

# Percutaneous Clot Removal Devices in Acute Ischemic Stroke

## A Systematic Review and Meta-analysis

Latha G. Stead, MD; Rachel M. Gilmore, MBBCh; M. Fernanda Bellolio, MD; Alejandro A. Rabinstein, MD; Wyatt W. Decker, MD

**W**e conducted a systematic review and meta-analysis of mechanical thrombectomy in the treatment of ischemic stroke and assessed factors for technical and clinical success and survival. We searched the literature using MEDLINE and EMBASE for January 1, 2000, through March 1, 2006. Studies were limited to those in human beings; there were no language or study design restrictions. Validity assessment was performed using the Newcastle-Ottawa Scale. The pooled cohort was compared with a historical cohort matched for sex, age, and National Institutes of Health Stroke Survey score. The search yielded 114 publications. Two authors determined inclusibility (interrater agreement,  $\kappa=0.94$ ). Mean preprocedure National Institutes of Health Stroke Survey score was 20.4. The middle cerebral artery (36%) and the posterior circulation (38%) were the most frequently occluded areas. The clot was accessible in 85% of the patients. Hemorrhage occurred in 22% of the patients. Of 81 patients with concurrent thrombolysis, 18.5% had hemorrhage compared with 27.3% of 66 patients without thrombolysis ( $P=.21$ ). Of the 126 patients with accessible clots, 36% had a good modified Rankin score ( $\leq 2$ ) and 29% died; in patients with inaccessible clots, 24% had a good modified Rankin score and 38% died. Factors associated with clinical success were younger age ( $P=.001$ ) and lower National Institutes of Health Stroke Survey score at admission to the hospital ( $P=.001$ ). Compared with a matched cohort, patients who received mechanical intervention were 14.8 times more likely to have a good modified Rankin score (95% confidence interval, 4.4-50.0;  $P<.001$ ). Percutaneous mechanical embolectomy in the treatment of acute ischemic stroke is feasible and seems to provide an option for some patients seen after the interval for administration of intravenous tissue plasminogen activator therapy has elapsed.

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On average, every 45 seconds in the United States<sup>1</sup> and every 10 minutes in Canada,<sup>2</sup> someone experiences a stroke. Stroke is the number 1 cause of disability: 20% of patients need help walking, 70% cannot return to their previous jobs, and 51% are unable to return to work. Each year, more than twice as many women in the United States die of stroke than breast cancer, and in women older than 45 years, stroke is more common than heart attack.

The current goal of treatment of acute ischemic stroke is to minimize damage to the brain by restoring blood flow.<sup>3</sup> To date, the only drug approved by the US Food and Drug Administration for treatment of stroke is intravenous tissue plasminogen activator (tPA)<sup>4</sup> in those patients seen within 180 minutes of stroke onset and who do not meet the exclusion criteria. Several factors including lack of awareness of symptoms of stroke, delay in being seen by a primary care physician, unavailability of tPA at all centers, and the inherent painful nature of stroke make this treatment an option in less than 5% of per-

**Author Affiliations:** Division of Research, Department of Emergency Medicine (Drs Stead, Gilmore, Bellolio, and Decker) and Department of Neurology (Dr Rabinstein), Mayo Clinic College of Medicine, Rochester, Minnesota.

sons who experience stroke.<sup>5</sup> For the remaining 95%, or 627 500 persons each year in the United States, treatment of stroke consists of brain optimization measures including administration of antiplatelet agents,<sup>6</sup> blood pressure management,<sup>7,8</sup> and, in certain cases, anticoagulation therapy.<sup>9</sup>

In the 12 years since intravenous tPA was approved, much work has focused on the percutaneous removal of thrombus from occluded cerebral vessels. The recent approval of the MERCI Retrieval System (Concentric Medical, Inc, Mountain View, California) has refocused the spotlight on this therapy, which has promise for extending the interval for treatment of stroke. The Food and Drug Administration gave clearance to market this device “to restore blood flow in the neurovasculature by removing thrombus in patients experiencing ischemic stroke, patients who are ineligible for IV tPA, or fail therapy,”<sup>10(p1)</sup> but to date, it has not proved either safe or effective.

This study was conducted to assess whether (1) any factors predict technical success; (2) any factors predict clinical success; (3) one particular device has advantages over others; and (4) percutaneous procedures result in a better chance of survival and functional outcome when compared with a historically concurrent matched cohort.

