Endovascular Thrombectomy for Anterior Circulation Stroke: Systematic Review and Meta-Analysis

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Background and Purpose—Stroke affects ≈700,000 patients annually. Recent randomized controlled trials comparing endovascular thrombectomy (ET) with medical therapy, including intravenous thrombolysis (IVT) with tissue-type plasminogen activator, have shown effectiveness of ET for some stroke patients. The study objective is to evaluate the effect of ET on good outcome in stroke patients.

Methods—We searched PubMed, Embase, Web of Science, SCOPUS, ClinicalTrials.gov, and Cochrane databases to identify original research publications between 1996 and 2015 that (1) reported clinical outcomes in patients for stroke at 90 days with the modified Rankin Scale; (2) included at least 10 patients per group; (3) compared outcome with a control arm, and (4) included anterior circulation strokes in each arm. Two authors reviewed articles for inclusion independently.

Results—Nine of 23 809 studies met inclusion criteria. In primary analysis, ET was associated with increased odds for good outcome (odds ratio [OR], 1.75; 95% confidence interval [CI], 1.20–2.54). In secondary analysis, younger patients (OR, 1.85; 95% CI, 1.50–2.28), older patients (OR, 1.93; 95% CI, 1.10–3.37), patients receiving intravenous thrombolysis (OR, 1.83; 95% CI, 1.46–2.31), patients with worse strokes (OR, 2.23; 95% CI, 1.56–3.18), and patients with more moderate strokes (OR, 1.72; 95% CI, 1.36–2.18) had increased odds for good outcome. Symptomatic intracranial hemorrhage and mortality were similar between ET and control patients. No evidence of publication bias was seen.

Conclusions—ET improves good outcomes after anterior circulation stroke. ET should be strongly considered for all patients presenting within 6 hours of onset with a stroke affecting a proximal, anterior circulation vessel without a contraindication to ET. (Stroke. 2015;46:3177-3183. DOI: 10.1161/STROKEAHA.115.009847.)

Key Words: intracranial hemorrhage • meta-analysis • review, systematic • stroke • thrombectomy

Intravenous thrombolysis (IVT) with tissue-type plasminogen activator (tPA) has been the only established therapy for acute management of ischemic stroke.1,2 The efficacy of IVT is time dependent and limited to within 4.5 hours of symptom onset.3 In addition, >90% of patients with ischemic stroke are ineligible for tPA because of contraindications, including recent surgery, history of intracranial hemorrhage (ICH), and late presentation.4,5

Despite its efficacy, IVT fails to achieve recanalization in over half of patients with middle cerebral artery occlusion and even more patients with more proximal occlusions.6–12 To improve rates of recanalization and increase the number of stroke patients with effective treatment, the emergence of local therapies, including intra-arterial thrombolysis and endovascular thrombectomy (ET), has generated great interest in the stroke community. The mechanisms of action for ET devices vary, often categorized as first or second generation methods. First generation techniques include mechanical disruption by catheter manipulation, aspiration through proximal suction, and removal by coil retrievers that wrap around thrombus before catheter removal. Second generation devices consist of stent retrievers that incorporate the thrombus within the device and remove the thrombus as the stent is removed.13

Early studies comparing intra-arterial thrombolysis agents with standard therapy were promising.14 However, the use of older or no intravenous thrombolytic agents among controls limited these results’ applicability for clinical practice.15,16 Furthermore, practitioners increasingly used a combination of pharmacological and mechanical approaches.17 Several following studies that included mechanical devices failed to show significant benefit over
standard therapy alone, leading to equipoise regarding the true efficacy of ET. Advocates of ET posited that delays in achieving reperfusion, lack of appropriate patient selection with advanced imaging, and first-generation devices contributed to the neutral results.

Within the last year, 5 randomized controlled trials (RCTs), Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke (MR CLEAN), Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times (ESCAPE), Extending the Time for Thrombolysis in Emergency Neurological Deficits- Intra-Arterial (EXTEND-IA), Solitaire FR With the Intention for Thrombectomy as Primary Endovascular Treatment of Acute Ischemic Stroke (SWIFT PRIME), and Randomized Trial of Revascularization With Solitaire FR Device Versus Best Medical Therapy (REVASCAT) have shown significant benefit of ET over standard therapy. The purpose of this meta-analysis is to investigate the overall effect of ET in aggregate and to examine the data for benefit in clinically important subgroups.

