Rescue Intracranial Stenting After Failed Mechanical Thrombectomy for Acute Ischemic Stroke: A Systematic Review and Meta-Analysis

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■ BACKGROUND: **Up to 20% of patients fail to achieve reperfusion with modified Thrombolysis in Cerebral Infarction (mTICI) scores of 0–1 after mechanical thrombectomy (MT). Furthermore, underlying intracranial atherosclerotic disease, particularly when associated with >70% residual or flow limiting stenosis, is associated with higher rates of failed MT and high failure risk MT. The aim of this study was to systematically review the procedural and clinical outcomes in patients with failed MT and high failure risk MT. We also explored differences between patients receiving acute rescue stenting compared with medical management alone.**

■ METHODS: **A systematic literature search was conducted in Ovid MEDLINE, PubMed, Embase, and Cochrane online scientific publication databases for English language publications from their date of inception until October 2018. Studies including adult patients with acute ischemic stroke because of emergent large vessel occlusion with failed (mTICI score 0–1) or high failure risk MT within the anterior circulation who underwent rescue stenting were included. A systematic review and meta-analysis of proportions was performed.**

■ RESULTS: **Rescue intracranial stenting after failed MT or high failure risk MT results in improved clinical outcomes compared with patients without stenting (48.5% vs. 19.7%, respectively; $P < 0.001$), without an increase in the rate of symptomatic intracranial hemorrhage, despite additional use of antiplatelet agents (9.7% vs. 14.1%, respectively; $P = 0.04$).**

■ CONCLUSIONS: **In patients who fail initial attempts at MT or are high risk for acute reocclusion, rescue intracranial stenting could be considered with the aim to improve functional outcomes. Antiplatelet agents do not increase the risk of hemorrhage in these patients.**

INTRODUCTION

Stroke is a leading cause of morbidity and mortality worldwide.[1] Cerebral reperfusion with mechanical thrombectomy (MT) is the standard of care for acute ischemic stroke (AIS) because of emergent large vessel occlusion.[2-10] MT is effective across different patient subgroups including elderly patients, those who are ineligible for intravenous

Key words
- Acute ischemic stroke
- Angioplasty
- Intracranial atherosclerosis
- Stenting
- Thrombectomy

Abbreviations and Acronyms
AIS: Acute ischemic stroke
CI: Confidence interval
IV tPA: Intravenous thrombolysis
mRS: Modified Rankin scale
MT: Mechanical thrombectomy
mTICI: Modified Thrombolysis in Cerebral Infarction
OR: Odds ratio
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
sICH: Symptomatic intracranial hemorrhage

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thrombolysis (IV tPA), and patients with tandem occlusions.[6] Recent trials have demonstrated efficacy of MT in selected patients with delayed presentation of up to 24 hours postictus.[11,12]

However, up to 20% of patients fail to achieve reperfusion with modified Thrombolysis in Cerebral Infarction (mTICI) scores of 0—1 after MT.[6] Failed MT may relate to thrombus burden, etiology, and/or endothelial injury during MT. Underlying intracranial atherosclerotic disease, particularly when associated with >70% residual or flow limiting stenosis, is associated with higher rates of failed MT and high failure risk MT. Recent observational studies suggest that this cohort of patients with failed and high failure risk MT may benefit from rescue stenting with more favorable clinical outcomes demonstrated after this treatment compared with medical management alone.[13-15]

The aims of this study were to systematically review the procedural and clinical outcomes in patients with failed and high failure risk MT, and to explore differences between patients receiving acute rescue stenting compared with medical management alone.

METHODS

Literature Search Strategy

This study was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[16,17] A systematic literature search was conducted in Ovid MEDLINE, PubMed, Embase, and Cochrane online scientific publication databases for English language publications using Medical Subject Headings and general search terms from their date of inception until October 2018. The search strategy used a combination of the following terms: "stroke," "middle cerebral artery," "MCA," "thrombectomy," "endovascular," "clot retrieval," "rescue," "stenting," "angioplasty," and "balloon angioplasty."

Selection Criteria

Eligible studies included those investigating rescue stenting or angioplasty treatment after failed (mTICI score 0—1) or high failure risk MT (defined as intracranial atherosclerosis prior to or after MT with >70% luminal narrowing or flow limiting stenosis) within the anterior circulation, with patient age >18 years and reporting successful reperfusion (defined as mTICI score 2b—3), and with relevant clinical outcome data using the modified Rankin scale (mRS). Studies with <10 patients and without anterior circulation strokes were excluded. Only studies published after 2015 were included in an attempt to capture modern MT results. When duplicate data were published, only the most up-to-date version was included. Abstracts, case reports, conference presentations, editorials, and expert opinions were excluded from the analysis.

Data Extraction

All data were extracted from the article text, tables, and figures by 2 reviewers (J. M. and K. P.). Discrepancies were resolved by consensus with input from a senior author (H. A.). Demographic data included study period, year of publication, single arm versus comparative study, number of patients, age, sex, hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, smoking, National Institutes of Health Stroke Scale score, target vessel occlusion location, Alberta Stroke Program Early CT Score, and use of IV tPA.

Treatment parameters included MT technique, type of stent deployed (Solitaire [Medtronic, Dublin, Ireland], Wingspan [Stryker Neurovascular, Kalamazoo, Michigan, USA], or Enterprise [Codman Neurovascular, Los Angeles, California, USA]), use of adjunct procedures (angioplasty or tirofiban use), successful recanalization with mTICI score of 2b—3, and groin-to-recanalization time.

Outcome parameters included total intracranial hemorrhage and symptomatic intracranial hemorrhage (sICH) rates, 90-day mRS score 0—2, mortality, and procedural complication rates.