Over the last few years, there has been an increase in the number of devices available to perform mechanical embolectomy. For this study, we divided these devices into 5 major categories: snares, laser devices, ultrasonographic devices, clot retrieval devices, and clot disruption or aspiration devices (**Table 1**).

Snare devices ensnare, incorporate, or interdigitate the thrombus and extract it through the guide catheter or sheath. Laser devices, such as the Endovascular Photo-Acoustic Recanalization (EPAR; EndoVasix, Inc, Belmont, California) system, use a microcatheter with a laser at the tip. Clot emulsification is achieved using acoustic energy generated by photo energy at the fiberoptic tip. Ultrasonographic devices, such as the MicroLysUs catheter (EKOS Corp, Bothell, Washington), are designed for augmented fibrinolysis. An ultrasound transducer is used to microfracture the embolic material and create microstreaming of the thrombolytic agent into the thrombus. These pulses help advance thrombolytic agents into the thrombus. With clot retrieval devices, such as the MERCI Retrieval System (Concentric Medical, Inc), the guidewire and microcatheter are placed beyond the clot, the retriever engages and ensnares the clot, the balloon is inflated, and the clot is pulled into the catheter and removed. In suction thrombectomy, a catheter is navigated over a guidewire into the thrombus within the internal carotid artery, and a syringe is used to aspirate the thrombus. The goal is to extract as much thrombus as possible to minimize the amount of thrombolytic agents needed to achieve recanalization. Thromboaspiration devices used in the present study included the Possis AngioJet System (Possis Medical, Inc, Minneapolis, Minnesota), which combines local vortex suction with mechanical disruption. The catheters use multiple retrograde high-pressure fluid jets directed into the primary evacuation lumen to create a hydrodynamic vortex that draws in, traps, and fragments the thrombus.

**Table 1. Types of Devices Used**

Device Type (Manufacturer)	No. of Patients
Snare	
Amplatz gooseneck snare (Microvena Corp, White Bear Lake, Minnesota)	27
Neuronet endovascular snare (Guidant Corp, Indianapolis, Indiana)	10
Soutenir microsnares (Solution, Kanagawa, Japan)	1
Laser	
Endovascular Photo-Acoustic Recanalization system (EndoVasix, Inc, Belmont, California)	34
Ultrasound	
MicroLysUs catheter (EKOS Corp, Bothell, Washington)	14
Clot retrieval	
MERCI retrieval system (Concentric Medical, Inc, Mountain View, California)	37
In-Time retrieval device (Boston Scientific Corp, Natick, Massachusetts)	1
Attracker-18 coil retriever (Target Therapeutics, Inc, Fremont, California)	1
Thromboaspiration with 50-, 60-, 61-, or 62-mL syringe	
AngioJet system (Possis Medical, Inc, Minneapolis, Minnesota)	16
Guidewire	2

## METHODS

The literature was searched using MEDLINE and EMBASE from January 1, 2000, through March 1, 2006. The studies were limited to those in human beings; no language restrictions were applied, and all study designs were included. The references from each article were examined, and relevant articles were retrieved. Missing data were requested from all authors whose articles were included in this review article. Wherever applicable, unpublished data were sought directly from the authors. Device manufacturers were also contacted. In addition, abstracts from the International Stroke Conference (2000-2006) were searched and the references reviewed.

The literature search yielded 114 publications. Two of us (L.G.S. and R.M.G.) independently read the articles to determine inclusibility. The interrater agreement yielded a  $\kappa$  statistic of 0.94 (SE, 0.08). There were no randomized or quasi-randomized controlled trials; thus, this review is based on observational case series and individual case reports. Of the 114 publications, 91 were review articles or comments or were inappropriate because the clot removal was either not percutaneous or not performed because of acute ischemic stroke, which we defined as symptom onset less than 24 hours before treatment, resulting from arterial occlusion. In case series that included both acute and nonacute strokes, we included in our meta-analysis only acute strokes. For the final analysis, 22 articles were included (**Figure**).

Validity assessment was performed on each of the studies based on the Newcastle-Ottawa Scale<sup>11</sup> (**Table 2**). However, because the technology of mechanical clot removal is relatively new, there is an expected paucity of data that precludes stringent selection criteria based on study method.