Methods
Search Methods for Identification of Studies
A detailed systematic biomedical literature search was executed in the following databases: PubMed, EMBASE, SCOPUS, Web of Science (WOS), the Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov. The search strategy was conducted using both the controlled vocabulary of each database and plain language keywords for the terms: stroke, brain infarction, cerebral infarction, anterior cerebral artery infarction, middle cerebral artery infarction, posterior cerebral artery infarction, brain ischemia, thrombectomy, endovascular procedures, embolocyte, and thrombolytic therapy. The final search results were limited to the range of years 1996 to 2015 (March 11, 2015). Two additional RCTs were published after the original search, but were included in this analysis at the discretion of the authors.

Inclusion Criteria
RCTs comparing mechanical thrombectomy with the standard of care in patients with acute ischemic stroke were eligible for analysis. The study population of interest included patients >18 years with ischemic stroke caused by an anterior circulation intracranial occlusion who underwent either ET using a mechanical device or standard therapy. In addition to the primary intervention with ET, patients in the intervention arm could also receive either intra-arterial thrombolysis or IVT as adjunctive treatment.

Inclusion criteria required that studies must (1) examine human subjects; (2) be published in full and in English; (3) directly compare ET using mechanical thrombectomy with the standard of care, which included IV+PA for eligible patients; (5) contain at least 10 subjects; (6) report modified Rankin Scale (mRS) at 90 days; (7) include confirmation of anterior circulation stroke defined either clinically or by imaging in each arm; and (8) define specifically the alternative treatments received in the control arm, which must be accrued concurrently. We did not require imaging confirmation of large-vessel occlusion for inclusion in this meta-analysis.

Selection of Studies
One review authors (C.J.O., C.K.Y., and A.B.B.) screened titles and abstracts obtained from database searches. Two of the authors (C.J.O., C.K.Y., and A.B.B.) independently reviewed each article of potentially relevant abstracts against inclusion criteria. We resolved disagreements in inclusion by discussion.

Assessment of Risk of Bias in Included Studies
Two review authors (C.K.Y. and A.B.B.) independently assessed the methodological quality of the included trials. We resolved any disagreements in inclusion by discussion. We assessed the methodological quality of the studies using an 11-category scoring system developed by the authors (Figure I in the online-only Data Supplement). The Quality Assessment Scoring System was created using criteria from the Jadad Scale for quality of RCTs and the Newcastle-Ottawa Scale for quality of observational studies and modified to fit the topic at hand. Scores ranged from 0 to 12 with a higher score indicating higher quality. A minimum score of 7 was required to be included for analysis (Table I in the online-only Data Supplement). A quality evaluation was performed to ensure that only studies with high methodological quality were included and to limit potential bias.

Data Extraction
The authors extracted data from the included studies in an unblinded fashion using published articles, as well as supplementary materials and post hoc analysis. The data extraction sheet contained sections on (1) study characteristics; (2) ET therapy patient characteristics; (3) ET therapy outcomes; (4) standard of care patient characteristics; (5) standard of care outcomes; and (6) reported outcomes for the subgroups based on age, National Institute of Health Stroke Scale (NIHSS), and administration of IV+IPA.

In studies reporting outcomes as a percentage of the total population, the number of subjects in each group was calculated using the total population and listed percentage for each group. In trials reporting outcomes only as an odds ratio (OR), the 95% confidence interval and total number of subjects were used to calculate the SE and weight the results.

Outcome Measures
The primary outcome of interest was the proportion of patients with a favorable mRS score of 0 to 2 at 90 days post intervention. The mRS score is a widely validated and accepted measure of clinical outcome reported in all major stroke trials and ranges from 0 (fully independent without symptoms or deficit) to 6 (death). Secondary outcome measures of death at 90 days and symptomatic ICH were also recorded. Patients were pooled into an ET arm and a standard of care arm for all trials. Patients were also stratified based on type of study.

In addition to the data mentioned above, the authors collected rate of IVT in ET and control arms, comorbid medical conditions (diabetes mellitus, coronary artery disease, heart failure, atrial fibrillation, sex, race, history of stroke, and tobacco use), source of stroke, NIHSS, stent(s) used, complication rates, and time to intervention. If available, the authors collected data on the conflicts of interest reported in the included studies.

