

Medical Policy Manual

Topic: Mechanical Embolectomy for Treatment of Acute Stroke

Date of Origin: February 6, 2007

Section: Surgery

Last Reviewed Date: June 2014

Policy No: 158

Effective Date: August 1, 2014

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

The majority of strokes are caused by thrombotic or embolic occlusion, and these frequently present as acute neurologic emergencies. Standard treatment options for acute stroke include thrombolysis with intravenous tissue plasminogen activator (tPA) if patients present early (within 4.5 hours of stroke symptom onset), and supportive medical care if patients present late or do not otherwise meet criteria for thrombolysis. Endovascular interventions, including mechanical embolectomy/thrombectomy, are another method of acute stroke treatment. Mechanical embolectomy/thrombectomy is a technique to physically remove an intracranial occlusion with a device inserted via percutaneous catheter to the site of the occlusion.

Mechanical embolectomy devices, also known as neurothrombectomy devices, are being studied as an alternative, or adjunct to intravenous tPA therapy, and, among patients contraindicated for tPA, as a primary therapy for the treatment of ischemic stroke. Mechanical embolectomy devices used to extract clots in ischemic stroke can be categorized into one of the following types: clot retriever, aspiration or suction device, snare, ultrasound technology or laser.^[1]

Regulatory Status

The following devices have received 510(k) clearance from the US Food and Drug Administration (FDA) for mechanical embolectomy in acute stroke. Marketing clearance via the 510(k) process does not require data regarding clinical efficacy.

- In August 2004, the Merci Retriever® (Concentric Medical) was cleared by the FDA. With the Merci® device, a microcatheter is passed through the thrombus from a larger, percutaneous catheter positioned proximal to the occlusion. A helical snare is deployed, and the catheter and clot are withdrawn together.
- A modified Merci Retriever, also manufactured by Concentric Medical, Inc., received 510(k) clearance from the FDA in May 2006. The clearance notes that the Modified Merci Retriever is intended to restore blood flow in the neurovasculature by removing thrombus in patients experiencing ischemic stroke. Patients who are ineligible for intravenous tPA, or who fail intravenous tPA therapy, are candidates for treatment. The device also has clearance for retrieval of foreign bodies misplaced during interventional radiological procedures in the neuro-, peripheral, and coronary vasculature.
- In December 2007, the Penumbra System® (Penumbra Inc.) was cleared through the 510(k) process. With the Penumbra device, an opening at the tip of a percutaneous catheter utilizes suction to extract the clot. The Penumbra System is intended for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease (in the internal carotid, middle cerebral - M1 and M2 segments, basilar, and vertebral arteries) within 8 hours of symptom onset.
- In March 2012, the Solitaire™ FR device was cleared for marketing by the FDA through the 510(k) process. The FDA determined that this device was substantially equivalent to the Merci Retriever device, based on a randomized controlled trial (RCT) of 113 patients submitted to the FDA comparing the Merci and Solitaire devices. Indications for the device are patients with ischemic stroke due to large intracranial vessel occlusion who are ineligible for intravenous tPA, or who fail intravenous tPA.
- In August 2012, the Trevo Pro Retriever™ device (Stryker Neurovascular) was cleared for marketing by the FDA through the 510(k) process. The FDA determined that this device was substantially equivalent to the Merci Retriever device, based on an RCT of 178 patients from 27 centers in the U.S. and Europe that compared the Trevo device with the Merci device. Indications for the device are patients with acute ischemic stroke due to large intracranial vessel occlusion who are ineligible for or fail intravenous tPA.

MEDICAL POLICY CRITERIA

Mechanical embolectomy is considered **investigational** in the treatment of acute stroke.

SCIENTIFIC EVIDENCE

The principal outcomes associated with treatment of acute ischemic stroke are clinically relevant improvements in short and long-term neurological outcomes, as measured by a validated instrument (such as the National Institutes of Health Stroke Scale [NIHSS]). Measures of disability, such as those provided by the Rankin Scale or modified Rankin Scale, may also be reported. Treatment with intravenous tissue plasminogen activator (tPA) is currently the only recommended intervention to restore perfusion following acute ischemic stroke.^[2]

Mechanical embolectomy devices are proposed as an alternative or adjunct to tPA or as a primary therapy for patients in whom tPA is contraindicated. Data from large, randomized controlled trials (RCTs) are required to control for baseline differences between treatment groups and determine whether any treatment effect provides a significant advantage over the standard of care in any of the proposed uses of any of the embolectomy devices. The appropriate control groups for comparison are as follows:

- Outcomes relating to use of mechanical embolectomy as an alternative to tPA are best understood in comparison with patients receiving tPA.
- For patients who would receive mechanical embolectomy in addition to tPA, the proper comparison is between mechanical embolectomy and no mechanical embolectomy, in patients receiving tPA.
- In patients for whom tPA is contraindicated (e.g., comorbidities; treatment over 3 hours after symptom onset), the ideal comparison is between mechanical embolectomy and standard medical management without tPA.