The information collected included patient age and sex, time from stroke symptom onset to beginning of mechanical clot removal, National Institutes of Health Stroke Scale (NIHSS) before the procedure, whether the artery was occluded, the device used, whether the clot was accessible with the device, whether concurrent thrombolysis was performed, the recanalization was defined angiographically by thrombolysis in myocardial infarction (TIMI) flow grade<sup>35</sup> after clot removal, occurrence of hem-

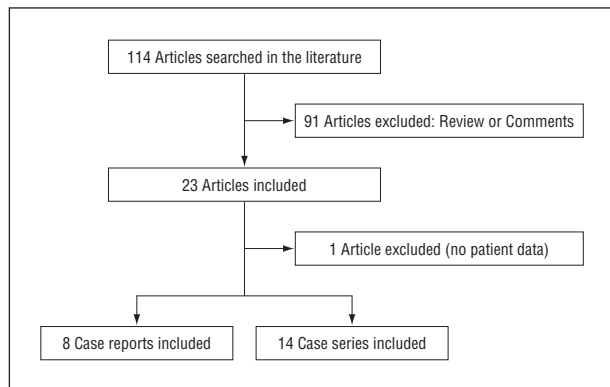


Figure. Literature search.

orrhage or death, and assessment of functional outcome. Arteries having a TIMI flow grade of 0 to 1 were considered not recanalized, those having grade 2 as partially recanalized, and those having grade 3 as completely recanalized.<sup>36</sup> Technical failure was defined as inability to access the clot with the device used, and clinical failure was defined as either death or moderate to severe disability (modified Rankin score [mRS]  $\geq 3$ ).

For the quantitative analysis, the pooled population was divided into patients in whom accessibility (the device reached the clot) and technical success (the flow was restored) were achieved vs those in whom they could not be achieved, and odds ratios and 95% confidence intervals were calculated for mortality and functional outcome (mRS  $\leq 2$ , good outcome; and mRS  $\geq 3$ , bad outcome). Hemorrhage after the procedure was considered a secondary end point. Univariate associations were assessed using the  $\chi^2$  test for nominal or categorical variables and the Wilcoxon rank sum test for continuously scaled variables. Statistical analyses were performed using commercially available software (SAS version 7.0 and JMP 6.0; SAS Institute, Inc, Cary, North Carolina).

The pooled population was also compared with a historically concurrent age ( $\pm 5$  years), sex-, and NIHSS score-matched cohort from the Mayo Clinic Emergency Department Acute Brain Ischemia Registry, in Rochester, Minnesota. This registry encompasses all patients having acute stroke or transient ischemic attack, with 31% seen within 2 hours of onset. For the analysis of functional outcome, 84 matched pairs were available. For the outcome of death, 70 pairs were available because the complete Mayo Clinic cohort was limited to those who had 90-day follow-up. Of the 147 patients obtained from the meta-analysis, 28 patients from the study by Gobin et al<sup>25</sup> did not have individual patient data for sex and, thus, were excluded for this portion of the analysis.

## RESULTS

A total of 298 patients were evaluated in the 23 studies. For 2 studies (Gobin et al<sup>25</sup> and Smith et al<sup>30</sup>), the authors referred us to the vice president of Clinical Affairs of the device manufacturing company (Concentric Medical, Inc) for our individual patient data request, but the company was not willing to provide those data. The study by Gobin et al<sup>25</sup> had enough aggregate data reported to be included for overall descriptive statistics and is, therefore, included; however, the study by Smith et al<sup>30</sup> did not and was, therefore, excluded (n=151). The following statistics are based on 22 studies comprising 147 patients.

The mean (SD) age of the patients was 62.6 (13.9) years (median age, 68 years). Seventy-three of 119

patients were men (61.3%). The mean NIHSS score before mechanical embolectomy was 20.5 (7.2) (median, 21; range, 6-41).

The posterior circulation vessels were the most frequently occluded arteries (n=56 [38.1%]), followed by the middle cerebral artery (n=53 [36.1%]) and the carotid artery (n=38 [25.9%]). The time from symptom onset to mechanical intervention was known for 109 patients. The mean (SD) time to intervention was 10.6 (27.2) hours (median, 5 hours; range, 1-216 hours).

The clot was accessible in 126 patients (86%). The TIMI flow grade was 0 in 21% (n=31), 10% in grade 1 (n=15), 23% in grade 2 (n=34), and 46% in grade 3 (n=67). In 9 of the 147 patients (6%), recanalization was achieved despite technical failure, and concurrent thrombolysis was used in 3 of these patients. A summary of the TIMI flow grade obtained with the various devices is given in **Table 3**.

