (16 of which were double-blinded) with a total of 5,727 patients who were treated with thrombolytics (streptokinase, rtPA, IV urokinase, or prourokinase) up to 6 hours after symptom onset; the analysis showed a significant reduction in death and dependency (modified Rankin Scale [mRS] score, 3–6) at the 3- to 6-month follow-up (odds ratio [OR] 0.84; 95% confidence interval [CI] 0.75–0.95).[7] This was in spite of a significant increase in the odds of death within the first 10 days (OR 1.81; 95% CI 1.46–2.24). A separate Cochrane review that analyzed different doses, routes of administration, and agents used for thrombolysis in AIS confirmed that higher doses of thrombolytic therapy were associated with a 3-fold increase in fatal intracerebral hemorrhage (ICH).[8]

Intra-arterial thrombolysis. Intra-arterial (IA) thrombolysis allows direct infusion of the fibrinolytic agent into the thrombus; thus, a smaller dose of drug can reach a higher local concentration than with an IV infusion. In theory, IA therapy could permit better rates of recanalization with reduced systemic complications and ICH, due to the smaller doses of thrombolytics used. IA thrombolysis gained validity on the basis of the results from 2 randomized trials and several case series.[9–12] The Prolyse in Acute Cerebral Thromboembolism II (PROACT II) trial[10] was a prospective randomized trial to test efficacy and safety of IA prourokinase plus heparin, vs heparin alone, in patients with occlusion of the middle cerebral artery (MCA) who could have initiation of treatment within 6 hours of symptom onset. Partial or complete recanalization was achieved in 67% of patients in the treatment group. Of the treated patients, 40% had an mRS score of 0–2 at 90 days, compared with 25% of control subjects ($p = 0.04$). Complete restoration of blood flow (Thrombolysis In Myocardial Infarction [TIMI] 3) was achieved in 20%, and an additional 46% in the treatment group had partial recanalization (TIMI 2) vs only 20% with TIMI 2–3 in the control group. Symptomatic ICH occurred in 10% of patients within the treatment group, compared with 2% of control patients ($p = 0.06$). The FDA required a confirmatory study prior to approval. No placebo-controlled, randomized studies have tested the use of IA rtPA therapy in AIS.

Bridging therapy. It is understandable that there are inherent delays in performing endovascular procedures, which is why IV rtPA therapy remains first-line treatment. Unfortunately, IV rtPA achieves recanalization rates of only approximately 9% for occluded extracranial internal carotid arteries (ICAs)[13] and 28% to 30% for occlusions of the M1 segment of the MCA.[13,14] Furthermore, early reocclusion occurs in 34% of patients treated with rtPA who had any initial recanalization.[14] Ideally, bridging therapy combines the rapidity of administration by the IV route with the better efficacy of the IA approach. The Interventional Management of Stroke (IMS) II study showed the feasibility and safety of a combined IV and IA treatment with rtPA.[15] The 81 subjects enrolled with NIH Stroke Scale (NIHSS) scores ≥10 had two-thirds the IV dose initiated within 3 hours of symptom onset, followed by IA thrombolysis. Previous studies evaluating the combined approach have shown better recanalization rates; however, they have shown only trends toward better outcomes, as compared with the IV rtPA–treated subjects in the NINDS rtPA Stroke Trial[15] or a database registry.[16] An additional study has shown the potential benefit of bridging therapy increases when the target population is limited to IV rtPA nonresponders (40% of IV-IA patients reached functional independence at 3 months, compared with 14.9% of IV nonresponders [$p = 0.012$]); however, the benefit came at the cost of a higher morbidity and mortality associated with the bridging therapy (OR 1.49 and 95% CI 0.70–3.16 for death; OR 2.14 and 95% CI 0.58–7.83 for symptomatic ICH).[17] The IMS III trial comparing IV and multimodal-approach IA therapy to IV rtPA only is currently underway.

Mechanical approaches to stroke therapy. The theoretical advantages of mechanical approaches include a reduced need for thrombolytics, faster rates of recanalization, and fragmentation of the thrombus, which increases the surface area accessible to the fibrinolytic agents. Early studies utilizing endovascular retrievers or aspiration devices did not show the anticipated rates of clinical improvement, despite achieving higher recanalization rates.[18,19] Three uncontrolled trials have led to FDA approval of 2 devices, the Merci Retriever (in 2004) and the Penumbra System (in 2008), for the indication of

intracranial clot retrieval in patients with AIS. The Merci clot retrieval device (Concentric Medical, Mountain View, CA) achieved 69.5% vessel recanalization (TIMI 2–3) with adjuvant IA rtPA.[19] The Penumbra thromboaspiration system (Penumbra, Inc., Alameda, CA) achieved an 81.6% recanalization rate (TIMI 2–3), though the ICH rate was 28% (11% symptomatic) within 24 hours of treatment.[18]

Self-expanding stents. The limitations of the currently approved therapies have driven the pursuit of devices that can further expedite and improve the degree of flow restoration. Starting in 2006, reports in the literature indicated that varied combinations of angioplasty alone, balloon-mounted stents, and self-expanding stents (SESs) were being utilized in the treatment of AIS. In a multicenter analysis of endovascular reperfusion therapies, in a cohort of 1,122 patients with AIS, stent deployment was an independent predictor of TIMI 2–3 recanalization (OR 1.91; 95% CI 1.23–2.96; $p < 0.001$).[20] Conceptually, the occlusive clot is rapidly displaced outwardly along the vessel wall and becomes entrapped in the interstices of an SES as it is completely or partially deployed.