Literature Appraisal

Until recent publications of randomized controlled trials (RCTs), the available literature consisted primarily of a large number of small, single-arm studies reporting outcomes following endovascular interventions. Some of these studies have included comparison groups, consisting either of historical controls or non-concurrent controls of patients treated with an alternative strategy. Systematic reviews of single-arm studies have also been published. The following evidence review focused on systematic reviews and RCTs, with less emphasis on nonrandomized studies.. Following is a summary of the key literature to date.

Systematic Reviews

- In a 2013 systematic review and meta-analysis, Singh and others consolidated the evidence from RCTs for the use of endovascular therapy (ET) in patients with acute ischemic stroke.^[3] Of the 1252 retrieved articles, 5 randomized trials enrolling 1197 patients with acute ischemic stroke were included. One of the reviewed studies did not include mechanical embolectomy devices in the trial.^[4] In addition, a trial included in the review defined endovascular therapy as intraarterial thrombolysis with recombinant tissue plasminogen activator [tPA], mechanical clot disruption or retrieval, or a combination of these approaches.^[5] Seven hundred eleven patients received ET, and 486 received intravenous (IV) tPA. There was no significant improvement in any of the outcomes in patients receiving ET compared with those receiving IV tPA. On subgroup analysis, ET was found to have better outcomes in patients with severe stroke (National Institutes of Health Stroke Scale score ≥ 20), showing a dose-response gradient and improving excellent, good, and fair outcomes by an additional 4%, 7%, and 13%, respectively, compared with IV thrombolysis. Authors concluded that ET was not superior to IV thrombolysis for acute ischemic strokes (level B recommendation).

- In 2012, Mokin et al. published a systematic review that evaluated clinical outcomes from endovascular therapy compared to thrombolysis.^[6] The authors selected studies that used either thrombolysis or endovascular therapy for patients with acute ischemic stroke due to internal carotid artery occlusion. Included studies reported on functional outcomes past 30 days, mortality rates beyond 30 days, and rates of symptomatic intracerebral hemorrhage. A total of 28 studies were reviewed, including 385 patients treated with thrombolysis and 584 patients treated with endovascular therapy. There were no differences in mortality between the thrombolysis and endovascular groups (27.3% vs. 32.0%, $p=0.12$). A favorable clinical outcome, defined as a Rankin scale of <2 or a Barthel index of 90-100, was attained by a greater percentage of patients in the endovascular group compared with the thrombolysis group (33.6% vs. 24.9%, $p=0.004$). Symptomatic intracranial hemorrhage was also more common in the endovascular group compared to thrombolysis (11.1% vs. 4.9%, $p=0.001$).
- In 2012, Almekhlafi et al. published a systematic review of observational studies of endovascular treatment.^[7] The authors identified 16 eligible studies and classified them according to the type of device used. There were 4 studies ($n=357$) that used the Merci device, 8 studies ($n=455$) that used the Penumbra system, and 4 studies ($n=113$) that used a retrievable stent. Mean procedural time was 120 minutes for the Merci device, compared to 65 and 55 minutes for the Penumbra and retrievable stents. The successful recanalization rate was 59.1% for the Merci group, 86.6% for the Penumbra system, and 92.9% for the retrievable stent group.
- In 2011, the Agency for Healthcare Research and Quality (AHRQ) published a comparative effectiveness report on the use of mechanical embolectomy devices for the treatment of acute ischemic stroke.^[1] A review of the available evidence on this technology concluded that no comparative research has been conducted and that short follow-up (typically 90 days or fewer) and inconsistent use of tPA (ranging from 0-100%) limit findings from this body of research. The report concluded: “There remains a need for further research on the topic, including randomized controlled trials to determine the optimal device(s) to use, and the patient populations most likely to benefit from their use.”
- A second publication on the AHRQ systematic review, published by the same authors, goes into more detail about the studies considered and the state of the evidence to date.^[8] A total of 87 articles reporting on non-randomized case series or registry reports met the inclusion criteria for this review. Rates of successful recanalization, defined as a Thrombolysis in Myocardial Infarction (TIMI) score of 2 or 3, ranged widely (from 43-100% across all studies). Higher rates of recanalization were reported with the Penumbra System (83-100%) compared to either the MERCI Retriever (43-78%) or other devices studying off-label use (50-90%). There was a wide range in clinical effectiveness, from 15% to 60% of treated patients. Common adverse events from treatment were asymptomatic intracranial hemorrhage (ranging from 1-43%) and symptomatic intracranial hemorrhage (ranging from 0-25%). A published comment on this review noted that revascularization, the main outcome of interest in these studies, is only a secondary health outcome, and stated, “Unfortunately, we lack randomized trials to document that neurothrombectomy devices improve patient outcomes.”^[9]
- In 2008, Stead and colleagues conducted a systematic review and meta-analysis of percutaneous clot removal devices.^[10] Of note, the authors were unable to obtain individual patient data for the MERCI trial described below; those 151 patients were not included in the meta-analysis. The authors identified 14 case series and 8 case reports with a total of 147 patients. The Merci Retriever was utilized for 17 patients; a variety of mechanical embolectomy devices (with coronary or peripheral vascular indications) were used in other studies. Patients were similar in that they were diagnosed with large vessel disease but were otherwise heterogeneous. Emboli were accessible in 85% of patients. In all studies, post-procedural blood flow was measured using the TIMI score. A flow rate representing full recanalization was achieved in 67 of 146 patients (45.6%). Partial or full recanalization was achieved in 101 of 146 patients (68.7%). When embolectomy methods were

compared, superiority of one device over others was not demonstrated in accessing the lesion, retrieving the clot, or in clinical outcome.