Hemorrhages (symptomatic and asymptomatic) occurred in 33 patients (22.5%). Of 81 patients with concurrent thrombolysis, 15 (18.5%) had hemorrhage compared with 18 of 66 patients without concurrent thrombolysis (27.3%) ( $P=.21$ ,  $\chi^2$  test). The mRS was recorded for 124 of 126 patients with accessible clots. Eighty patients (65%) had a poor mRS compared with 16 of 21 clots (76%) that were not accessible ( $P=.30$ ,  $\chi^2$  test).

The overall 90-day death rate was 31% (n=45). Of the 126 patients with accessible clots, 37 (29%) died compared with 8 of 21 patients (38%) with clots that were inaccessible ( $P=.42$ ,  $\chi^2$  test). The odds of death were 2.4-fold higher in patients with a TIMI flow grade of 0, 1, or 2 compared with those with a TIMI flow grade of 3 after the procedure (95% confidence interval, 1.14-5.03;  $P=.02$ ).

The odds of having a good mRS increased with the TIMI score after mechanical thrombectomy in patients with a TIMI score of 3 (odds ratio, 3.94; 95% confidence interval, 1.90-8.17;  $P=.002$ ). This relation remains statistically significant after adjusting for initial NIHSS score.

There was no statistically significant difference across device categories for technical success or overall 90-day mortality (**Table 4**). However, for the outcome of clinical success, patients in whom a snare device was used were significantly more likely to be independent (mRS  $\leq 2$ ) at 90 days compared with patients in whom other devices were used. Other factors associated with clinical success were younger age ( $P=.001$ ) and lower NIHSS score ( $P<.001$ ) at presentation.

The location of the occlusion was only significant for 90-day mortality; mortality was higher in patients having posterior circulation vessel occlusion compared with those having middle cerebral artery or internal carotid artery lesions. The arterial territory occluded did not affect the technical success of the procedure across device types or the 90-day functional outcome.

Time to mechanical intervention, concurrent lytic administrations, and occurrence of hemorrhage were not associated with accessibility, 90-day mortality, or technical or clinical success. To assess whether having mechanical intervention resulted in better odds of survival and functional outcome, we compared the present cohort with a historically concurrent cohort from the Mayo Clinic Emergency Department Acute Brain Ischemia registry, matched for age, sex, and NIHSS score (termed

**Table 2. Validity Assessment of Included Studies**

Source	Year	Study Design			Was Selection of Patients Based on A Priori Criteria?	Was Follow-up Long Enough for Outcomes to Occur?	Was Outcome Assessment Blinded?	Method Quality Score (4=Best)
		Prospective		Retrospective				
		Selected	Consecutive					
Chopko et al <sup>12</sup>	2000	X	...	...	No	Yes	No	1
Bellon et al <sup>13</sup>	2001	...	...	X	No	Yes	No	1
Chapot et al <sup>14</sup>	2002	X	...	...	No	Yes	No	1
Kerber et al <sup>15</sup>	2002	X	...	...	No	Yes	No	1
Lutsep et al <sup>16</sup>	2002	X	...	...	No	Yes	No	1
Mayer et al <sup>17</sup>	2002	X	...	...	No	Yes	No	1
Quereshi et al <sup>18</sup>	2002	...	X	...	Yes	Yes	Yes	4
Bush et al <sup>19</sup>	2003	X	...	...	No	Yes	No	1
Mahon et al <sup>20</sup>	2003	X	...	...	Yes	Yes	Yes	3
Schumacher et al <sup>21</sup>	2003	X	...	...	No	Yes	No	1
Wikholm <sup>22</sup>	2003	...	X	...	No	Yes	No	2
Yu et al <sup>23</sup>	2003	X	...	...	No	Yes	No	1
Berlis et al <sup>24</sup>	2004	X	...	...	Yes	Yes	No	2
Gobin et al <sup>25</sup>	2004	X	...	...	Yes	Yes	No	2
Martinez et al <sup>26</sup>	2004	X	...	...	No	Yes	No	1
Imai et al <sup>27</sup>	2005	X	...	...	No	Yes	No	1
Lansberg et al <sup>28</sup>	2005	X	...	...	No	Yes	No	1
Mayer et al <sup>29</sup>	2005	...	X	...	Yes	Yes	Yes	4
Smith et al <sup>30</sup>	2005	X	...	...	Yes	Yes	No	2
Sugg et al <sup>31</sup>	2005	...	...	X	Yes	Yes	Yes	3
Versnick et al <sup>32</sup>	2005	...	X	...	Yes	Yes	No	2
Zaidat et al <sup>33</sup>	2005	X	...	...	No	Yes	No	1
Bergui et al <sup>34</sup>	2006	...	X	...	Yes	Yes	No	3