Statistical Analysis

A systematic review and meta-analysis of proportions was performed. Proportions were combined using DerSimonian-Laird random effects models to account for heterogeneity within the sample. Subgroup analysis according to stenting subgroups was performed using meta-regression analysis. Heterogeneity was evaluated using Cochran Q and I^2 tests. If the study provided medians and interquartile ranges instead of means and SDs, we imputed the means and SDs as described by Hozo et al.[18] All analyses were performed using the metaphor package for R version 3.01 (Bell Laboratories, Madison, Wisconsin, USA). $P < 0.05$ was considered statistically significant.

RESULTS

Search Strategy

A total of 4599 articles were identified through a comprehensive search of relevant databases. After removal of duplicates, 3344 articles were available for title and abstract screening. After removal of irrelevant articles based on title and abstract screening, 50 were retrieved for full-text analysis. Figure 1 outlines the search strategy following PRISMA guidelines, including reasons for exclusion after full-text review. Twelve studies were identified with a total of 530 patients who underwent MT and either failed MT or were deemed high risk for early reocclusion.[14,15,19-28] Of these, 365 patients from 12 studies underwent rescue stenting or angioplasty and 165 patients from 4 studies did not undergo rescue treatment.

Study Characteristics

All studies were retrospective in design. Four studies included patients stented after failed MT compared with patients without stenting in failed MT. Three studies included patients stented after failed MT compared with patients without stenting who underwent successful thrombectomy, and 4 single-arm studies did not have a comparison cohort. A single study compared Solitaire AB stenting (Medtronic) with other self-expandable stents for similar patient cohorts. Additional study characteristics are outlined in Table 1.

Definition of Failed or High-Risk MT

The definitions of failed or high-risk MT varied among the included studies and are outlined in Table 1. In general, those with persistent occlusion or early reocclusion after stent retrieval or severe (>70%) or flow limiting stenosis were generally considered appropriate candidates for rescue stenting. Woo et al.,[14] Baek et al.,[25] and Nappini et al.[22] defined a maximum number of attempts of MT prior to consideration of stenting. Cornelissen et al.[27] had no predetermined number of failed MT

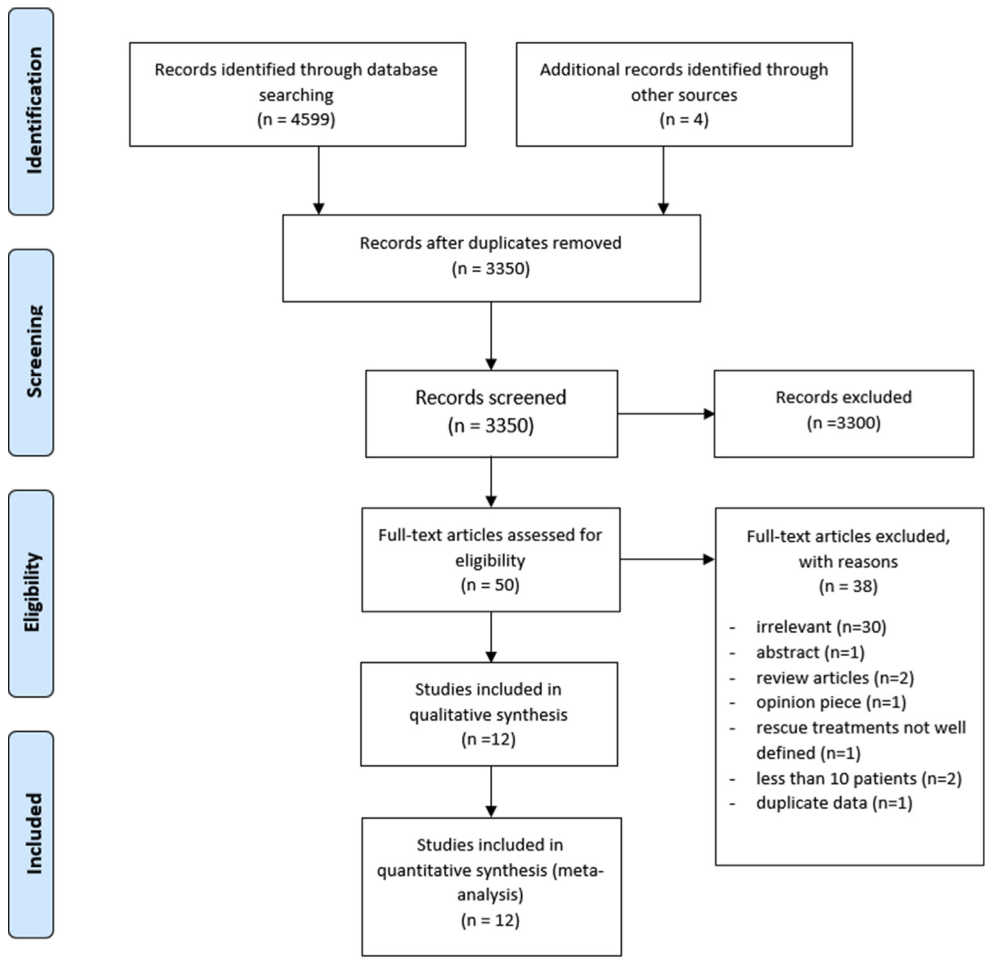

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart outlining the search strategy for the systematic review and meta-analysis.

attempts, whereas Yoon et al.[20] and Kim et al.[24] required intra-arterial vasodilator delivery with persistent stenosis at 3–5 minutes prior to stenting. Interestingly, Baracchini et al.[26] considered lesions appropriate for stenting when they were associated with calcified plaque or where lesions were deemed too distal for safe attempts at multiple MT passes because of a high risk of endothelial damage, dissection, or perforation.

Baseline Characteristics

Overall, patients were older adults with a mean age of 66.6 years. There was a significant difference in age between patients with and without stents, with younger patients seen in the stented group ($P = 0.002$). There were no differences in sex or baseline cardiovascular risk factors. IV tPA was administered in 35.7% of cases overall and was used more frequently in patients who did not undergo stenting ($P = 0.04$). The reasons for withholding IV tPA were not clearly defined in the included studies. There were no differences in target vessel occlusions or stroke severity.