Statistical Analysis
Statistical analysis was performed using STATA CORP LP (TX) to create a random effects model for each outcome. The authors chose a random effects model over a fixed effects model because of possible heterogeneity among studies and patient populations. We assessed primary and secondary outcomes using an OR weighted by inverse variance of the measure in each individual trial. Subgroup analysis was performed for patients receiving IVT versus no IVT; patients classified as older versus younger age groups, and patients classified as severe NIHSS score versus less severe NIHSS score. We assessed heterogeneity using Cochrane’s Q test and the F statistic and used Egger’s test and visual inspection of the forest plot to assess for publication bias. Meta-regression was used to determine whether study-related factors could account for some portion of heterogeneity. We were not able to analyze the impact of symptom onset to puncture times because of the heterogeneity in study design. Previous meta-analyses have studied the impact of symptom onset to puncture times on recanalization.
Results

Search Results and Study Characteristics

Figure 1 outlines the search and selection process for the meta-analysis. Our detailed search gathered 23,809 studies total from PubMed, EMBASE, SCOPUS, WOS, Cochrane, and ClinicalTrials.gov. After excluding studies, article review was performed on 162 studies. One hundred fifty-three studies were excluded after article review. Data were extracted from 9 articles. One study provided only data from the larger Interventional Management of Stroke III (IMS III) trial, so was extracted for possible use in subgroup analysis. Data from the larger trial were included in all subsequent analyses. A total of 8 studies comprising 2049 patients were included for analysis.

Table shows salient characteristics of the included studies. Included studies were published between 2011 and 2015. Earlier studies did not meet our inclusion and quality criteria. All studies reported follow-up data at 90 days. Eight RCTs consisting of 2049 patients met inclusion criteria.

Baseline Characteristics

Mean or median age was similar between intervention arms in all studies (Table). Baseline covariates were measured in all studies, although several studies did not report baseline characteristics. No study reported significant differences between intervention arms.

Clinical Outcomes

Primary Outcome

The primary outcome measure of this study was good outcome, defined by mRS score of 0 to 2 at 90 days of follow-up. Figure 2 shows the pooled odds for good outcome among all included studies. Because of its requirement for inclusion, all studies reported this outcome measure. RCTs showed pooled odds of 1.75 (1.20–2.54) for good outcome. Restricting to those 6 studies—all except Local Versus Systemic Thrombolysis for Acute Ischemic Stroke (SYNTHESIS) trial—requiring confirmed large arterial occlusion, patients undergoing ET had even stronger odds for good outcome (OR, 2.00; 95% CI, 1.48, 2.71; Figure II in the online-only Data Supplement).

In all studies, ET patients showed good outcome in 43.2% of patients, whereas control arm showed good outcome in 30.9% of patients for an absolute risk reduction of 12.3% and a number needed to treat of 8. In the RCTs reported in 2015, 46.1% of ET patients had good outcome, whereas only 26.4% of control patients had good outcome, for a number needed to treat of 5.

Secondary Outcomes

Subgroup Analysis for Good Clinical Outcome (mRS score, 0–2 at 90 days)

In all subgroup analyses, ET demonstrates an increased OR for good outcome. Subgroups of younger patients had increased odds of mRS score 0 to 2 at 90 days, (OR, 1.85; 95% CI, 1.50–2.28), as did subgroups of older patients (OR, 1.93; 95% CI, 1.10–3.37; Figure III in the online-only Data Supplement).

The age cutoff for younger and older subgroups differed by study and only 4 of 8 studies reported age-stratified results. Despite varying rates of IVT in intervention arms, 6 of 8 studies reported either 100% IVT in the ET arm or reported subgroup analysis of patients receiving IVT in ET and control arms (Figure IV in the online-only Data Supplement). For patients receiving IVT (Figure IVA in the online-only Data Supplement), patients in all study designs showed increased odds for a good outcome (OR, 1.83; 95% CI, 1.46–2.31). Patients not receiving prior IVT had increased odds for good outcome as well (OR, 1.59; 95% CI, 0.86, 2.95; Figure IVB in the online-only Data Supplement), although only 4 studies presented data for this subgroup of patients and the odds ratio did not achieve statistical significance.

Similar to subgroup analysis by age, severe and less severe strokes were defined heterogeneously according to NIHSS (Figure V in the online-only Data Supplement). Despite this limitation, ET was shown to be superior in both subgroups of patients with severe and moderate strokes (OR, 2.23; 95% CI, 1.56–3.18; OR, 1.72; 95% CI, 1.36–2.18). The effect of ET was higher in subgroups with higher NIHSS cutoff (Figure V in the online-only Data Supplement).