Retrievable stents. A completely deployed SES requires dual antiplatelet therapy, and in the acute setting IV glycoprotein IIb/IIIa inhibitors are often used. The additional risk of hemorrhagic complications from the combination of thrombolytics and glycoprotein IIb/IIIa inhibitors, as well as the long-term risk of in-stent stenosis, has brought about the concept of RSs. In the literature, restenosis and reocclusion rates of 25% and 32.3% for SESs used in atherosclerotic lesions have been reported.[21,22] Also called stentrievers, RSs offer the advantage of immediate flow restoration after deployment and the ability to retrieve the stent after mechanical embolectomy. Some models of RSs allow permanent detachment for resistant lesions or underlying intracranial stenosis. In theory, an RS offers the rapidity of the SES to open the vessel, while maintaining navigability of the intracranial vessels and the capability of thrombus extraction, all the while diverting the long-term risks associated with SESs. Furthermore, RSs negate the long-term need for dual antiplatelet therapy and IV glycoprotein IIb/IIIa inhibitors in the acute setting (figure).

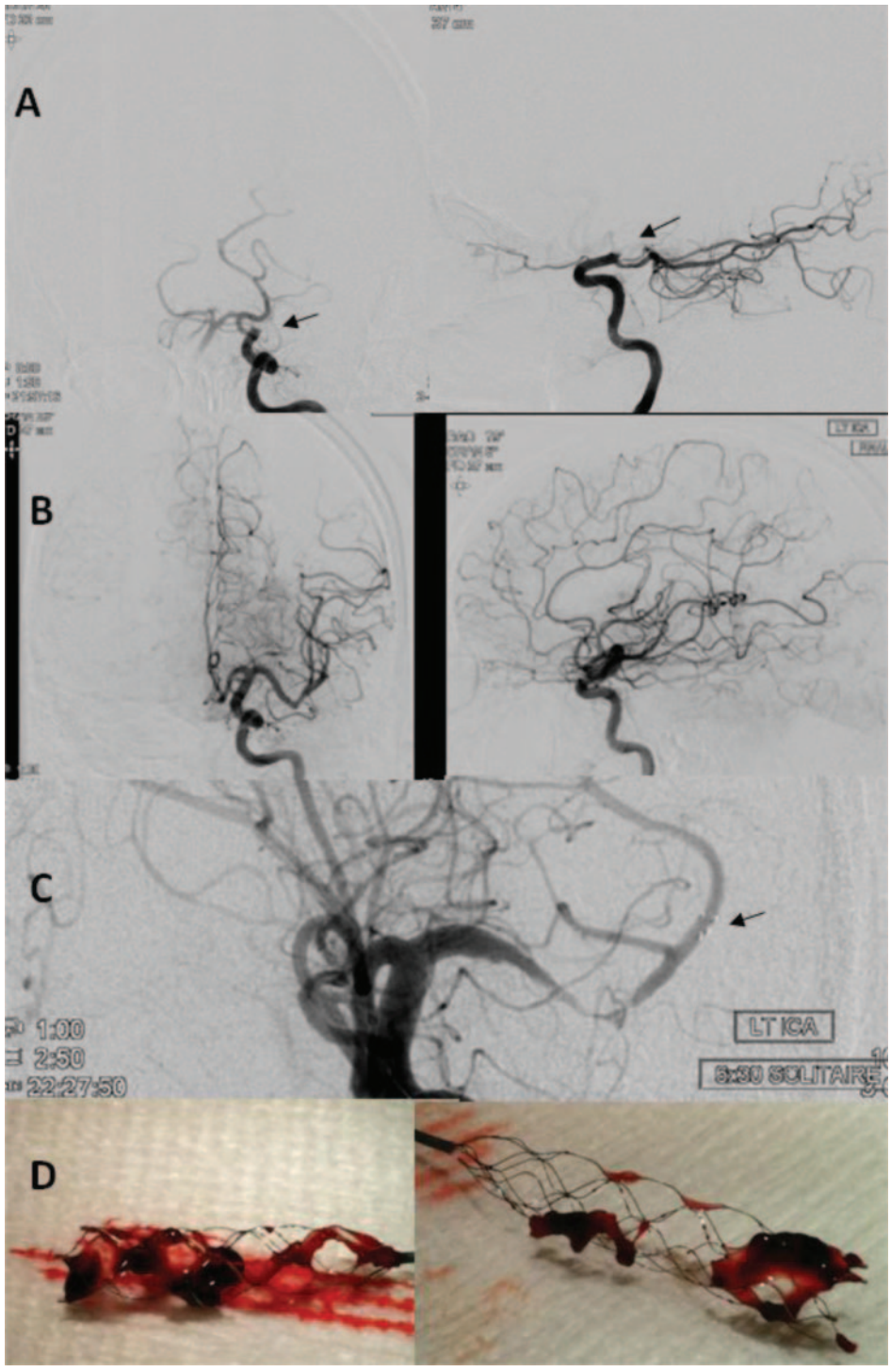
The safety and efficacy evaluation of RSs in animal models provided important technical data with clinical implications. Jahan[23] performed mechanical thrombectomy in swine. Successful TIMI 3 recanalization was achieved in all 6 cases within 1 to 2 passes with the Solitaire device (ev3 Inc., Irvine, CA). No distal embolization, vessel damage, or thrombosis was noted. Postprocedure vasospasm was encountered but resolved in all cases. Postprocedure angiography at 30 days showed no evidence of vessel damage. Microscopic examination of the treated vessels at 30 and 90 days showed mild intimal thickening with approximately 1% to 5% narrowing of the vessel lumen.