Treatment Characteristics

Importantly, stenting did not increase the overall procedure time, with no significant difference in groin puncture-to-recanalization times demonstrated (Table 2); however, reporting was inconsistent across the studies.

Stent Types

A variety of intracranial stents were deployed in the studies and included the following: Wingspan, Enterprise, Neuroform (Stryker Neurovascular), PRECISE (Cordis Corp., Miami Lakes, Florida, USA), Solitaire AB, and Solitaire FR (Medtronic) stent devices. Interestingly, Woo et al.[14] compared the Solitaire FR device with other self-expanding stents; however, the specific stent types and number were not detailed. In this series, reported rates of favorable outcome (mRS score 0–2) at 3 months were statistically significant in favor of the Solitaire FR device.

Table 1. Summary of Methodologic Characteristics of Included Studies

Study	Country	Number of Patients (Included in Analysis)	Criteria for Rescue Stenting	Rescue Stenting Type
Chang et al., 2018[28]	South Korea	148	1. ICAS suspected as a cause of LVO 2. Repeat reocclusion shortly after MT 3. Clinical infarct core mismatch 4. Good antegrade flow with stent retriever for 10 minutes but instant reocclusion after retrieval 5. Aggravating flow compromise because of residual stenosis after MT	Solitaire AB: 37, Wingspan: 8, Enterprise: 2, balloon expandable: 1
Zhou et al., 2018[15]	China	193	1. mTICI score <2b/3	Solitaire: 24, Apollo:16, Enterprise: 5, Wingspan: 6, Neuroform: 4
Cornelissen et al., 2018[27]	Sweden	26	1. Persistent reocclusion after withdrawal of thrombectomy device (mTICI score 0—1) 2. No predetermined number of failed attempts	Enterprise: 8, Solitaire: 4
Nappini et al., 2018[22]	Italy	17	1. Flow restoration with device in situ with reocclusion or residual severe stenosis after retrieval 2. Retrieval attempted 4—6 times	Solitaire AB
Baracchini et al., 2017[26]	Italy	109	1. Effective with device in place but reocclusion or severe stenosis after retrieval 2. Calcified plaque or distal occlusion which contraindicates multiple retrieval maneuvers where stent retriever may cause endothelial damage, dissection, or perforation 3. ASPECTS ≥6 with a good mismatch on CT perfusion	Solitaire AB
Woo et al., 2018[14]	South Korea	27	1. Refractory occlusion or residual flow limiting stenosis after 3—7 attempts of MT, suction thrombectomy, or chemical thrombolysis	Solitaire FR
Delgado et al., 2017[23]	Spain	42	1. Failed MT or intracranial stenosis	Enterprise
Baek et al., 2016[25]	South Korea	45	1. Refractory occlusion after 3—7 attempts 2. Stented only after other reperfusion therapies exhausted (Penumbra aspiration, IA urokinase, IA glycoprotein IIb/IIIa)	Solitaire AB/FR: 10 Wingspan: 7
Al Kasab et al., 2017[19]	USA	36	1. ICAS 2. Significant fixed focal stenosis at occlusion site which became evident during MT or on final angiography	Wingspan: 30, Precise: 1, Enterprise: 1
Kim et al., 2016[24]	South Korea	46	1. Severe (>70%) underlying ICAS on initial or follow-up angiogram determined by WASID criteria 2. Must be persistent 3—5 minutes after IA injection of vasodilatory via guide catheter	Wingspan
Seo et al., 2016[21]	South Korea	10	1. Acute stroke caused by ICAS (>70%) or persistent occlusive disease	Wingspan
Yoon et al., 2015[20]	South Korea	172	1. Severe (>70%) underlying ICAS on initial or follow-up angiogram determined by WASID criteria 2. Must be persistent 3—5 minutes after IA injection of vasodilatory via guide catheter	Wingspan

ICAS, intracranial atherosclerosis; LVO, large vessel occlusion; MT, mechanical thrombectomy; mTICI, modified Thrombolysis in Cerebral Infarction; ASPECTS, Alberta Stroke Program Early CT Score; CT, computed tomography; WASID, warfarin-aspirin symptomatic intracranial disease; IA, intra-arterial.

Clinical Outcomes

The pooled primary outcome of favorable 90-day mRS score among patients with stents was 48.5% (95% confidence interval [CI], 41.2—55.9) compared with 19.7% (95% CI, 14.2—26.7) in patients without stents ($P < 0.001$) (**Figure 2**). This was associated with significant heterogeneity ($I^2 = 73.3\%$ overall).

Overall mortality was 21.9%, with a trend favoring patients with stents compared with patients without stents (18.5% vs. 31.0%, $P = 0.06$) (**Figure 3**). This was associated with moderate

Table 2. Baseline Demographic Data of Included Patients

Variable	Overall	No Stenting	Stenting	*P* Value for Difference
Age (years)	66.6 (64.7—68.5)	70.6 (67.1—74.0)	65.3 (63.3—67.2)	0.002*
Male (%)	58.5 (53.6—63.2)	53.4 (44.3—62.3)	60.5 (55.1—65.7)	0.10
Hypertension (%)	65 (56.4—72.7)	73.2 (45.1—90.1)	62.8 (53.8—71.0)	0.38
Hyperlipidemia (%)	33.4 (21.7—47.7)	20.2 (8.4—41.0)	38.4 (25.1—53.8)	0.23
Diabetes (%)	35.4 (29.2—42.1)	33.2 (18.2—52.7)	36.3 (29.6—43.6)	0.50
Atrial fibrillation (%)	23.6 (15.0—35.1)	39.2 (22.5—59.0)	19.9 (11.9—31.4)	0.09
Smoking history (%)	29.0 (25.0—33.4)	31.9 (24.9—39.7)	27.6 (22.9—32.8)	0.34
IV tPA use (%)	35.7 (30.7—41.1)	43.2 (35.8—50.9)	32.9 (27.2—39.2)	0.04*
NIHSS score at baseline	15.5 (14.4—16.6)	16.3 (14.7—17.9)	15.2 (13.6—16.8)	0.49
Target vessel occlusion				
MCA	58.4 (46.1—69.7)	73.3 (45.1—90.2)	54.2 (40.7—67.0)	0.19
ICA	26.8 (18.9—36.6)	15.8 (2.5—57.6)	28.1 (19.7—38.3)	0.63
Basilar artery	20.0 (13.2—29.0)	6.6 (0.7—42.5)	22.5 (15.1—32.1)	0.25
Vertebral artery	3.5 (1.8—6.4)	1.5 (0.3—7.1)	4.0 (2.0—7.9)	0.26
Groin puncture to recanalization time	93.3 (72.4—114.2)	118.8 (50.9—186.7)	88.2 (66.8—109.6)	0.25