Mortality and Postintervention Symptomatic ICH

The authors gathered 90-day mortality data in all studies (Figure 3). Pooled ORs suggest lower odds of death in patients...
receiving ET versus those not receiving ET (OR, 0.78; 95% CI, 0.57–1.08). This finding did not achieve statistical significance, but is suggestive of an effect. Mortality at 90 days was 15.36% of patients receiving ET and 18.24% of controls. Additional data show that symptomatic ICH rates were similar between patients receiving ET and those not receiving ET (OR, 1.26; 95% CI, 0.80–1.98; Figure VI in the online-only Data Supplement).

Heterogeneity of Studies
Analysis of our primary outcome suggested significant heterogeneity among all studies ($F=71.8\% \; P=0.001$). We performed meta-regression to assess whether covariates and study quality explain the heterogeneity of the study for the primary outcome measure. Using meta-regression, publication year and study type explained 32.7% of heterogeneity among all studies ($\chi^2=0.635 \; P=0.001$). We performed meta-regression to assess whether covariates and study quality explain the heterogeneity of the study for the primary outcome measure. Using meta-regression, publication year and study type explained 32.7% of heterogeneity among all studies ($\chi^2=0.635 \; P=0.001$). We performed meta-regression, publication year and study type explained 32.7% of heterogeneity among all studies ($\chi^2=0.635 \; P=0.001$).

Publication Bias
Publication bias was assessed using Egger’s test and funnel plot analysis (Figure 4). Egger’s test ($P=0.635$) did not demonstrate evidence of publication bias. Funnel plot analysis did not suggest bias in included studies.

Discussion
As the recent positive trials suggest,22–26 and in accordance with recent systematic reviews and meta-analyses before publication of the most recent trials,53,54 a pooled analysis of all studies that directly compared ET with standard therapy demonstrated improved likelihood of achieving a good functional outcome (defined as mRS score, 0–2) at 90 days. This is despite the large weights accorded to the previous neutral trials of IMS III and SYNTHESIS. Using the most recent data in the 5 RCTs reported in 2015, the pooled number needed to treat was 5 for ET for patients with stroke secondary to radiographically confirmed proximal occlusion of the anterior circulation, provided that the interventional team is able to begin treatment within the 6- to 8-hour window after symptom onset. One RCT23 showed positive results with patients enrolled ≤12 hours after symptom onset, although the study is not powered to evaluate the efficacy of ET near the 12-hour window. Thus, this analysis does not pinpoint the optimal time frame for ET. Previous work has shown the benefit of streamlined time to recanalization in promoting good clinical outcome.31,32 The authors hypothesize that shorter time to recanalization promotes improved outcome from proximal occlusion of the middle cerebral artery or internal carotid artery. However, various other imaging and clinical factors may affect the effective time window for ET, requiring further study to further define the appropriate patient population for ET.

Several factors are likely responsible for the differences in results between earlier and more recent RCTs. The recent review by Prabhakaran et al32 nicely demonstrates the association of reperfusion rate and time to reperfusion with good clinical outcome. In addition to advances in device engineering, interventionalists have become more accustomed to using these mechanical devices, stroke centers have become more familiar with how to expedite intervention, and patient selection is more sophisticated. The limitation of eligible patients to those with confirmed large vessel occlusions homogenized the patient population in more recent trials. The lack of vascular imaging selection in almost half of patients in IMS III led to the inclusion of distal or no artery occlusions in 21% of patients in the treatment arm.37 However, when IMS III investigators