Several small case series utilizing the Solitaire device demonstrate recanalization (TIMI 2–3) rates from 88% to 90% following 1 or 2 passes with the device.[24–27] One of the first reported case series of 20 subjects treated with the Solitaire device was published in 2010.[24] The device was used as rescue therapy in 2 patients refractory to IA rtPA and in 3 patients after unsuccessful recanalization with the Merci device. Following a mean of 1.4 passes, successful revascularization (Thrombolysis in Cerebral Ischemia [TICI] grade 2b or 3) was achieved in 90% of treated vessels, with a mean time to recanalization of 50 minutes and a symptomatic ICH rate of 10%. At the 90-day follow-up, 45% of patients had good functional outcome (mRS score ≤2), and the mortality rate was 20%. Similarly, in a second series of 26 patients with AIS who underwent Solitaire device–assisted thrombectomy, 42.3% had a favorable clinical outcome (mRS ≤2); the lowest rate was seen in patients with basilar artery occlusion (20%).[25] In addition, a series of 22 patients with AIS and ICA occlusions were treated with the Solitaire device, and successful revascularization was achieved in 90.9% of patients (TICI grade 2a/b in 36.3%; TICI grade 3 in 54.5%).[27] The mean time from stroke symptom onset to recanalization was 277 minutes. Fifty percent of patients showed favorable outcome at 90 days, and mortality was 18.1%. ICH occurred in 3 patients (2 symptomatic).

One of the larger reported studies with an RS was presented at the 2011 International Stroke Conference.[28,29] Among the 89 subjects enrolled, 48% of the patients received rtPA prior to the intervention. The location of the thrombus was in the M1 segment in 44%, vertebrobasilar artery in 15%, ICA terminus in 14%, and ICA and MCA (tandem occlusions) in 14%. Both the Trevo (Concentric Medical, Mountain View, CA) and Solitaire systems were utilized in the study. Following a mean of 1.4 passes per patient, the average recanalization time was 45 minutes (27–60 minutes), and no case of technical failure was reported. The recanalization rate achieved was 91% (TIMI 2–3). ICH occurred in 11% of patients (9% symptomatic). Follow-up data at 90 days was available for 74 patients, and good clinical outcome (mRS ≤2) was achieved in 47%; mortality rate was 20%.

Results with the Trevo device were presented at the 2010 European Stroke Conference.[30] Thirty patients were enrolled, with a mean NIHSS score of 17.36. Recanalization (TIMI 2–3) was achieved in 93.3%; however, no ICH, clinical outcomes, or mor-

Figure **A 51-year-old man with history of stroke, whose baseline modified Rankin Scale (mRS) score was 3, presented within 2 hours of sudden onset of right-sided hemiplegia and neglect**



NIH Stroke Scale (NIHSS) score was 22. IV recombinant tissue plasminogen activator (rtPA) was administered, without improvement in his NIHSS score. The patient was taken to the angio-suite and treated with a Solitaire device. (A) Baseline left internal carotid artery (ICA) angiogram in anteroposterior (AP) and lateral projections with complete carotid terminus occlusion distal to the posterior communicating artery origin (arrows); (B) final AP and lateral left ICA angiogram, following 2 passes of the stentreivers, with complete recanalization; (C) AP left ICA run with an open stentreiver (6 mm × 30 mm) and distal markers (arrow); (D) the retrieved clots after the first pass (left) and second pass (right) of the device. In the final 3 months, the NIHSS score went down to 6 and the mRS score improved to 3.