Values are presented as weighted mean (95% confidence interval).
IV tPA, intravenous thrombolysis; NIHSS, National Institutes of Health Stroke Scale; MCA, middle cerebral artery; ICA, internal carotid artery.
*Statisically significant.

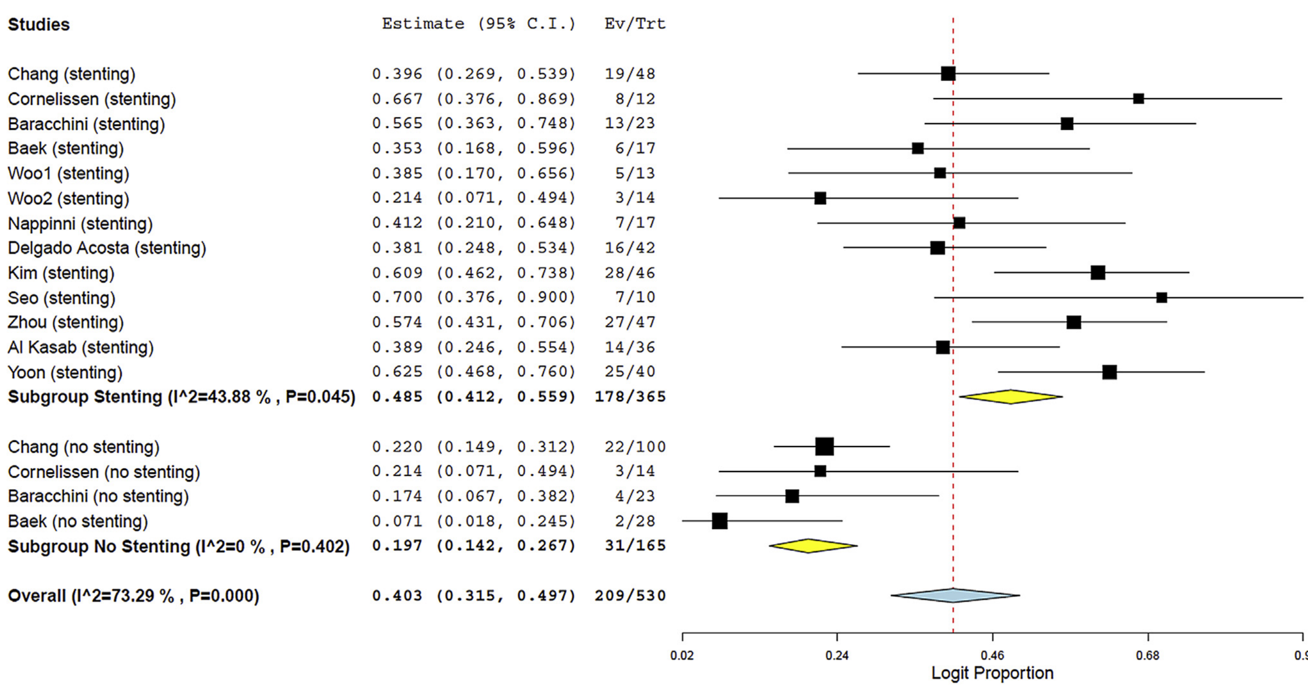

Figure 2. Ninety-day modified Rankin scale scores in patients with versus without stents. C.I., confidence interval; Ev, events; Trt, number treated.