Table. Characteristics of Studies Included in This Meta-Analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Design</th>
<th>Countries</th>
<th>No. of Sites</th>
<th>NIHSS (Mean or Median)</th>
<th>Window for IVT, h</th>
<th>Window for ET, h</th>
<th>% Patients in ET Arm Receiving IVT</th>
<th>ET Arm Mean Age n</th>
<th>Control Arm Mean Age n</th>
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<tbody>
<tr>
<td>ESCAPE23</td>
<td>2015</td>
<td>RCT</td>
<td>Canada, United States, South Korea, Ireland, and United Kingdom</td>
<td>22</td>
<td>16</td>
<td>4.5</td>
<td>12</td>
<td>73</td>
<td>165</td>
<td>71</td>
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<tr>
<td>MR CLEAN22</td>
<td>2015</td>
<td>RCT</td>
<td>The Netherlands</td>
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<td>17</td>
<td>4.5</td>
<td>6</td>
<td>87.1</td>
<td>233</td>
<td>65.8</td>
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<td>RCT</td>
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<td>17</td>
<td>3</td>
<td>5</td>
<td>100</td>
<td>434</td>
<td>69</td>
</tr>
<tr>
<td>IMS III21</td>
<td>2014</td>
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<td>United States, Canada, Australia, and Europe</td>
<td>58</td>
<td>17</td>
<td>3</td>
<td>5</td>
<td>100</td>
<td>190</td>
<td>70</td>
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<tr>
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<td>RCT</td>
<td>Italy</td>
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<td>13</td>
<td>4.5</td>
<td>6</td>
<td>0</td>
<td>181</td>
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<tr>
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<td>RCT</td>
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<td>22</td>
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<td>4.5</td>
<td>8</td>
<td>43.8</td>
<td>64</td>
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<tr>
<td>SWIFT PRIME25</td>
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<td>RCT</td>
<td>Global</td>
<td>39</td>
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<td>4.5</td>
<td>6</td>
<td>100</td>
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<td>65</td>
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<tr>
<td>EXTEND-IA24</td>
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<td>Australia</td>
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<td>4.5</td>
<td>6</td>
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<tr>
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</table>

ESCAPE indicates Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion With Emphasis on Minimizing CT to Recanalization Times; ET, endovascular thrombectomy; EXTEND-IA, Extending the Time for Thrombolysis in Emergency Neurological Deficits-Intra-Arterial; IMS III, Interventional Management of Stroke III; IVT, intravenous thrombolysis; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke; MR RESCUE, Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy; NIHSS, National Institute of Health Stroke Scale; RCT, randomized controlled trial; REVASCAT, Randomized Trial of Revascularization With Solitaire FR Device Versus Best Medical Therapy; SWIFT PRIME, Solitaire FR With the Intention for Thrombectomy as Primary Endovascular Treatment of Acute Ischemic Stroke; and SYNTHESIS, Local Versus Systemic Thrombolysis for Acute Ischemic Stroke.
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retrospectively studied patients with confirmed large vessel occlusion, their results favored the use of ET.21 We used the data for patients with confirmed large artery occlusion from IMS III to present a more accurate picture of the state of ET.

Among subgroups, patients receiving IV-tPA prior to ET had a significant improvement in outcome (OR, 1.83; 95% CI, 1.46–2.31; Figure IV in the online-only Data Supplement). In patients with more clinically severe stroke (varying among studies between an NIHSS delineation of 14–20), likelihood of mRS score of 0 to 2 was most pronounced (OR, 2.23; 95% CI, 1.56–3.18; Figure VA in the online-only Data Supplement), suggesting that this subset of patients may benefit most from intervention. Thrombectomy was also favored in a pooled analysis of those determined to have clinically moderate stroke under a range of 14 to 20 (OR, 1.72; 95% CI, 1.36–2.18; Figure VB in the online-only Data Supplement). The increased effectiveness of ET in patients with higher NIHSS may be a direct result of the confluence of 3 effects—the increase in stroke severity with proximal occlusion,38 the decreased recanalization rate of IV-tPA in proximal occlusions,6–10 and worse outcomes in patients not achieving recanalization after stroke.37

In studies that performed analysis on older subgroups, patient age ranged from 70 to >80 years. Overall, their benefit favored ET (OR, 1.93; 95% CI, 1.10–3.37; Figure III in the online-only Data Supplement). Our analysis revealed no significant increase in symptomatic ICH in patients who underwent ET. In addition, there was no difference in mortality at 90 days between ET and standard therapy.

Although publication bias is a potential problem in any meta-analysis, an examination of such bias graphically with a funnel plot and statistically with Egger’s test showed no evidence of bias (Figure 4). This is unsurprising for the included RCTs, given their careful study design and execution.

Limitations

Our study is limited by the following factors. First, despite the increasing use of mechanical devices, the studies examined used a variety of devices, as well as chemical thrombolytic methods, within their endovascular treatment arms, contributing to heterogeneity. Second, there is always inherent risk in meta-analysis of bias within the component studies that cannot be completely addressed. Despite these limitations, our study has multiple strengths. We conducted a comprehensive and rigorous search of studies in
multiple databases with the use of a professional librarian. Data analysis included 9 studies comprising data from 8 RCTs, strengthening the overall methodological rigor in the included studies. We included a quality assessment on all articles and used a randomized effects model to mitigate heterogeneity within studies.