Table Summary of the literature on stentrievers

First author, year	No. occluded vessels	Mean NIHSS (range)	Occlusion site, n	IV/IA thrombolysis %	MTR, min (range)	MPP	Recan rate, %	sICH, %	Mortality, %	mRS ≤2, % (n)	Device	Notes
Andersson 2010	30	17.4	NA	IV 70	77	2.46	93.3	0	NA	NA	Trevo	70% MM
							TIMI 2–3					6 vasospasm
							80					2 dissections
							TICI 2b/3					1 ISD
Aleu 2011	89	18 (15–22)	M1 44%, TO 14%, VB 15%, ICAt 14%	IV 48	45 (27–60)	1.4	91	9	20	47 (35/74)	Solitaire	
							TICI 2–3			(90-day)	And Trevo	
							70					
							TICI3					
Brekenfeld 2011	17	19 (14–22)	M1–7, M2–2, BA-3, ICA-5	IV 35	52.5 (37.5–61)	1.4	94	0	NA	43 (90-day)	Solitaire	76% MM
				IA 53			TIMI 2–3					2 SESs permanently placed
												2 eICA stents
Castano 2010	20	19 (15–23)	M1–11, M2–1, TO-3, ICAt-5	IV 50	50 (38–71)	1.4	90	10 (30 aICH)	20	45 (9/20)	Solitaire	1 SAH
							TICI 2b/3			(90-day)		1 fICH
												2 eICA stents
Castano 2009	1	23	M1–1	IV 100	NA	1	100	0	0	0	Solitaire	100% MM
							TICI 3			mRS 3 (90-day)		
Cohen 2011	4	22 (18–24)	M1–1, M2–1, TO-1, ICAt-1	IV 0	34 (22–52)	1	100	0	0	100 (30-day)	Solitaire	1 eICA stent for occlusion
				IA 0			TICI 3					
Costalat 2011	50	14.7	MCA-20, ICA-14, BA-16	IV 80	54 (15–243)	2	92	2 (10 tICH)	12	54 (27/50)	Solitaire	2 SAH
							TIMI 2–3			(90-day)		4 adverse embolic infarcts in new territory
							88					
							TICI 2b/3					
Liebig 2010[b]	104 (108[e])	15.3 (3–23)	M1–54, M2–6, ACA-6, ICAt-18, VB-24	IV 55.8	47 (5–186)	2.46	92.5[e]	(6.7 tICH)	23	25.6 (at D/C)	Solitaire	76.9% MM
				IA 13.9			TIMI 2–3					1 SAH
							79[e]					1 fICH
							TICI 2b/3					

—Continued

Table Continued

First author, year	No. occluded vessels	Mean NIHSS (range)	Occlusion site, n	IV/IA thrombolysis %	MTR, min (range)	MPP	Recan rate, %	sICH, %	Mortality, %	mRS ≤2, % (n)	Device	Notes
Menon 2010	14	12.7 (5–22)	M1–8, M2–1, BA-5	IV 50	84 (26–164)	NA	85.7	(28.6 tICH)	14.3	57.1 (8/14)	Solitaire	64.3% MM
		NA for 3					TIMI 2–3			(90-day or D/C)		1 fICH/SAH
							28.6					
							TICI 3					
Miteff 2011	26[e] (29)	21.4 (3–35)	M1–4, M2–3, ACA-1, ICAt-5, ICA-3, TO-3, BA-10	IV 0	95.6 (38–181)	NA	96.1[e]	7.7	19.2	42.3 (11/26)	Solitaire	38.5% MM
							TIMI 2–3			55.6		1 USD
										(5/9)		1 eICA stent
										(90-day)		1 entangled[a]
										35.3 (at D/C)		1 fICH/SAH
												1 fICH
Mpotsaris 2011	26	16 (7–31)	MCA-17, ICAt-6, BA-2, VA-1	IV 73	NA	2.12	88	NA	7.7	38.5 (10/26)	Solitaire	12 eICA stents
							TIMI 2–3			(at D/C)		
							69					
							TIMI3					
Nayak 2010	7	19 (14–23)	M1–4, M1/M2- 1, TO-2	IV 100	84 (40–145)	1.86	100	0	0	57 (4/7)	Solitaire	1 eICA stent for stenosis
							TIMI 2–3	(14.3 tICH)		(30-day)		1 USD
Park 2011	8	18.3 (8–24)	M1–4, M1/M2- 1, M2–1, TO-1, BA-1	IV 62.5	40.9 (17–70)	1.5	100	0	0	50 (4/8)	Solitaire	1 eICA stent for stenosis
				IA 12.5			TICI 2b/3			(90-day)		
Rohde 2011	10	19	MCA-5, TO-5, BA-1	IV 90	88.7	3	100	20	30	NA	Revive[d]	1 eICA stent for stenosis
				IA 20			TICI 2b/3					
Roth 2010	22	19.4	M1–12, ICAt -2, BA-8	IV 59	NA	1.77	90.9	4.5	18.1	50 (11/22)	Solitaire	6 eICA stents for occlusion
							TICI 2a/b-3	(13.6 tICH)		(90-day)		
Seifert 2011	4	24.3 (13–34)	M1–1, BA-3	IV+IA 100	116.3 (62–142)	1.25	100	0	25	66.7 (2/3)	Solitaire	100% MM
							TIMI 2–3			(90-day)		2 ISD
Stampfl 2011	18[e] (19)	21 (7–35)	MCA-9, TO-5, BA-5	IV 27.8	48.3	2.5	88.8[e]	(16.7 tICH)	27.8	33.3 (6/18)	Solitaire	1 eICA stent for occlusion