Abbreviation: Ellipses, not applicable.

matched cohort). There were 116 patients in the devices group (termed *procedure group*) with complete data on age, sex, and NIHSS score.

In the analyses with the matched cohort, 29 of 84 patients in the procedure group and 9 (10.7%) in the matched-cohort had a good mRS (unadjusted odds ratio, 4.4; 95% confidence interval, 1.9-10.0;  $P < .001$ ). Fitting a multivariate logistic regression model (adjusted for age, sex, and NIHSS score) to evaluate the association between procedure (yes or no) and good mRS suggests that patients in the procedure group were 14.9 times more likely to have a good mRS (95% confidence interval, 4.4-50.0;  $P < .001$ ).

For the outcome of death, 18 of 116 patients in the procedure group (25.7%) and 27 of 70 in the matched-cohort group (38.6%) died within 90 days. Fitting a multivariate logistic regression model (adjusted for age, sex, and NIHSS score) to evaluate the association between procedure (yes or no) and death suggests that patients not in the procedure group were 2.2 times more likely to die (95% confidence interval, 0.98-5.1;  $P = .06$ ).

**COMMENT**

Mechanical thrombectomy to treat acute ischemic stroke has been evolving since the first case was reported in 1958.<sup>37</sup> There has been increasing interest in this therapy over the last number of years, in particular because it has been realized that thrombolytic therapies are only of benefit in the minority of patients with acute ischemic stroke.

In our meta-analysis, we found that the clot was accessible in 126 patients (86%). A TIMI flow grade of 2 or 3 was obtained in 101 patients overall (68.7%) and in 92 of 126 patients with accessible clots. However, TIMI grade 3 flow was restored in 67 patients (45.6%). This is still a large improvement on the spontaneous recanalization rate of 18% observed in the PROACT (Prolyse in Acute Cerebral Thromboembolism)-II trial.<sup>38</sup> In the PROACT-II trial the recanalization rates in those patients who received intra-arterial tPA was 66% or that 66% of the patients who received tPA had recanalization. However, concurrent thrombolysis was used in 81 patients (55.1%) in this meta-analysis. Therefore, it is difficult to fully ascertain whether the recanalization was secondary to the mechanical embolectomy or the concomitant thrombolysis.

One of the largest single studies of mechanical embolectomy is the MERCI (Mechanical Embolus Removal in Cerebral Ischemia) trial.<sup>30</sup> This was a prospective single-armed trial in which the device was deployed in all patients and compared with results in a historical control group. The trial included 151 patients but could not be included in this analysis because insufficient patient information data were available. Of the 151 patients in whom the device was deployed, revascularization was successful in 46%. This is a much lower rate of revascularization than what we observed in the present study and that was observed in the PROACT-II trial. This low rate may be related to the lack of thrombolytic agents. Another 17 patients underwent recanalization after intra-arterial thrombolysis in the MERCI trial, increasing the