Conclusions
We conducted an up-to-date and comprehensive systematic review and meta-analysis of mechanical thrombectomy based on literature over the past 20 years. Our results reinforce the most current RCTs that ET improves good outcomes after anterior circulation stroke, regardless of prior IV therapy. Our results suggest that older patients with good premorbid functional status may benefit from ET as well. Symptomatic ICH risk and mortality are similar between those who undergo ET and those who undergo standard therapy. Recent large, well-executed RCTs suggest a number needed to treat of $\approx 5$ for ET. Given these findings, ET should be strongly considered for all patients with moderate to severe strokes affecting a proximal vessel of the anterior circulation.

Acknowledgments
We would like to thank Methodius Tuuli, MD, MPH who provided guidance and suggestions for analysis. We would like to thank Graham Colditz, MD, PhD for his guidance and recommendations.

Disclosures
Dr Derdeyn is a consultant for Microvention Inc, Silk Road Inc, and Penumbra, Inc. Dr Derdeyn shares stock ownership: Pulse Therapeutics. The other authors report no conflicts.
References
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http://stroke.ahajournals.org/content/suppl/2016/05/30/STROKEAHA.115.009847.DC2
http://stroke.ahajournals.org/content/suppl/2015/09/22/STROKEAHA.115.009847.DC1

Data Supplement (unedited) at:
http://stroke.ahajournals.org/content/suppl/2015/09/22/STROKEAHA.115.009847.DC1
http://stroke.ahajournals.org/content/suppl/2016/05/30/STROKEAHA.115.009847.DC2

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In the article by Yarbrough et al (Yarbrough CK, Ong CJ, Beyer AB, Lipsey K, Derdeyn CP. Endovascular thrombectomy for anterior circulation stroke: systematic review and meta-analysis. *Stroke*. 2015;46:3177–3183. DOI: 10.1161/STROKEAHA.115.009847.), which published online ahead of print on September 22, 2015, and appeared in the November 2015 issue of the journal, a correction was needed.

On page 3177, Abstract section Results, “In secondary analysis, younger patients (OR, 1.85; 95% CI, 1.50–2.28), older patients (OR, 1.93; 95% CI, 1.10–3.37), patients receiving intravenous thrombolysis (OR, 1.83; 95% CI, 1.46–2.31), patients not receiving intravenous thrombolysis (OR, 1.59; 95% CI, 0.86–2.95), patients with worse strokes (OR, 2.23; 95% CI, 1.56–3.18), and patients with more moderate strokes (OR, 1.72; 95% CI, 1.36–2.18) had increased odds for good outcome” has been changed to read “In secondary analysis, younger patients (OR, 1.85; 95% CI, 1.50–2.28), older patients (OR, 1.93; 95% CI, 1.10–3.37), patients receiving intravenous thrombolysis (OR, 1.83; 95% CI, 1.46–2.31), patients with worse strokes (OR, 2.23; 95% CI, 1.56–3.18), and patients with more moderate strokes (OR, 1.72; 95% CI, 1.36–2.18) had increased odds for good outcome.”

On page 3181, Discussion section, the first sentence of the third paragraph, “Among subgroups, the improvement in outcome remained significant regardless of whether patients received IV-tPA before therapy or not (OR, 1.83; 95% CI, 1.46–2.31; OR, 1.59; 95% CI, 0.86–2.95; Figure IV in the online-only Data Supplement)” has been changed to read, “Among subgroups, patients receiving IV-tPA prior to ET had a significant improvement in outcome (OR, 1.83; 95% CI, 1.46–2.31; Figure IV in the online-only Data Supplement).”

The authors regret the errors.

This correction has been made to the online and print version of the article, which is available at http://stroke.ahajournals.org/content/46/11/3177.
Supplemental Material

This supplement provides additional information for readers of the following manuscript:

## Supplemental Table I. Quality scores of studies included in this meta-analysis.

<table>
<thead>
<tr>
<th>Study</th>
<th>Inclusion Criteria (0-2)</th>
<th>Device Used</th>
<th>Time to Intervention</th>
<th>NIHSS Reported</th>
<th>Covariates</th>
<th>Adequate Randomization</th>
<th>Control=Standard of Care</th>
<th>Follow Up</th>
<th>Loss to F/U</th>
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Supplemental Figure I. Quality Assessment of Included Studies.