—Continued

Table Continued

First author, year	No. occluded vessels	Mean NIHSS (range)	Occlusion site, n	IV/IA thrombolysis %	MTR, min (range)	MPP	Recan rate, %	sICH, %	Mortality, %	mRS ≤2, % (n)	Device	Notes
				IA 22.2			TICI 2a/b-3			(at D/C)		5 ISD
				IV+IA 44.4			50[e]					
							TICI 3					
Wehrschuetz 2011	11	16.1	MCA-5, ICAt-2, BA-4	IV 100	94	2.27	100	0	9	30 (3/10)	Solitaire	
				IA aggrastat			TICI 2a/b-3			(90-day)		
				82			18					
							TICI3					
Total	461 (469)	18.6[c]			67.4[c]	1.8[c]	93.3 (430/461)	6.7[f]	17.4	49.2 (90-day) (104/211)		
							TIMI 2-3/TICI 2-3	(29/435)	(72/414)	50.5 (30- or 90-day)		
										(112/222)		

Abbreviations: a/s/t ICH = asymptomatic/symptomatic/total intracerebral hemorrhage in %; BA = basilar artery; D/C = at discharge; eICA = extracranial internal carotid artery; fICH = fatal intracerebral hemorrhage; IA = intra-arterial; ICA = internal carotid artery; ICAt = internal carotid artery terminus; ISD = intentional stent detachment; M1 = middle cerebral artery, main stem; M2 = middle cerebral artery, superior or inferior division; MCA = middle cerebral artery; MPP = mean passes per patient; MTR = mean/median time to recanalization from start of procedure, in minutes, or when not available, duration of procedure; n = patients; NA = not assessable; NIHSS = mean NIH Stroke Scale score on admission; MM = multimodality; Recan = recanalization; SAH = subarachnoid hemorrhage; TICI = thrombolysis in cerebral ischemia; TIMI = thrombolysis in myocardial infarction; TO = tandem occlusion; USD = unintentional stent detachment; VB = vertebrobasilar.

[a] During retrieval, the Solitaire stent became entangled with the proximal ICA stent that was placed during the procedure.

[b] Henkes et al. 2009 and Liebig et al. 2010 were not included in the table separately because of concern for overlapping patient database.

[c] Number was derived from mean number presented in table.

[d] Revive (Micrus Endovascular, San Jose, CA).

[e] Number used as denominator in the recanalization rate calculation by study's author.

[f] Where rate of sICH was not given, tICH was used in the calculation.

tality rates were reported. Nonsignificant vasospasm was noted in 6 patients, and 1 device had to be permanently implanted because of significant friction.

Retrievable stent trials in the United States. Solitaire FR With the Intention for Thrombectomy (SWIFT) is an open-label, randomized trial comparing the efficacy and safety of the Solitaire RS system with the Merci device.[31] The primary outcome is recanalization rate of an occluded target vessel to TIMI 2 or 3. Secondary outcomes are time to initial recanalization as well as NIHSS score, Barthel index, and mRS score at 30 and 90 days postprocedure. Morbidity and mortality rates and the incidence of symptomatic ICH are also recorded at these time points. The study includes patients with NIHSS scores of 8–30 presenting within 8 hours of stroke symptom onset. Patients included in the trial may be those who are ineligible for IV rtPA or whose IV rtPA failed before the procedure. The SWIFT study was halted by the data monitoring board in early 2011 after 126 patients of the anticipated 250 were enrolled. The company is currently seeking FDA approval based on the study results.

Thrombectomy REvascularization of Large Vessel Occlusions in Acute Ischemic Stroke 2 (TREVO 2) is a nonrandomized, open-label trial evaluating the efficacy of the Trevo device in large-vessel occlusions in AIS patients.[32] The primary outcome is revascularization, defined as at least TICI 2a in the target vessel. The secondary outcomes are mRS score, NIHSS score, and mortality at 90 days. Device-related serious adverse events and symptomatic ICH rates are also recorded. The exclusion criteria are similar to those of the SWIFT trial, described previously.

DISCUSSION Although the number of RSs for AIS therapy has been growing, none of the devices has gained FDA approval in the United States. The devices that are currently in clinical trials or being investigated include Solitaire FR, Trevo, Revive (Codman Neurovascular, San Jose, CA), Pulse (Penumbra, Inc., Alameda, CA), and Flow/Capture (MindFrame, Inc., Lake Forest, CA).