Pooled data were compared to the placebo arm and intra-arterial thrombolysis arm of the PROACT II (Prolyse in Acute Cerebral Thromboembolism II) study, comparing intravenous and intra-arterial tPA use.^[11] Partial or full recanalization rate in the placebo group was 18%; the rate was 66% in the intra-arterial group. However, the authors acknowledge that 81 patients (55.1%) in the meta-analysis also received thrombolytics, and the comparative role of thrombolytics against mechanical thrombectomy is unknown. The authors concluded that there was a modest survival benefit in the mechanical thrombectomy patients compared to historical controls, while recognizing the limitation of small study sizes and non-randomized comparator groups.

The systematic reviews reported above should be interpreted with caution as reviews may be biased by methodological limitations in the original studies. These limitations include but are not limited to non-random allocation of treatment, lack of adequate comparison groups, and extrinsic limitations including small sample sizes and short follow-up.

Randomized Controlled Trials (RCTs)

The strongest evidence on the efficacy of endovascular mechanical embolectomy compared with standard treatment for acute ischemic stroke comes from three large RCTs published in 2012 and 2013. These RCTs failed to demonstrate significant benefits from the use of endovascular mechanical embolectomy compared with usual therapy. Following is a summary of those RCTs:

- Kidwell and colleagues reported on the MR RESCUE (Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy) trial in 2013.^[12] MR RESCUE was a randomized, controlled, open-label, blinded outcome trial of 118 patients from 22 North American sites. All patients had large vessel, anterior circulation ischemic strokes and were stratified by penumbral pattern as determined by pretreatment computed tomography (CT) or magnetic resonance imaging (MRI) of the brain. Patients were randomly assigned to standard stroke treatment (n=54) or mechanical embolectomy (n=64) using the Merci Retriever or Penumbra System within 8 hours after presentation of symptoms. Eight patients in the embolectomy group also received tissue plasminogen activator (tPA). The primary hypothesis of the study was that patients with favorable penumbral patterns (at-risk area of viable ischemic cerebral tissue of 70% or less and a small, 90 ml or less, area of predicted core infarct) would benefit more from mechanical embolectomy than patients with nonpenumbral patterns (large infarct area and small or absent penumbra [viable ischemic cerebral tissue]) as determined by the 90-day modified Rankin scale, ranging from a score of 0 (no symptoms) to 6 (dead). In the embolectomy group, 67% achieved revascularization but this was not superior to standard care. Mean modified Rankin scale scores were the same (3.9) in both groups and pretreatment imaging patterns did not show any relationship to treatment outcomes in any group. Overall mortality (21% at 90 days) and symptomatic intracranial hemorrhage (4%) did not differ across groups.
- In 2013 Ciccone et al. reported on the SYNTHESIS Expansion trial of 362 patients randomized within 4.5 hours of the onset of various types of acute ischemic strokes to receive endovascular therapy (n=181) or IV tPA (n=181).^[5] Endovascular therapy consisted of intraarterial tPA, mechanical embolectomy (using the Solitaire, Penumbra, Trevo, or Merci devices) or a combination of these treatments. Endovascular treatment was completed in 163 of the 181 patients randomized to endovascular therapy. No significant differences in 90-day survival without disability (modified Rankin score 0-1) occurred between the endovascular therapy group and TPA group (30.4% vs.

34.8%, respectively, 0.71; 95% confidence interval (CI), 0.44 to 1.14; $p=0.16$). Within 7 days, fatal or nonfatal symptomatic intracranial hemorrhage occurred in each group at a rate of 6%. Rates of other serious adverse events were also not significantly different between groups. While there were different treatment approaches in the endovascular group, these results suggest endovascular therapy is not superior to tPA.

- In 2013 Broderick et al. reported the results of the IMS 3 trial, an open-label RCT that compared IV thrombolysis with either mechanical thrombectomy or endovascular tPA at the site of the occlusion. In the latter group, the treatment choice was made at the discretion of the treating physician.^[13] The study had a planned enrollment of 900 patients, but was halted prematurely in April 2012 for futility when an interim analysis showed no significant between-group differences in outcomes.

Strengths of these three trials include their randomized design and multi-site recruitment. A potential strength was that, in general, the endovascular intervention was left to the discretion of the treating physician which could allow for greater generalizability; however, the variability in specific endovascular treatments used may make it difficult to reach conclusions about the efficacy of mechanical embolectomy.