Categories for Quality Evaluation:

1. There is a clear description of inclusion criteria (0-2)
   a. 0- None reported
   b. 1- Inclusion criteria reported
   c. 2 - Inclusion criteria includes occlusion established with imaging procedure (CTA, MRA, DSA)
2. There is a clear description of device used. (0-1)
3. Time to intervention is reported (0-1)
4. Initial NIHSS Score reported (0-1)
5. Subjects in the treatment and control groups are similar in respect to prognostic variables. (0-1)
6. RCT Only: Adequate Randomization, including concealment and equal distribution of potential confounders among groups. (0-1)
7. Observational Studies Only: Possible confounders are acknowledged and controlled for. (0-1)
8. Control Group is treated with standard of care. (0-1)
9. There is adequate time for follow up reported. (0-1)
10. Loss to follow up is less than 20% and there is a description of withdrawals and dropouts. (0-1)
11. Assessment of outcomes is independent to subject group allocation. (0-1)
12. Authors reported funding sources/ conflicts of interest. (0, .5, 1)
   a. 0- No mention of potential conflicts of interest or funding resources.
   b. 0.5- Authors report conflicts of interest or industry support.
   c. 1- Authors report no conflicts on interest or industry support.

Supplemental Figure II. Secondary Outcome: Confirmed Large Arterial Occlusion.

Random effects model favored ET over IVT in patients with confirmed large arterial occlusion.
Supplemental Figure III. Secondary Outcome: Age subgroups. Random effects model favored ET over IVT in both older (A) and younger (B) patients, though studies define these differently.

Supplemental Figure IV. Secondary Outcome: With and without t-PA. Random effects model favored ET over control in as-treated analyses of patients receiving IVT plus ET versus IVT (A), and in patients receiving ET versus no IVT (B).
Supplemental Figure V. Secondary Outcome: Stroke Severity. Random effects model favored ET over IVT in both more severe (A) and less severe (B) strokes, though studies define what NIHSS constitutes a severe stroke differently.

Supplemental Figure VI. Secondary Outcome: Symptomatic Intracranial Hemorrhage. Random effects model showed similar rates of symptomatic ICH in patients receiving ET and standard care.
SUPPLEMENTAL REFERENCES


前景および目的：脳卒中を発症する患者は1年で約70万人にあたり、血管内血栓除去術（ET）と、組織プラスマリンノゲン活性化因子による静脈内血栓溶解療法（IVT）などの薬物療法を比較した最近の無作為化比較試験では、一部の脳卒中患者においてはETが有効であることが示されている。本研究は、脳卒中患者の平均的な転帰（mRS 0-2）に対するETの効果を評価することを目的としている。

方法：PubMed、Embase、Web of Science、SCOPUS、ClinicalTrials.gov、およびCochraneデータベースを検索し、1996年から2015年までに発表された原著研究論文で下記の条件を満たす論文を同定した。（1）変更Rankinスケールによる90日後の脳卒中の臨床転帰を報告した研究、（2）1群に10名以上の患者を含めた研究、（3）転帰を対照群と比較した研究、（4）各群に前方循環系脳卒中患者を組み入れた研究。論文選択するために、2名の研究者が別個に検討した。

結果：23,809報中9報が選択基準を満たしていた。主解析では、ETは良好な転帰のオッズ増加と関連していた（オッズ比（OR）= 1.75, 95%信頼区間（CI）: 1.20 〜 2.54）。二次解析では、比較的若年の方（OR = 1.85, 95% CI: 1.50 〜 2.28）、高齢の方（OR = 1.93, 95% CI: 1.10 〜 3.37）、静脈内血栓溶解療法を受けた患者（OR = 1.83, 95% CI: 1.46 〜 2.31）、脳卒中が比較的重症の方（OR = 2.23, 95% CI: 1.56 〜 3.18）、および軽度の脳卒中患者（OR = 1.72, 95% CI: 1.36 〜 2.18）で転帰良好のオッズが増加していた。症候性頭痛内血栓および死亡率は、ET群と対照群で類似していた。公表バイアスのエピデンスは認められなかった。

結論：ETは前方循環系脳卒中後の良好な転帰を改善する。ETに対する禁忌がない場合、近位前方循環系脳卒中発症後6時間以内の患者にはETの実施を検討するべきである。

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