**Table 3. TIMI Flow Grade Obtained in Included Studies**

Source	Device <sup>a</sup>	No. of Patients	TIMI Flow After Device Use, Mean (Range)
Chopko et al <sup>12</sup>	Amplatz snare	1	3
Bellon et al <sup>13</sup>	AngioJet	3	3
Chapot et al <sup>14</sup>	Syringe	1	3
Kerber et al <sup>15</sup>	Amplatz snare	5	3
Lutsep et al <sup>16</sup>	Syringe	3	3
Mayer et al <sup>17</sup>	Neuronet	5	1.6
Quereshi et al <sup>18</sup>	Amplatz snare	5	3
Bush et al <sup>19</sup>	AngioJet	1	3
Mahon et al <sup>20</sup>	MycroLysUs	14	1.9
Schumacher et al <sup>21</sup>	Attractor-18	1	0
Versnick et al <sup>32</sup>	Neuronet	4	2.3
Wikholm <sup>22</sup>	Amplatz snare	4	3
Yu et al <sup>23</sup>	MERC1 retrieval system	1	3
Berlis et al <sup>24</sup>	EPAR	34	1.2
Gobin et al <sup>25</sup>	MERC1 retrieval system	28	1.3
Martinez et al <sup>26</sup>	MERC1 retrieval system	1	3
Imai et al <sup>27</sup>	Soutenir snare	1	3
Lansberg et al <sup>28</sup>	MERC1 retrieval system	1	3
Mayer et al <sup>29</sup>	AngioJet	12	2.8
Lansberg et al <sup>28</sup>	Neuronet	1	3
Sugg et al <sup>31</sup>	Guidewire	2	2
Versnick et al <sup>32</sup>	MERC1 retrieval system	6	2.5
Zaidat et al <sup>33</sup>	In-Time retrieval device	1	3
Bergui et al <sup>34</sup>	Amplatz snare	12	2.1
Total and weight mean		<b>147</b>	1.93

Abbreviations: EPAR, Endovascular Photo-Acoustic Recanalization laser system (EndoVasix, Inc, Belmont, California); TIMI, thrombolysis in myocardial infarction.

<sup>a</sup>Amplatz gooseneck snare, Microvena Corp, White Bear Lake, Minnesota; AngioJet system, Possis Medical, Inc, Minneapolis, Minnesota; Attractor-18, coil retriever, Target Therapeutics, Inc, Fremont, California; In-Time retrieval device, Boston Scientific Corp, Natick, Massachusetts; MERC1 retrieval system, Concentric Medical, Inc, Mountain View, California; MycroLysUs catheter, EKOS Corp, Bothell, Washington; Neuronet endovascular snare, Guidant Corp, Indianapolis, Indiana; and Soutenir microsnare, Solution, Kanagawa, Japan.

recanalization rate to 57%. In the present study, if the 81 patients who received thrombolysis are excluded, the rate of recanalization is 68.2% (45 patients). However, it is difficult to interpret this percentage because revascularization was achieved in these patients and, thus, further therapy was unnecessary and no thrombolysis was given. Moreover, there is a risk that the high revascularization rate was affected by publication bias.

In the present study, the middle cerebral artery was occluded in 36% of patients, the posterior circulation vessels in 38%, and the internal carotid artery in 26%. It seems that the anterior circulation vessels were more accessible than the posterior circulation vessels. The internal carotid and middle cerebral arteries were accessible in more than 90% of patients (83 of 91), whereas the posterior circulation vessels were accessible in 77% (43 of 56).

For outcome measures, we compared the procedure group with a similar matched cohort who underwent no procedures. The procedure group had good functional recovery (mRS ≤2) in 34.5% of patients compared with 10.7% of patients matched for age, sex, and NIHSS score. This suggests that the procedure group was nearly

**Table 4. Comparison of Device Types for Clot Accessibility, Technical Success, Clinical Success, and Survival**

Variable	Clot Accessibility, No. (%)		P Value <sup>a</sup>
	Yes	No	
<b>Device type</b>	<b>(n=126)</b>	<b>(n=21)</b>	
Laser	30 (24)	4 (19)	.19
Clot D/T	19 (15)	3 (14)	
Snare	29 (23)	9 (43)	
Ultrasound	11 (9)	3 (14)	
Clot retrieval	37 (29)	2 (10)	
<b>Technical success</b>	<b>(n=104)</b>	<b>(n=43)</b>	
Laser	19 (18)	15 (35)	.16
Clot D/T	19 (18)	3 (7)	
Snare	27 (26)	11 (26)	
Ultrasound	11 (11)	3 (7)	
Clot retrieval	28 (27)	11 (26)	
<b>Clinical success<sup>b</sup></b>	<b>(n=49)</b>	<b>(n=97)</b>	
Laser	5 (10)	29 (30)	.02
Clot D/T	6 (12)	16 (17)	
Snare	20 (41)	18 (19)	
Ultrasound	5 (10)	8 (8)	
Clot retrieval	13 (27)	26 (27)	
<b>Death</b>	<b>(n=45)</b>	<b>(n=102)</b>	
Laser	13 (29)	21 (21)	.56
Clot D/T	6 (13)	16 (16)	
Snare	8 (18)	30 (29)	
Ultrasound	5 (11)	9 (9)	
Clot retrieval	13 (29)	26 (26)	

Abbreviation: D/T, disruption/thromboaspiration.