These trials also had methodological limitations, particularly related to relatively low use of embolectomy devices in general and of newer stent-retriever devices in particular. For example, in the IMS III and SYNTHESIS Expansion trials, sizable proportions of the endovascular therapy groups did not receive an endovascular device; in IMS III, 138/334 of those who received endovascular therapy received intra-arterial tPA only^[13]; 109/165 of those who received endovascular therapy received intra-arterial tPA with clot fragmentation with a guidewire but without device deployment. In addition, the three trials all had relatively low utilization of the newer generation retrievable stents (Solitaire FR and Trevo devices), which may be relevant as several studies have demonstrated superiority of the newer generation retrievable stents compared with older neuroendovascular devices. For the IMS III trial, there was a longer time to endovascular procedure than in early trials of endovascular interventions; given evidence that longer time to reperfusion is associated with poorer outcomes, the delay in revascularization in the endovascular group may have contributed to worse clinical outcomes in that group.

A number of studies compared different mechanical embolization devices including the following RCTs. These RCTs document the improvements in the most recent generation of these devices.

- In the SWIFT (Solitaire FR With the Intention for Thrombectomy) study, recanalization rates with Solitaire were compared with the Merci Retrieval System in a randomized, prospective, noninferiority trial of 113 patients with moderate or severe large vessel occlusion strokes.^[14] Treatment was initiated within 8 hours of symptom onset in patients who had unsuccessful IV tPA or were ineligible for IV tPA. This trial was halted early after an interim analysis found revascularization without symptomatic intracranial hemorrhage occurred in 61% of Solitaire patients compared with 24% of Merci patients. Mortality rates at 90 days were 17% with Solitaire versus 38% with Merci ($p=0.001$).
- A follow up analysis of complications of endovascular procedures using the SWIFT study data was published in 2013.^[15] This analysis included 144 patients with acute ischemic stroke (31 patients treated with the Solitaire FR device during the SWIFT trial roll-in period and 113 patients randomly assigned to the Solitaire FR or Merci device). Major periprocedural complications, including symptomatic intracranial hemorrhage, air emboli, vessel dissection, major groin complications, and emboli to new vascular territories, were seen in 18/144 (12.5%) of all patients. Complication rates were similar for patients receiving the Solitaire FR and Merci devices, with the

exception of symptomatic cerebral hemorrhage, which was significantly less common in the Solitaire FR group (10.9% vs 1.1%, $p=0.013$).

- In the TREVO 2 (Thrombectomy Revascularization of large Vessel Occlusions) Study, 178 patients were randomized to receive mechanical embolectomy with either the Trevo Retriever or the Merci Retriever for large vessel occlusion strokes.^[16] Revascularization rates were 86% in the Trevo group versus 60% in the MERCI group ($p<0.001$). Procedure-related adverse events occurred in 15% of the Trevo group and 23% in the Merci group; $p=0.183$). Mortality rates at 90 days were 33% versus 24% ($p=0.18$), respectively.

Nonrandomized Studies

A number of nonrandomized, comparative and noncomparative studies have been published. Results from these studies should be interpreted with caution due to the following limitations:

- Inadequate comparison with a control group, including comparison with a group which was found to have different demographic or disease characteristics. In particular, concerns have been raised about using the patients from the PROACT II study as historic controls.^[17] These concerns include the fact that the MERCI trial included patients with different types of occlusions; PROACT II had M1 and M2 occlusions while the MERCI trial also included internal carotid and vertebral basilar systems. Groups with baseline differences may not be directly comparable in terms of forming conclusions about the relative performance of this device.
- Low participation rates which have the potential to over-estimate the relative performance of the device (if more complicated cases self-selected out of the analysis).
- Concurrent treatment with tPA among some, but not all, of the mechanical embolectomy group. This has the potential to confound the treatment effect of mechanical embolectomy with tPA.
- Results from small sample sizes ($n<100$), limit our ability to rule out the role of chance as an explanation of study findings.
- Study of intermediate health outcomes (i.e., rates of recanalization), while useful from a research perspective, do not permit conclusions about improvement in short- or long-term primary health outcomes.
- Retrospective study designs, which are at high risk of bias and may not be appropriate for establishing valid and reliable conclusions concerning the use of this treatment for a broad patient population.

Following is a summary of articles that are representative of the current body of nonrandomized studies:

- Rai et al. included 223 patients with acute strokes involving the internal carotid artery, the middle cerebral artery, or the bifurcation of the middle cerebral artery.^[18] A total of 100 patients were treated with IV thrombolysis, and 123 patients were treated with an endovascular intervention. The primary outcome measure was a good clinical outcome at 3 months, defined as a modified Rankin score of 2 or less. A good clinical outcome was achieved by 44.7% in the endovascular group and 26% in the IV thrombolysis group (odds ratio for good outcome 2.3, 95% confidence interval [CI]: 1.3 to 4.1, $p=0.003$). There were no differences in the rate of death or the rate of intracranial hemorrhage.
- Alexandrov et al. treated 125 patients presenting with acute stroke with the Penumbra System and compared their outcomes to that of historical controls who were treated with IV TPA in a previous clinical trial.^[19] Embolectomy patients had a similar stroke severity score, but were younger and had a longer time from onset of treatment to symptoms. The rate of recanalization was 82% for the embolectomy patients; this was higher than the 40% recanalization rate reported with TPA.

However, mortality at three months was higher in the embolectomy group compared to TPA (32.8% vs. 14.1%, $p=0.008$), and the rate of favorable functional outcome was lower (25% vs. 39%, $p=0.046$).