Since the development of these devices is relatively new, only a limited number of publications with small case series are available in the literature (table).[23–30,33–46] If we summarize the data from the studies listed in the table, the average recanalization rate is 93.3% to achieve a TICI 2–3/TIMI 2–3 score in a mean of 1.8 passes. Favorable outcome, as measured by mRS score of 0–2, was achieved in 49.2% of patients at 90 days, with an average mortality rate of about 17.4%. The overall incidence of symptomatic intracranial hemorrhage was 6.7%, which is comparable to the rate of symptomatic intracranial

hemorrhage in other clinical trials (10% in PROACT II,[10] 11% in the Penumbra trial,[18] and 9.8% in the Multi-MERCI trial[19]). Reversible vasospasm and spontaneously detached stents were seen in a few cases; however, overall complication rates were low.

It is difficult to evaluate the efficacy and safety of the RS alone in these small case series. In a significant number of cases, the RS was used in a multimodal approach, and in some cases the RS device was used as a salvage maneuver after other mechanical devices failed. Perhaps the overall mean duration of treatment of 67.4 minutes would improve if the RS was utilized as first-line treatment in IA therapy. Furthermore, lack of uniformity in primary and secondary outcome measures makes interpretation of the overall outcome difficult.

CONCLUSION Multimodal combination therapies for AIS achieve faster and better rates of recanalization. Faster recanalization should result in improved outcome in AIS.[47–50] Ideally, the optimal therapy should not only increase the likelihood of a favorable outcome but also reduce the likelihood of ICH. Currently, recanalization rates of endovascular treatment are around 67% for IA thrombolysis[10] and 68% to 81.6% for the combination of mechanical thrombectomy with IV and IA thrombolysis.[18,19] An impetus for the endovascular field is to develop recanalization devices that safely exceed the efficacy of IV and IA pharmacologic therapy.

The available nonrandomized, uncontrolled data on RSs from case series show promising results with better and faster recanalization rates, possibly better short-term outcomes than with other reported endovascular devices, and mortality and ICH rates comparable with published results of previous neurointerventional studies. Larger clinical trials are ongoing to assess the advantages of RSs in AIS therapy. Perhaps FDA approval of such devices is looming in the near future.

AUTHOR CONTRIBUTIONS

Dr. Novakovic: drafting/revising the manuscript, study concept or design, analysis or interpretation of data. Dr. Toth: drafting/revising the manuscript. Dr. Narayanan: drafting/revising the manuscript, supervision or coordination. Dr. Zaidat: drafting/revising the manuscript, study concept or design, contribution of vital reagents/tools/patients, acquisition of data.

DISCLOSURE

Dr. Novakovic performs endovascular treatments for acute ischemic strokes but has not used a retrievable stent. Dr. Toth reports no disclosures. Dr. Narayanan serves on the Editorial Board of the *Journal of Stroke and Cerebrovascular Diseases* and serves as Review Editor for *Frontiers in Neurology* (Interventional Neurology section). Dr. Zaidat serves on the scientific advisory board for Talecris; served on the adjudication committee for Stryker; received speaker honoraria from Stryker; served on the editorial board of *Frontiers in Neurology* (Endovascular & Interventional Neurology Section), serves as Editor of *The Journal of Neurointerventional Surgery*, and serves as Associate Editor and is a member of the Editorial Board of *Journal of Stroke & Cerebrovascular Diseases*; served as a consultant for Stryker Neurovascular–Commercial, Codman Neurovascular–Commercial, and Microvention Inc.–Commercial; and has received research support from a Society of Vascular & Interventional Neurology (SVIN) grant for this educational activity. **Go to Neurology.org for full disclosures.**

Received July 2, 2011. Accepted in final form October 7, 2011.

REFERENCES

1. Brekenfeld C, Remonda L, Nedeltchev K, et al. Endovascular neuroradiological treatment of acute ischemic stroke: techniques and results in 350 patients. Neurol Res 2005;27:29–35.
2. Rha JH, Saver JL. The impact of recanalization on ischemic stroke outcome: a meta-analysis. Stroke 2007;38:967–973.
3. The ATLANTIS, ECASS, and NINDS rt-PA Study Group Investigators. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. Lancet 2004;363:768–774.
4. Marler JR, Brott T, Broderick J, et al., for The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med 1995;333:1581–1587.
5. Marler JR, Tilley BC, Lu M, et al., for the NINDS rt-PA Stroke Study Group. Early stroke treatment associated with better outcome: the NINDS rt-PA Stroke Study. Neurology 2000;55:1649–1655.
6. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med 2008;359:1317–1329.
7. Wardlaw JM, del Zoppo GJ, Yamaguchi T, Berge E. Thrombolysis for acute ischaemic stroke. Cochrane Database Syst Rev 2003;3:CD000213.
8. Mielke O, Wardlaw JM, Liu M. Thrombolysis (different doses, routes of administration and agents) for acute ischemic stroke. Cochrane Database Syst Rev 2004;4:CD000514.
9. del Zoppo GJ, Higashida RT, Furlan AJ, Pessin MS, Rowley HA, Gent M. PROACT: a phase II randomized trial of recombinant pro-urokinase by direct arterial delivery in acute middle cerebral artery stroke. Stroke 1998;29:4–11.
10. Furlan A, Higashida R, Wechsler L, et al. Intra-arterial prourokinase for acute ischemic stroke: the PROACT II study: a randomized controlled trial. JAMA 1999;282:2003–2011.
11. Ogawa A, Mori E, Minematsu K, et al., for the MELT Japan Study Group. Randomized trial of intraarterial infusion of urokinase within 6 hours of middle cerebral artery stroke: the Middle cerebral artery Embolism Local fibrinolytic intervention Trial (MELT) Japan. Stroke 2007;38:2633–2639.
12. Macleod MR, Davis SM, Mitchell PJ, et al. Results of a multicentre, randomized controlled trial of intra-arterial urokinase in the treatment of acute posterior circulation ischaemic stroke. Cerebrovasc Dis 2005;20:12–17.
13. Wolpert SM, Bruckmann H, Greenlee R, et al. Neuroradiologic evaluation of patients with acute stroke treated with recombinant tissue plasminogen activator. AJNR 1993;14:3–13.