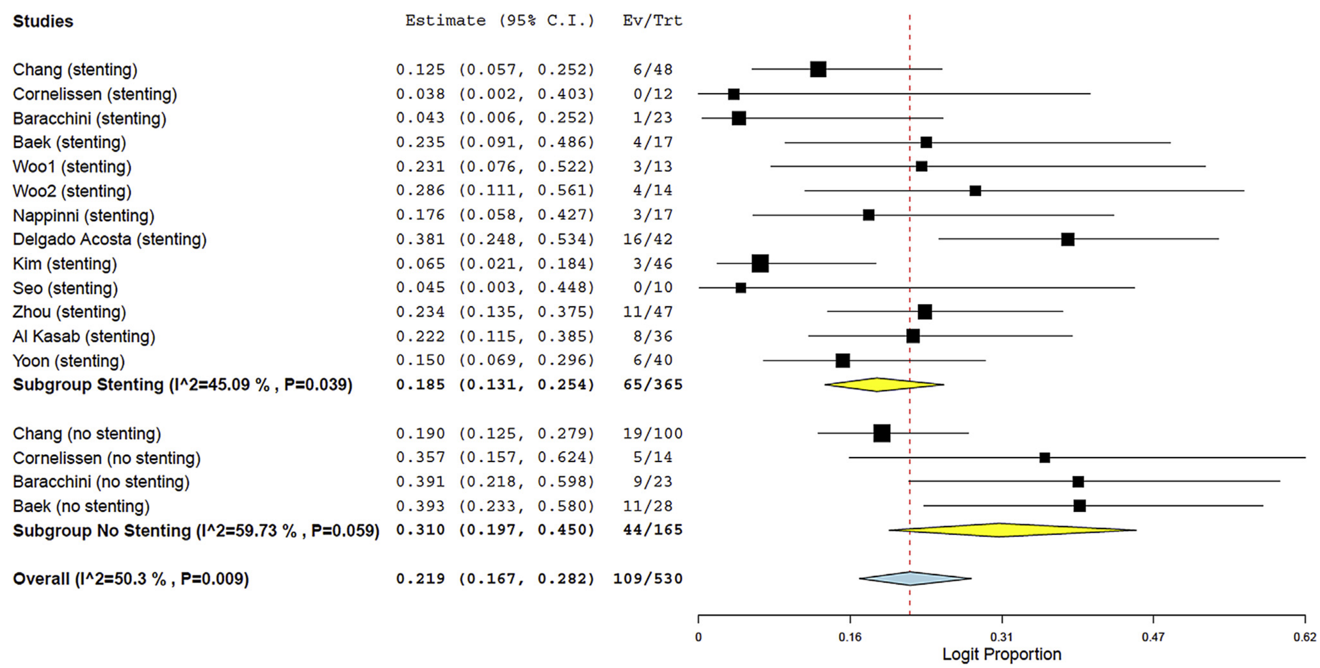

Figure 3. Mortality rate of patients with versus without stents. C.I., confidence interval; Ev, events; Trt, number treated.

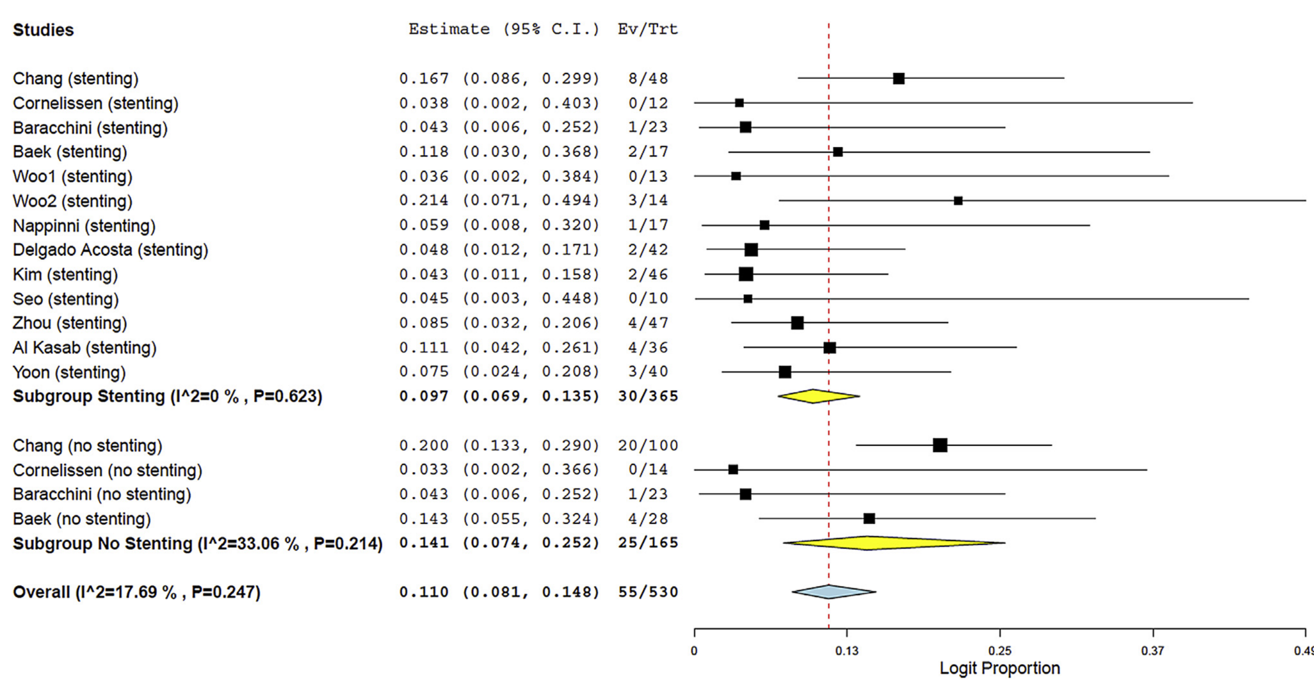

Figure 4. Symptomatic intracranial hemorrhage in patients with versus without stents. C.I., confidence interval; Ev, events; Trt, number treated.

heterogeneity ($I^2 = 50.3\%$ overall). The mortality rate in the stenting group ranged between 0% and 23.5% compared with 35.7% and 39.3% in the nonstented group.

sICH was reported in 0%–16.7% of patients with stents with a significant reduction compared with patients without stents (9.7% vs. 14.1%, $P = 0.04$) (**Figure 4**). This was associated with low heterogeneity ($I^2 = 17.7\%$ overall).

The overall successful recanalization rate (mTICI score 2b/3) for patients with stents was 79% (weighted mean, 95% CI, 71.3–85.1), varying from as low as 61.1% to 95.7% among the included studies. Follow-up stent primary patency between 24 hours and 24 months was assessed in 11 studies using transcranial color Doppler, computed tomography angiography, magnetic resonance angiography, or digital subtraction angiography. Of 365 patients with stents, 35 stents demonstrated in-stent restenosis (defined as >50% stenosis) or occlusion. These data are outlined in **Table 3** along with the varying periprocedural antiaggregate and postprocedural antiplatelet regimens. In general, intravenous or intra-arterial glycoprotein IIb/IIIa inhibitors were favored, followed by long-term dual antiplatelet therapy.

DISCUSSION

The results from this systematic review and meta-analysis suggest a significant benefit in clinical outcome to performing rescue stenting in patients with failed and high failure risk MT, without an increase in the rate of sICH, despite additional use of antiplatelet agents. There was also a numerically lower mortality in patients who received rescue stenting. **Figure 5** demonstrates and highlights the use of intracranial angioplasty and stenting using the Wingspan device in a patient with a high grade stenosis who underwent MT during the same procedure.