- In 2005, Smith and colleagues reported the results of the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) trial.^[20] This was a multicenter (25 centers), prospective nonrandomized trial of this device for patients with symptoms of acute stroke for less than 8 hours who were not candidates for thrombolytic therapy, either because of contraindications (approximately 25%) or because symptoms were present for more than 3 hours. A total of 1,809 patients were screened to identify the 151 patients enrolled in the trial. Chief reasons for exclusion were National Institutes of Health stroke score too low or improving, intracranial hemorrhage, or inability to obtain consent. The MERCI investigators compared their patients to the placebo arm of the PROACT II study to determine safety and efficacy of mechanical embolectomy. Of the 151 patients, recanalization was achieved in 46% (69/151) of patients on an intent-to-treat analysis and in 48% (68/141) of patients in whom the device was employed. Clinically significant procedural complications occurred in 10 patients (7.1%), and symptomatic intracranial hemorrhages were observed in 11 (7.8%). Good neurological outcomes were more frequent at 90 days in those with successful recanalization compared to those with unsuccessful recanalization (46% vs. 10%, respectively; $p<0.0001$), and there were fewer deaths (32% vs. 54%, respectively; $p=0.01$). Of note, up to 6 passes could be made to remove the clot, and at least 2 devices were used in each patient in the MERCI trial.
- In 2008, Smith and colleagues reported the results of the Multi MERCI trial, a prospective, international, multicenter, single-arm study.^[21] As with the MERCI trial, patients were eligible if they presented with 8 hours of onset of symptoms from large-vessel stroke. In addition to the MERCI indications, patients were eligible if they received intravenous tPA but failed to completely recanalize their occluded vessel. A total of 1,088 patients were screened to enroll 177 patients. Of these, 164 patients had the device deployed. A newer generation device was available for 131 of the 164 patients, and patients could be treated with adjuvant intra-arterial tPA, depending on the operator. Recanalization was achieved in 55% (90/164) on intention-to-treat analysis. Procedural complications occurred in 9 patients (5.5%), and symptomatic intracranial hemorrhage was observed in 16 (9.8%). In comparison with patients who did not recanalize, 90-day neurological outcomes favored patients in whom flow was restored (49% vs. 10%, respectively; $p=0.001$). An average of 3 attempts was made on each patient. This report also compared their results to the placebo arm of the PROACT II trial. Questions have been raised regarding the outcome measure of recanalization since the MERCI study did not look for distal emboli. Also, there are concerns about the reliability of the TIMI perfusion score as reported in this trial and, thus, questions concerning whether the recanalization rates can be compared among studies.^[22]
- In 2010, Shi and colleagues published a retrospective subgroup analysis of 178 patients from the MERCI and Multi MERCI trials, comparing patients with middle cerebral artery occlusions of the first (M1) or second (M2) large vessel branch.^[23] The relatively smaller M2 occlusions were associated with higher recanalization rates. Recanalization was also improved in patients who had received intravenous tPA. However, an accompanying editorial pointed out that no difference in 90-day morbidity or mortality was noted.^[24] Molina further commented that in published literature of patients undergoing mechanical embolectomy, recanalization was often achieved without improvement in clinical outcomes at 3 months post procedure. Rates of “futile” recanalization range from 26% to 51% in various studies.
- Numerous smaller (less than 100 patients) non-comparative case series have also been identified.^[25-30]
- Other case series have compared outcomes of different devices or studied only intermediate outcomes such as vessel recanalization.^[29,31-46]

Clinical Practice Guidelines

Society of Interventional Radiology (SIR)^[47]

In a 2013 position statement the SIR indicated that, despite clinical trials finding mechanical thrombectomy is *not* a proven therapy, rapid treatment with mechanical thrombectomy devices improves outcomes for occlusions in large vessels. However, this statement was not based on a systematic review of the published evidence.^[47] Three references were provided to support the SIR position.^[5,12,13] The SIR statement included the following conclusions:

- 1) Intraarterial stroke revascularization is beneficial to patients in whom IV tPA fails or who are not eligible for IV tPA;
- 2) Patients with a large vessel occlusion who are treated rapidly (even with first-generation techniques) have improved outcomes compared those treated with IV tPA alone;
- 3) Second-generation mechanical thrombectomy devices are the most effective therapy for large vessel occlusion;
- 4) Randomized trials of second-generation mechanical thrombectomy devices compared with IV tPA alone need to be performed and/or a national registry needs to be established;
- 5) Participation in research is critically important, but reimbursement for IA stroke revascularization should not be restricted to clinical trials; and
- 6) All IA cases should be contributed to a trial or national registry, including 90-day clinical outcomes.