14. Alexandrov AV, Grotta JC. Arterial reocclusion in stroke patients treated with intravenous tissue plasminogen activator. Neurology 2002;59:862–867.
15. The IMS II Trial Investigators. The Interventional Management of Stroke (IMS) II study. Stroke 2007;38:2127–2135.
16. Mazighi M, Serfaty JM, Labreuche J, et al. Comparison of intravenous alteplase with a combined intravenous-endovascular approach in patients with stroke and confirmed arterial occlusion (RECANALISE study): a prospective cohort study. Lancet Neurol 2009;8:802–809.
17. Rubiera M, Ribo M, Pagola J, et al. Bridging intravenous-intra-arterial rescue strategy increases recanalization and the likelihood of a good outcome in nonresponder intravenous tissue plasminogen activator-treated patients: a case-control study. Stroke 2011;42:993–997.
18. Penumbra Pivotal Stroke Trial Investigators. The Penumbra Pivotal Stroke Trial: safety and effectiveness of a new generation of mechanical devices for clot removal in intracranial large vessel occlusive disease. Stroke 2009;40:2761–2768.
19. Smith WS, Sung G, Saver J, et al. Mechanical thrombectomy for acute ischemic stroke: final results of the Multi MERCI trial. Stroke 2008;39:1205–1212.
20. Gupta R, Tayal AH, Levy EI, et al. Intra-arterial thrombolysis or stent placement during endovascular treatment for acute ischemic stroke leads to the highest recanalization rate: results of a multicenter retrospective study. Neurosurgery 2011;68:1618–1623.
21. Albuquerque FC, Levy EI, Turk AS, et al. Angiographic patterns of Wingspan in-stent restenosis. Neurosurgery 2008;63:23–28.
22. Zaidat OO, Klucznik R, Alexandar MJ, et al. NIH Multicenter Wingspan Intracranial Stent Registry Group: the NIH registry on use of the Wingspan stent for symptomatic 70–99% intracranial arterial stenosis. Neurology 2008;70:1518–1524.
23. Jahan R. Solitaire flow-restoration device for treatment of acute ischemic stroke: safety and recanalization efficacy study in a swine vessel occlusion model. Am J Neuroradiol 2010;31:1938–1943.
24. Castaño C, Dorado L, Guerrero C, et al. Mechanical thrombectomy with the Solitaire AB device in large artery occlusions of the anterior circulation: a pilot study. Stroke 2010;41:1836–1840.
25. Miteff F, Faulder KC, Goh AC, Steinfort BS, Sue C, Harrington TJ. Mechanical thrombectomy with a self-expanding retrievable intracranial stent (Solitaire AB): experience in 26 patients with acute cerebral artery occlusion. AJNR Am J Neuroradiol 2011;32:1078–1081.
26. Mpotsaris A, Bussmeyer M, Loehr C, Oelerich M, Buchner H, Weber W. Mechanical thrombectomy in severe acute stroke: preliminary results of the Solitaire stent. J Neurol Neurosurg Psychiatry 2012;83:117–118.
27. Roth C, Papanagiotou P, Behnke S, et al. Stent-assisted mechanical recanalization for treatment of acute intracerebral artery occlusions. Stroke 2010;41:2559–2567.
28. Aleu A, Dorado L, Castano C, et al. Endovascular therapy for acute ischemic stroke using retrievable stents (stentrievers). Stroke 2011;42:70.
29. Zoler ML. Retrievable stents produce fast recanalization in acute stroke. Available at: http://www.medconnect.com.au/tabid/311/ct1/c340385/Retrievable-Stents-Produce-Fast-Recanalization-in-Acute-Stroke/Default.aspx. Accessed September 1, 2011.
30. Andersson T, Liebig T, Macho J, et al. Multi-center first-in-man experience with a new thrombectomy device: the Trevo. Presented at the European Stroke Conference, 2010, Barcelona, Spain.
31. Thrombectomy REvascularization of Large Vessel Occlusions in Acute Ischemic Stroke (TREVO). Available at clinicaltrials.gov/ct2/show/NCT01088672?term=trevo&rank=1. Accessed September 7, 2011.
32. SOLITAIRE FR With the Intention For Thrombectomy (SWIFT) Study. Available at clinicaltrials.gov/ct2/show/NCT01054560?term=swift&rank=1. Accessed September 7, 2011.
33. Menon BK, Kochar P, Ah-Seng A, et al. Initial experience with a self-expanding retrievable stent for recanalization of large vessel occlusions in acute ischemic stroke. Neuroradiol 2012;54:147–154.
34. Park H, Hwang GJ, Jin SC, et al. A retrieval thrombectomy technique with the Solitaire stent in a large cerebral artery occlusion. Acta Neurochir 2011;153:1625–1631.
35. Nayak S, Ladurner G, Killer M. Treatment of acute middle cerebral artery occlusion with a Solitaire AB stent: preliminary experience. Br J Radiol 2010;83:1017–1022.
36. Cohen JE, Gomori JM, Leker RR, Eichel R, Arkadir D, Itshayek E. Preliminary experience with the use of self-expanding stent as a thrombectomy device in ischemic stroke. Neurol Res 2011;33:439–443.
37. Brekenfeld C, Schroth G, Mordasini P, et al. Impact of retrievable stents on acute ischemic stroke treatment. Am J Neuroradiol 2011;32:1269–1273.
38. Castaño C, Serena J, Dávalos A. Use of the new Solitaire AB device for mechanical thrombectomy when Merci clot retriever has failed to remove the clot. Interv Neuroradiol 2009;15:209–214.
39. Henkes H, Liebig T, Miloslavski E, Guethe T, Schmid E, Wiethoelter H. Endovascular acute ischemic stroke treatment using the self-expanding and fully retrievable Solitaire stent. Stroke 2009;40:e247.
40. Liebig T, Lockau H, Stehle S, Dorn F, Prothmann S, Henkes HH. Temporary endovascular bypass in acute stroke: experience after 50 patients. Stroke 2010;41:e259.
41. Liebig T, Lockau H, Stehle S, et al. The potential of stent-trievers: experience in 108 acute ischemic stroke treatments. Available at: http://www.wfnrs.org/newsite/PPT/08-10-2010/AUDITORIUM/14.30%20-%2016.00/541-Liebig%20T/Liebig-T.ppt. Accessed September 1, 2011.
42. Seifert M, Ahlbrecht A, Dohmen C, Spuentrup E, Moeller-Hartmann W. Combined interventional stroke therapy using intracranial stent and local intraarterial thrombolysis (LIT). Neuroradiology 2011;53:273–282.
43. Stampfl S, Hartmann M, Ringleb PA, Haehnel S, Bendszus M, Rohde S. Stent placement for flow restoration in acute ischemic stroke: a single-center experience with the Solitaire stent system. Am J Neuroradiol 2011;7:1245–1248.
44. Costalat V, Machi P, Lobotesis K, et al. Rescue, combined, and stand-alone thrombectomy in the management of large vessel occlusion stroke using the Solitaire device: a prospective 50-patient single-center stud: timing, safety, and efficacy. Stroke 2011;42:1929–1935.