<sup>a</sup>Univariate analysis.

<sup>b</sup>Modified Rankin score 2 or lower.

15 times more likely to have good functional recovery compared with the control group. When outcome was assessed depending on the degree of flow achieved, good outcome was noted only in patients with a TIMI grade 3 and not those with a TIMI grade 2; this is similar to findings in previous cardiac studies. This suggests that normal arterial flow is required to improve functional outcome and not just some return of flow. This has some important implications because a TIMI grade 3 flow was achieved in only 19% of patients with intra-arterial thrombolysis in the largest intra-arterial thrombolysis study (PROACT). Therefore, a combination of both intra-arterial thrombolysis and mechanical embolectomy may be the ultimate best solution to reduce clot burden and improve prognosis. All of the studies cited are limited in that they are single-armed studies compared with historical controls. The efficacy of embolectomy in comparison with intra-arterial or even intravenous tPA has not been established because intra-arterial thrombolysis is not approved by the Food and Drug Administration. The overall mortality of 30.6% is high when compared with most stroke registries. However, the patients selected for these studies had large-vessel intracranial occlusions and, thus, had more severe stroke with a mean NIHSS score of 20.5, and, therefore, much higher mortality is expected. When compared with the matched cohort, a modest survival benefit was noted in patients in the procedure group.

Several potential risks are associated with the introduction of mechanical devices into intracranial arter-

ies. These include technical difficulties such as arterial dissection. When reperfusion is achieved, there is also a risk of intracranial hemorrhage from the damaged vessels in the previously infarcted zone. This was found in the systemic tPA trials with an intracranial hemorrhage rate of 6%, and in the PROACT-II trial, the rate of intracranial hemorrhage was even higher at 10%. In our meta-analysis, however, the rate of intracranial hemorrhage was more than twice that seen in the PROACT-II trial, with 22% of patients developing a hemorrhage. This can be secondary to differences in the definition of hemorrhage, but we do not have sufficient information from the individual studies to categorize these hemorrhages as symptomatic or asymptomatic.

In our study, the mean time from symptom onset to procedure was 10.5 hours (median, 5 hours); therefore, most patients were seen well outside the narrow therapeutic interval for systemic thrombolysis. A more invasive approach was the only option available.

The results of the present study are to be interpreted with caution. First, the methodological quality of the studies included is suboptimal. Because there are no randomized control trials that compare devices, our meta-analysis included only comparative case reports and case series with nonrandomized data. These studies are likely to have significant publication bias because series with negative findings are frequently not published. Meta-analysis of nonrandomized studies is, however, useful in the absence of randomized controlled trials and also helps guide the direction of further research in the area.

Second, the procedure cohort was not a homogeneous cohort and was compared with a single-center historically concurrent cohort, although matched for important variables. There were few patients in each device category, and the patient populations were not comparable for each device; therefore, comparisons of one category with another are potentially misleading. In addition, because individuals were not randomly allocated to treatment, the influence of confounding variables cannot be fully evaluated, and all studies did not adjust for the same confounders. We were, however, able to adjust for NIHSS score. Also, most patients had an mRS at follow-up, which is reproducible and easily comparable between studies.

In conclusion, percutaneous mechanical embolectomy to treat acute ischemic stroke is feasible. Although our findings are promising, there remains a need for structured, randomized, clinical trials to further decipher the short- and long-term outcomes.

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**Correspondence:** Latha G. Stead, MD, Division of Research, Department of Emergency Medicine, Generose Bldg, Ste G-410, 200 First St SW, Rochester, MN 55905 (stead.latha@mayo.edu).

**Author Contributions:** Dr Stead had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. **Study concept and design:** Stead, Gilmore, and Decker. **Acquisition of data:** Stead and Gilmore. **Analysis and inter-**

**pretation of data:** Stead, Bellolio, and Rabinstein. **Drafting of the manuscript:** Stead, Gilmore, and Bellolio. **Critical revision of the manuscript for important intellectual content:** Stead, Gilmore, Bellolio, Rabinstein, and Decker. **Statistical analysis:** Stead and Bellolio. **Administrative, technical, and material support:** Stead, Gilmore, Bellolio, and Decker. **Study supervision:** Stead.

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