The American Heart Association and American Stroke Association (AHA/ASA)^[48]

The AHA/ASA 2013 Guidelines for the Early Management of Patients with Acute Ischemic Stroke included the following conclusions related to mechanical thrombectomy:

- Recanalization with mechanical thrombectomy devices with or without pharmacological fibrinolysis can be useful even though improvements in patient outcomes have not been established (Class IIa; Level of Evidence B).
- The need for randomized controlled trials is noted.
- Intra-arterial fibrinolysis or mechanical thrombectomy is reasonable in patients who have contraindications to the use of IV fibrinolysis (Class IIa; Level of Evidence C; the weight of the evidence or opinion is in favor of the procedure or treatment; consensus opinion of experts, case studies, or standard of care)
- Rescue intra-arterial fibrinolysis or mechanical thrombectomy may be reasonable in patients with large artery occlusions who have not responded to IV fibrinolysis (Class IIb; Level of Evidence B, usefulness/efficacy is less well established by evidence or opinion; data derived from a single randomized trial or nonrandomized study)
- Using stent retrievers such as the Solitaire FR and Trevo devices are generally preferred over coil retrievers like the Merci device (Class I; Level of Evidence A, sufficient evidence for favorable recommendation). Recommendations on the use of stent retrievers versus the Penumbra device have not been determined.
- The usefulness of mechanical thrombectomy devices other than the Merci retriever, the Penumbra System, Solitaire FR, and Trevo is not well established; those devices should be used in the setting of clinical trials (Class IIb; Level of Evidence C, defined as the weight of the evidence or opinion is in favor of the procedure or treatment; consensus opinion of experts, case studies, or standard of care).

Summary

Current evidence has shown that mechanical embolectomy does not produce superior outcomes compared with standard acute stroke treatment. While recanalization rates of infarcted vessels may be high, overall improvements in functional outcomes have not differed significantly between embolectomy and standard care. Additionally, rates of mortality, symptomatic intracranial hemorrhage, and other serious adverse events have not differed significantly between embolectomy and standard care. While there may be a role for mechanical embolectomy in patients that fail or are not candidates for fibrinolysis, evidence is lacking to address this population. Given the evidence that embolectomy does not improve patient outcomes over standard acute stroke care and the limitations in the evidence base as to the identification of appropriate patient selection criteria, the use of mechanical embolectomy devices for acute stroke is considered investigational.

REFERENCES

1. Baker, WL, Colby, JA, Tongbram, V, et al. Neurothrombectomy Devices for Treatment of Acute Ischemic Stroke Comparative Effectiveness Technical Briefs, No. 4. University of Connecticut/Hartford Hospital Evidence-based Practice Center Rockville (MD): Agency for Healthcare Research and Quality; January 2011. Report No.: 11-EHC020-EF. 2011 Jan. PMID: 21433335
2. Adams, HP, Jr., del Zoppo, G, Alberts, MJ, et al. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. *Circulation*. 2007 May 22;115(20):e478-534. PMID: 17515473
3. Singh, B, Parsaik, AK, Prokop, LJ, Mittal, MK. Endovascular therapy for acute ischemic stroke: a systematic review and meta-analysis. *Mayo Clin Proc*. 2013 Oct;88(10):1056-65. PMID: 24079677
4. Sen, S, Huang, DY, Akhavan, O, Wilson, S, Verro, P, Solander, S. IV vs. IA TPA in acute ischemic stroke with CT angiographic evidence of major vessel occlusion: a feasibility study. *Neurocrit Care*. 2009;11(1):76-81. PMID: 19277904
5. Ciccone, A, Valvassori, L, Nichelatti, M, et al. Endovascular treatment for acute ischemic stroke. *N Engl J Med*. 2013 Mar 7;368(10):904-13. PMID: 23387822
6. Mokin, M, Kass-Hout, T, Kass-Hout, O, et al. Intravenous thrombolysis and endovascular therapy for acute ischemic stroke with internal carotid artery occlusion: a systematic review of clinical outcomes. *Stroke*. 2012 Sep;43(9):2362-8. PMID: 22811456
7. Almekhlafi, MA, Menon, BK, Freiheit, EA, Demchuk, AM, Goyal, M. A Meta-Analysis of Observational Intra-Arterial Stroke Therapy Studies Using the Merci Device, Penumbra System, and Retrievable Stents. *AJNR Am J Neuroradiol*. 2012 Jul 26. PMID: 22837311
8. Baker, WL, Colby, JA, Tongbram, V, et al. Neurothrombectomy devices for the treatment of acute ischemic stroke: state of the evidence. *Ann Intern Med*. 2011 Feb 15;154(4):243-52. PMID: 21242342
9. Khatri, P. Neurothrombectomy devices for acute ischemic stroke: a state of uncertainty. *Ann Intern Med*. 2011 Feb 15;154(4):285-7. PMID: 21242343