Our results are in agreement with another recent meta-analysis, in which 43.4% (weighted mean, 95% CI, 34.2%–53.0%) of patients achieved independence at 3 months with low rates of sICH.[29] However, our analysis included twice as many patients with stents, included a comparison group of patients without stents, and only included studies published after 2015 in an attempt to capture more modern thrombectomy results. In addition, our analysis demonstrates favorable clinical and imaging outcomes in those undergoing rescue stenting over the nonstented group, with higher overall mortality rates in nonrecanalized patients. The current analysis included 365 patients with stents and 165 patients without stents, more than twice as many patients with stents as the previous meta-analysis, and remains significantly in favor of rescue stenting.

Early retrospective and prospective data investigating the use of intracranial stenting was predominantly for secondary prevention in intracranial stenosis and reported mixed results. Early studies using coronary stents were associated with higher rates of 30-day and delayed stroke or death.[30] The introduction of newer dedicated intracranial stents, Wingspan in particular, was associated with a reduction in periprocedural and long-term events; however, these analyses were retrospective.[30] The Wingspan system is composed of nitinol with improved trackability and radial outward strength, which is deployed with gentle balloon angioplasty. Despite this, the Stenting and

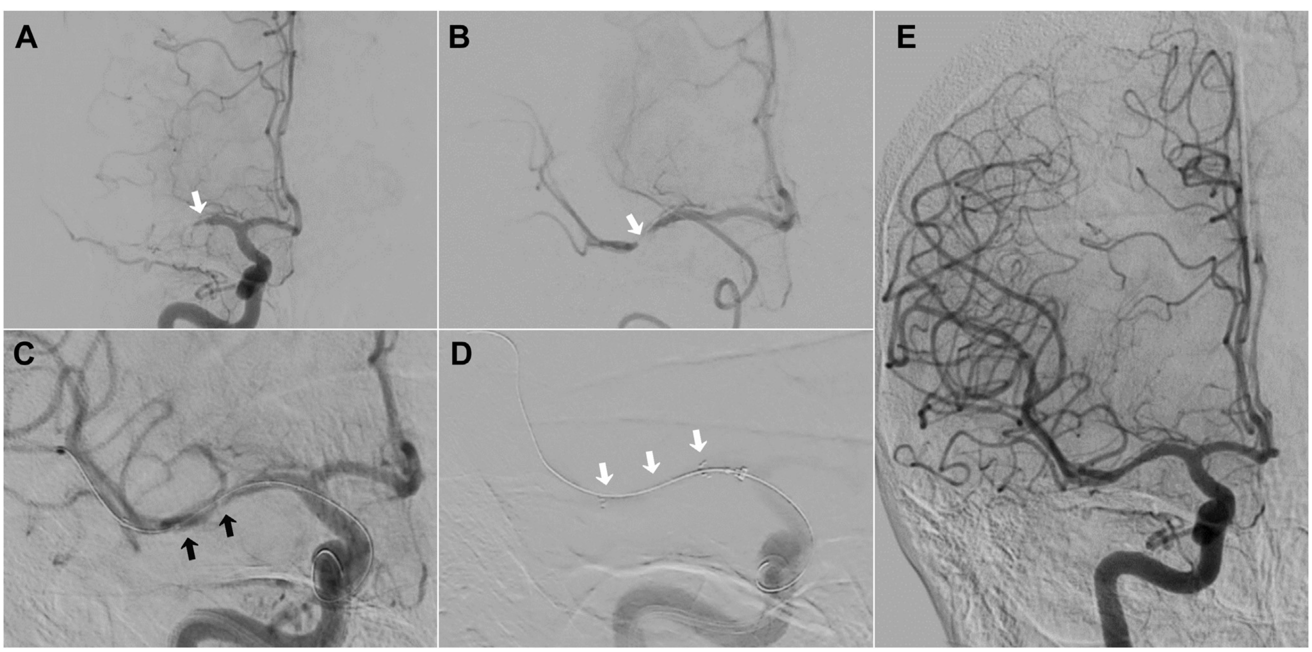

Figure 5. (**A**) Acute right M1 segment middle cerebral artery (MCA) occlusion (*white arrow*). A perfusion abnormality was present in the right MCA territory (not shown). (**B**) After mechanical thrombectomy with a stent retriever, a high-grade stenosis (>70%) was revealed with associated flow limitation (*white arrow*). (**C**) After balloon angioplasty, improved luminal diameter was noted (*black arrows*). (**D**) A Wingspan stent was deployed (*white arrows*) using over the wire exchange with an 0.014-in 300-cm exchange length microwire. (**E**) The final image demonstrated modified Thrombolysis in Cerebral Infarction score 3 reperfusion.

Table 3. Successful Recanalization, Long-Term Stent Patency, and Antiaggregate Therapy for Patients with Stents