45. Rohde S, Haehnel S, Herweh C, et al. Mechanical thrombectomy in acute embolic stroke: preliminary results with the Revive device. Stroke 2011;42:2954–2956.
46. Wehrschuetz M, Wehrschuetz E, Augustin M, et al. Early single center experience with Solitaire thrombectomy device for the treatment of acute ischemic stroke. Interv Neuroradiol 2011;17:235–240.
47. Schulte-Altedorneburg G, Hamann GF, Mull M, et al. Outcome of acute vertebrobasilar occlusions treated with intra-arterial fibrinolysis in 180 patients. AJNR Am J Neuroradiol 2006;27:2042–2047.
48. Arnold M, Nedeltchev K, Schroth G, et al. Clinical and radiological predictors of recanalisation and outcome of 40 patients with acute basilar artery occlusion treated with intra-arterial thrombolysis. J Neurol Neurosurg Psychiatry 2004;75:857–862.
49. Rha JH, Saver JL. The impact of recanalization on ischemic stroke outcome: a meta-analysis. Stroke 2007;38:967–973.
50. Eckert B, Kucinski T, Pfeiffer G, Groden C, Zeumer H. Endovascular therapy of acute vertebrobasilar occlusion: early treatment onset as the most important factor. Cerebrovasc Dis 2002;14:42–50.

Retrievable stents, ''stentrievers,'' for endovascular acute ischemic stroke therapy

Roberta L. Novakovic, Gabor Toth, Sandra Narayanan, et al.

Neurology 2012;79;S148-S157
DOI 10.1212/WNL.0b013e3182697e9e