10. Stead, LG, Gilmore, RM, Bellolio, MF, Rabinstein, AA, Decker, WW. Percutaneous clot removal devices in acute ischemic stroke: a systematic review and meta-analysis. *Arch Neurol*. 2008 Aug;65(8):1024-30. PMID: 18695052
11. Furlan, A, Higashida, R, Wechsler, L, et al. Intra-arterial prourokinase for acute ischemic stroke. The PROACT II study: a randomized controlled trial. Prolyse in Acute Cerebral Thromboembolism. *JAMA*. 1999 Dec 1;282(21):2003-11. PMID: 10591382
12. Kidwell, CS, Jahan, R, Gornbein, J, et al. A trial of imaging selection and endovascular treatment for ischemic stroke. *N Engl J Med*. 2013 Mar 7;368(10):914-23. PMID: 23394476
13. Broderick, JP, Palesch, YY, Demchuk, AM, et al. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. *N Engl J Med*. 2013 Mar 7;368(10):893-903. PMID: 23390923
14. Saver, JL, Jahan, R, Levy, EI, et al. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. *Lancet*. 2012 Oct 6;380(9849):1241-9. PMID: 22932715
15. Akins, PT, Amar, AP, Pakbaz, RS, Fields, JD. Complications of Endovascular Treatment for Acute Stroke in the SWIFT Trial with Solitaire and Merci Devices. *AJNR Am J Neuroradiol*. 2014;35:524-8. PMID: 24029392
16. Nogueira, RG, Lutsep, HL, Gupta, R, et al. Trevo versus Merci retrievers for thrombectomy revascularisation of large vessel occlusions in acute ischaemic stroke (TREVO 2): a randomised trial. *Lancet*. 2012 Oct 6;380(9849):1231-40. PMID: 22932714
17. Becker, KJ, Brott, TG. Approval of the MERCI clot retriever: a critical view. *Stroke*. 2005 Feb;36(2):400-3. PMID: 15653576
18. Rai, AT, Carpenter, JS, Raghuram, K, Roberts, TD, Rodgers, D, Hobbs, GR. Endovascular therapy yields significantly superior outcomes for large vessel occlusions compared with intravenous thrombolysis: is it time to randomize? *J Neurointerv Surg*. 2012 Jul 28. PMID: 22842210
19. Alexandrov, AV, Schellinger, PD, Saqqur, M, et al. Reperfusion and outcomes in Penumbra vs. systemic tissue plasminogen activator clinical trials. *Int J Stroke*. 2011 Apr;6(2):118-22. PMID: 21371272
20. Smith, WS, Sung, G, Starkman, S, et al. Safety and efficacy of mechanical embolectomy in acute ischemic stroke: results of the MERCI trial. *Stroke*. 2005 Jul;36(7):1432-8. PMID: 15961709
21. Smith, WS, Sung, G, Saver, J, et al. Mechanical thrombectomy for acute ischemic stroke: final results of the Multi MERCI trial. *Stroke*. 2008 Apr;39(4):1205-12. PMID: 18309168
22. Tomsick, TA. Mechanical embolus removal: a new day dawning. *Stroke*. 2005 Jul;36(7):1439-40. PMID: 15994450
23. Shi, ZS, Loh, Y, Walker, G, Duckwiler, GR. Clinical outcomes in middle cerebral artery trunk occlusions versus secondary division occlusions after mechanical thrombectomy: pooled analysis of the Mechanical Embolus Removal in Cerebral Ischemia (MERCI) and Multi MERCI trials. *Stroke*. 2010 May;41(5):953-60. PMID: 20378867
24. Molina, CA. Futile recanalization in mechanical embolectomy trials: a call to improve selection of patients for revascularization. *Stroke*. 2010 May;41(5):842-3. PMID: 20378862
25. Kim, D, Jahan, R, Starkman, S, et al. Endovascular mechanical clot retrieval in a broad ischemic stroke cohort. *AJNR Am J Neuroradiol*. 2006 Nov-Dec;27(10):2048-52. PMID: 17110664
26. Devlin, TG, Baxter, BW, Feintuch, TA, Desbiens, NA. The Merci Retrieval System for acute stroke: the Southeast Regional Stroke Center experience. *Neurocrit Care*. 2007;6(1):11-21. PMID: 17356186
27. Bose, A, Henkes, H, Alfke, K, et al. The Penumbra System: a mechanical device for the treatment of acute stroke due to thromboembolism. *AJNR Am J Neuroradiol*. 2008 Aug;29(7):1409-13. PMID: 18499798