Study	Successful Recanalization of Patients with Stents, % (95% CI)	Postprocedural Stent Patency	Periprocedural Antiaggregate Therapy	Postprocedural Antiplatelet Therapy Regimen
Chang et al., 2018[28]	64.6 (50.2—76.7)	3-day follow-up MRA or CTA 3 occluded, associated with not using glycoprotein IIb/IIIa inhibitor, $P = 0.03$	4 treatment regimens determined by consensus between the treating interventionalist and stroke physician 1. Glycoprotein IIb/IIIa inhibitor just before or after RS (loading tirofiban 0.3—1.0 mg or Abciximab 5—10 mg) followed by an intravenous maintenance dose of the same drug for 6—12 hours 2. Oral dual antiplatelet medication just before or after RS (100—500 mg aspirin and 300 mg clopidogrel) 3. Oral antiplatelet monotherapy just after RS (75—300 mg clopidogrel) 4. No antiaggregation therapy was done until follow-up nonenhanced CT or MRI was obtained next day	Dual antiplatelet therapy
Zhou et al., 2018[15]	80.9 (67.1—89.7)	6-month follow-up DSA >50% ISR in 4 of 21 followed-up patients	IV heparin with an activated clotting time of 250—300 seconds IV tirofiban 8.0 g/kg bolus over 3 minutes then IV tirofiban maintenance 0.10 g/kg/min for up to 24 hours IA tirofiban was used at the discretion of the treating interventionalist in 2 patients	Dual antiplatelet therapy loading 300 mg clopidogrel and 300 mg aspirin followed by 75 mg clopidogrel and 100 mg aspirin for 3—6 months
Cornelissen et al., 2018[27]	91.7 (58.7—98.8)	10 patients followed-up with CTA or DSA up to 24 months 1 patient occluded at 6-month CTA	Half or full bolus dose of weight adapted abciximab in 11 patients IV aspirin in 1 patient	Dual antiplatelet therapy with aspirin in combination with clopidogrel or prasugrel for 3—6 months (antiplatelet resistance testing performed) 100 mg aspirin lifelong
Nappini et al., 2018[22]	70.6 (45.8—87.2)	3-month CTA/MRA All stents patent in remaining alive patients	IV bolus tirofiban 25 μg/kg in 3 minutes IV maintenance 0.1 μg/kg	Dual antiplatelet therapy loading 300 mg clopidogrel and 300 mg aspirin followed by 75 mg clopidogrel and 100 mg aspirin for 3 months Lifelong aspirin thereafter
Baracchini et al., 2017[26]	73.9 (52.8—87.8)	24-hour control DSA was performed to verify stent patency and distal recanalization followed by TCCD at discharge and at 1, 3, 6, and 12 months; in case of restenosis, the diagnosis was confirmed by CTA/MRA 1 patient reoccluded at 24 hours	IA bolus of glycoprotein IIb/IIIa inhibitor (tirofiban) was injected (25 μg/kg in 3 minutes) followed by a 12-hour IV infusion (0.1 μg/kg)	Dual antiplatelet therapy for 3 months

Continues

Table 3. Continued

Study	Successful Recanalization of Patients with Stents, % (95% CI)	Postprocedural Stent Patency	Periprocedural Antiaggregate Therapy	Postprocedural Antiplatelet Therapy Regimen
Woo et al., 2018[14]	84.6 (54.9—96.1)	Angiographic follow-up at discharge and 3 months with DSA or CTA Discharge ISR in 18.2% ($P = 1.0$) 3-month ISR in 28.6% ($P = 0.633$)	If the patient was about to undergo permanent stent insertion and had not taken proper antithrombotic medication before the procedure, IV glycoprotein IIb/IIIa inhibitor (tirofiban) loading dose (0.4 μg/kg) for 30 minutes, followed by continuous infusion for prevention of acute in-stent thrombosis (0.1 μg/kg/min)	Dual antiplatelet therapy 300 mg aspirin and 75 mg clopidogrel after excluding symptomatic hemorrhagic transformation
Woo et al., 2018[14] (other self-expanding stents)	78.6 (50.6—92.9)	Discharge ISR in 9.9% ($P = 1.0$) 3-month ISR in 44.4% ($P = 0.633$) In those receiving a glycoprotein IIb/IIIa inhibitor, 0% versus 50% stenosis at discharge ($P = 0.013$) 18.2% versus 80% at 3 months ($P = 0.036$)		
Delgado et al., 2017[23]	71.4 (56.1—83.0)	Not reported	Dual antiplatelet therapy 300 mg clopidogrel and 300 mg aspirin orally or via nasogastric After October 2013, IV abciximab 0.1 mg/kg bolus	Dual antiplatelet therapy 75 mg clopidogrel and 100 mg aspirin for 1 year 100 mg aspirin for life
Baek et al., 2016[25]	82.4 (57.3—94.2)	24-hour MRA or CTA 3- to 12-month DSA or CTA follow-up All patients patent except for 1 with biliary sepsis who did not receive ReoPro maintenance	IA glycoprotein IIb/IIIa inhibitor (ReoPro 5—10 mg) IV maintenance for 24 hours	Dual antiplatelets for 3 months
Al Kasab et al., 2017[19]	61.1 (44.6—75.4)	Not reported	Loaded with abciximab intraprocedurally	Dual antiplatelet therapy
Kim et al., 2016[24]	95.7 (84.2—98.9)	48-hour CTA in 45 patients (97.8%) 120-hour CTA in 1 patient Acute reocclusion in 6 patients (13%)	Neither heparin nor glycoprotein IIb/IIIa inhibitor was used IV or IA	Dual antiplatelet therapy 300 mg aspirin and 300 mg clopidogrel orally or via nasogastric then 100 mg aspirin and 75 mg clopidogrel for 3 months
Seo et al., 2016[21]	90.0 (53.3—98.6)	1 patient with reocclusion on TCCD postprocedure	Dual antiplatelet therapy prior to the procedure IA urokinase, abciximab, or tirofiban if residual stenosis	Dual antiplatelet therapy
Yoon et al., 2015[20]	95.0 (82.1—98.7)	Follow-up CTA before discharge Reocclusion in 3 patients (8.8%)	Neither heparin nor glycoprotein IIb/IIIa inhibitor was used IV or IA	Dual antiplatelet therapy aspirin and clopidogrel orally or via nasogastric immediately after the procedure Dual antiplatelet therapy was continued for at least 3 months

CI, confidence interval; MRA, magnetic resonance angiography; CTA, computed tomography angiography; RS, rescue stenting; CT, computed tomography; MRI, magnetic resonance imaging; DSA, digital subtraction angiography; ISR, in-stent restenosis; IV, intravenous; IA, intra-arterial; TCCD, transcranial color Doppler.

Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial, which only used the Wingspan system, failed to demonstrate efficacy and was ceased after enrolling 451 patients from 50 centers because of higher-than-expected periprocedural events at 30 days in the stented group (14.7% vs. 5.8%; $P = 0.002$).[31]

Concerns over the need for over-the-wire exchange after balloon angioplasty for stent deployment (potentially resulting in increased rate of hemorrhage and stroke from dissection and perforation) were addressed in the Vitesse Intracranial Stent Study for Ischemic Stroke Therapy (VISSIT) trial, which used a balloon-mounted intracranial stent. Enrollment was ceased after 112 patients because of higher-than-expected rates of stroke in the stented group and lower-than-expected rates in the medical group, respectively (23.7% vs. 9.4% at 30 days; P = 0.05 and 36.2% vs. 15.1% beyond 30 days; P = 0.02).[32]

However, there were criticisms of the SAMMPRIS trial, including low rates of enrollment from participating centers, raising concerns over operator experience, varying underlying lesion etiologies, and perforator occlusion (a large proportion of events were perforator strokes), which may have impacted results.[30] In comparison with intracranial stenosis, AIS because of large vessel occlusion is associated with worse outcomes. The Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials meta-analysis, and Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3 (DEFUSE3) and Diffusion Weighted Imaging (DWI) or Computerized Tomography Perfusion (CTP) Assessment With Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention (DAWN) trials, demonstrated clear benefit of MT.[6,11,12] In the current study, the prevalence of functional independence at 90 days was 19.7% in nonrecanalized patients versus 48.5% in patients with stents (P = 0.001), with a higher mortality rate of 31.0% (vs. 18.5% in patients with stents; P = 0.06). Correspondingly, rates of functional independence in patients ineligible for intravenous alteplase from the control group in the Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials meta-analysis were also low at 22.3% versus 43.5% in those undergoing MT.[6] These data suggest that when MT fails, additional procedures to open the target vessel occlusion should be attempted. The studies included in the current analysis predominantly included the Wingspan and a newer detachable Solitaire stent. The use of newer and modern detachable intracranial stents may improve recanalization and therefore clinical outcome, particularly in the acute setting.

Additional stent types included in the reviewed studies were the Enterprise and, more recently, the detachable Solitaire AB or Solitaire FR devices. Of the included studies, a single study compared the Solitaire FR device with other self-expanding stents. Reported rates of functionally independent outcome (mRS score 0–2) at 3 months were in favor of the Solitaire FR device; however, the specific stent types and numbers were not mentioned in the comparison self-expanding stent group.[14] It is possible that a trend toward improved recanalization rates and clinical outcomes may be seen as technology, device deliverability, and interventional techniques improve.

Interestingly, a recent study evaluating primary angioplasty and stenting against stent retriever thrombectomy in patients with large vessel atherosclerosis demonstrated higher rates of functional independence at 90 days (69.7% vs. 47.6%, P = 0.02), lower rates of asymptomatic intracranial hemorrhage (30.5% vs. 9.1%, P = 0.01), and no difference in rates of sICH (11.5% vs. 9.1%, P > 0.99.).[33] Given these findings and the results of the current analysis, further studies evaluating a primary stenting strategy is warranted to evaluate a potential role as first-line therapy in appropriately selected patients.

The use of periprocedural antiplatelet agents and early institution of dual antiplatelet therapy after stroke and stenting needs to be considered because there are concerns surrounding the risk of hemorrhagic complications after their use. There was significant variability in the use of antiplatelet agents, with no clear recommendations from major societies. Only Yoon et al.[20] and Kim et al.[24] did not use periprocedural heparin or a glycoprotein IIb/IIIa inhibitor in their series. Chang et al.[28] reported that as part of their protocol, some patients did not receive antiaggregation or antiplatelet therapy until follow-up computed tomography scan excluded hemorrhage; however, exact numbers were not reported. Overall, rates of sICH were higher among patients without stents. Although this could be attributed to a significantly higher rate of IV tPA use in the nonstented cohort, the data suggest safety of periprocedural antiaggregation therapy and early institution of dual antiplatelet treatment. Several studies not included in our analysis confirm these findings.[34,35] The multicenter Safety of Tirofiban in Acute Ischaemic Stroke trial and several further observational studies have demonstrated favorable results with intra-arterial and intravenous tirofiban infusions in AIS. The Safety of Tirofiban in Acute Ischaemic Stroke trial randomized 260 patients to tirofiban or placebo and investigated the rate of intracerebral hemorrhage and early neurologic and functional performance after 2–7 days and after 5 months. Overall, there was no significant difference in hemorrhagic transformation between groups (odds ratio [OR], 1.18; 95% CI, 0.66–2.06); however, mortality was significantly lower in patients treated with tirofiban (2.3% vs. 8.7%; OR, 4.05; 95% CI, 1.1–14.9), without differences in functional outcome (mRS score 1–5) after 5 months.[34] A single-center prospective registry study by Zhao et al.[35] demonstrated similar results in patients undergoing MT with a lower odds of death (23% vs. 44%, P = 0.005) and better odds of long-term functional independence (OR, 4.37; 95% CI, 1.13–16.97; P = 0.033).

There are several limitations to this study. There was significant heterogeneity in some components of the analysis. The underlying reasons for failed MT, criteria for proceeding to stent deployment, treatment approaches and stents used, and number of thrombectomy attempts varied across the studies, which may impact results and limit generalizability. Furthermore, some of the analyzed studies included patients with posterior circulation occlusion, potentially impacting clinical outcomes. The use of periprocedural angioplasty and antiaggregation therapy also varied between studies. There was a high risk of selection bias because those patients undergoing stenting tended to be younger with lower rates of concomitant IV tPA use, which further limits generalizability. Nevertheless, the results from this analysis favour stenting, supporting the results of a smaller comparable meta-analysis. These analyses support the investigation of a primary stenting strategy in AIS in a randomized setting.

CONCLUSIONS

This meta-analysis suggests that rescue stenting is safe and efficacious in patients presenting with AIS in the setting of failed MT or with high-risk MT, with significant improvement in clinical outcomes and no corresponding risk of sICH. However, current data are limited to relatively small retrospective studies and should be cautiously interpreted. The data are not generalizable to all patients, given the variability in the underlying etiology of the failed MT therapy, and given the heterogeneity of treatments used, and even variation in the number of treatment attempts. These data provide guidance for future prospective registries and randomized controlled trials to strengthen the evidence base in this area of AIS therapy.

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