28. Taschner, CA, Treier, M, Schumacher, M, Berlis, A, Weber, J, Niesen, W. Mechanical thrombectomy with the Penumbra recanalization device in acute ischemic stroke. *J Neuroradiol.* 2011 Mar;38(1):47-52. PMID: 21255841
29. Flint, AC, Duckwiler, GR, Budzik, RF, Liebeskind, DS, Smith, WS. Mechanical thrombectomy of intracranial internal carotid occlusion: pooled results of the MERCI and Multi MERCI Part I trials. *Stroke.* 2007 Apr;38(4):1274-80. PMID: 17332445
30. Broussalis, E, Trinka, E, Wallner, A, Hitzl, W, Killer, M. Thrombectomy in patients with large cerebral artery occlusion: a single-center experience with a new stent retriever. *Vasc Endovascular Surg.* 2014;48:144-52. PMID: 24249122
31. Restrepo, L, Bang, OY, Ovbiagele, B, et al. Impact of hyperlipidemia and statins on ischemic stroke outcomes after intra-arterial fibrinolysis and percutaneous mechanical embolectomy. *Cerebrovasc Dis.* 2009;28(4):384-90. PMID: 19713698
32. Abou-Chebl, A. Endovascular treatment of acute ischemic stroke may be safely performed with no time window limit in appropriately selected patients. *Stroke.* 2010 Sep;41(9):1996-2000. PMID: 20651271
33. Castano, 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 Aug;41(8):1836-40. PMID: 20538693
34. Abelson, M, Roos, J. Mechanical embolectomy for large vessel ischemic strokes: a cardiologist's experience. *Catheter Cardiovasc Interv.* 2010 Sep 1;76(3):309-15. PMID: 20506287
35. Lin, R, Vora, N, Zaidi, S, et al. Mechanical approaches combined with intra-arterial pharmacological therapy are associated with higher recanalization rates than either intervention alone in revascularization of acute carotid terminus occlusion. *Stroke.* 2009 Jun;40(6):2092-7. PMID: 19390066
36. Fesl, G, Patzig, M, Holtmannspoetter, M, et al. Endovascular Mechanical Recanalisation After Intravenous Thrombolysis in Acute Anterior Circulation Stroke: The Impact of a New Temporary Stent. *Cardiovasc Intervent Radiol.* 2011 Dec 9. PMID: 22160095
37. Broussalis, E, Trinka, E, Hitzl, W, Wallner, A, Chroust, V, Killer-Oberpfalzer, M. Comparison of Stent-Retriever Devices versus the Merci Retriever for Endovascular Treatment of Acute Stroke. *AJNR Am J Neuroradiol.* 2012 Jul 12. PMID: 22790249
38. Cheang, MY, Manning, N, Churilov, L, Mitchell, P, Dowling, R, Yan, B. Recanalisation success is associated with good clinical outcome despite advanced age and stroke severity in patients treated with the Solitaire stentriever. *J Clin Neurosci.* 2014 Mar;21(3):401-5. PMID: 24161340
39. Cohen, JE, Rabinstein, AA, Ramirez-de-Noriega, F, et al. Excellent rates of recanalization and good functional outcome after stent-based thrombectomy for acute middle cerebral artery occlusion. Is it time for a paradigm shift? *J Clin Neurosci.* 2013 Sep;20(9):1219-23. PMID: 23602573
40. Gratz, PP, Jung, S, Schroth, G, et al. Outcome of standard and high-risk patients with acute anterior circulation stroke after stent retriever thrombectomy. *Stroke.* 2014;45:152-8. PMID: 24262328
41. Mokin, M, Dumont, TM, Veznedaroglu, E, et al. Solitaire Flow Restoration thrombectomy for acute ischemic stroke: retrospective multicenter analysis of early postmarket experience after FDA approval. *Neurosurgery.* 2013 Jul;73(1):19-25; discussion -6. PMID: 23719060
42. Pereira, VM, Gralla, J, Davalos, A, et al. Prospective, multicenter, single-arm study of mechanical thrombectomy using Solitaire Flow Restoration in acute ischemic stroke. *Stroke.* 2013;44:2802-7. PMID: 23908066
43. Sanak, D, Kocher, M, Veverka, T, et al. Acute combined revascularization in acute ischemic stroke with intracranial arterial occlusion: self-expanding solitaire stent during intravenous thrombolysis. *J Vasc Interv Radiol.* 2013 Sep;24(9):1273-9. PMID: 23973019

44. Mohlenbruch, M, Stampfl, S, Behrens, L, et al. Mechanical Thrombectomy with Stent Retrievers in Acute Basilar Artery Occlusion. *AJNR Am J Neuroradiol*. 2013. PMID: 24287087
45. Ademuyiwa, FO, Miller, A, O'Connor, T, et al. The effects of oncotype DX recurrence scores on chemotherapy utilization in a multi-institutional breast cancer cohort. *Breast Cancer Res Treat*. 2011 Apr;126(3):797-802. PMID: 21197567
46. Park, BS, Kang, CW, Kwon, HJ, et al. Endovascular mechanical thrombectomy in basilar artery occlusion: initial experience. *Journal of cerebrovascular and endovascular neurosurgery*. 2013 Sep;15(3):137-44. PMID: 24167791
47. Sacks, D, Connors, JJ, 3rd, Black, CM. Society of interventional radiology position statement on endovascular acute ischemic stroke interventions. *J Vasc Interv Radiol*. 2013 Sep;24(9):1263-6. PMID: 23891633
48. Jauch, EC, Saver, JL, Adams, HP, Jr., et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2013;44:870-947. PMID: 23370205
49. BlueCross BlueShield Association Medical Policy Reference Manual "Mechanical Embolectomy for Treatment of Acute Stroke." Policy No. 2.01.76

CROSS REFERENCES

[Endovascular Angioplasty and/or Stenting for Intracranial Arterial Disease \(Atherosclerotic and Aneurysms\)](#), Surgery, Policy No. 141

CODES	NUMBER	DESCRIPTION
CPT	37184	Primary percutaneous transluminal mechanical thrombectomy, noncoronary, arterial or arterial bypass graft, including fluoroscopic guidance and intraprocedural pharmacological thrombolytic injection(s); initial vessel
	37185	second and all subsequent vessel(s) within the same vascular family (List separately in addition to code for primary mechanical thrombectomy procedure)
HCPCS	None	