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Original research

Reocclusion after successful endovascular treatment in acute ischemic stroke: systematic review and meta-analysis

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ABSTRACT

Background Endovascular treatment (EVT) is the standard of care for selected patients with acute ischemic stroke (AIS) due to large vessel occlusion (LVO).

Objective To systematically review the available data on: (1) incidence, predictors, and outcomes of patients with reocclusion after successful EVT for AIS and, (2) the characteristics, complications, and outcomes of patients with reocclusion treated with repeated EVT (rEVT) within 30 days of the first procedure.

Methods PubMed was searched (between January 2012 and April 2021) to identify studies reporting reocclusion following successful EVT (Thrombolysis in Cerebral Infarction $\geq 2b$) in patients with AIS due to LVO. Pooled incidence of reocclusion per 100 patients with successful recanalization following EVT was calculated using a random-effects model with Freeman-Tukey double arcsine transformation. Extracted incidences of reocclusion according to etiology and use of intravenous thrombolysis were pooled using random-effects meta-analytic models.

Results A total of 840 studies was identified and seven studies qualified for the quantitative analysis, which described 91 same-vessel reocclusions occurring within the first 7 days after treatment among 2067 patients (4.9%; 95% CI 3% to 7%, $I^2=70.2\%$). Large vessel atherosclerosis was associated with an increased risk of reocclusion (OR=3.44, 95% CI 1.12 to 10.61, $I^2=50\%$). We identified 90 patients treated with rEVT for recurrent LVO, described in five studies. The rates of procedural complications, mortality, and unfavorable functional outcome at 3 months were 18.0%, 18.9%, and 60.3%, respectively.

Conclusion In cohorts of patients with AIS due to LVO, 5% of patients experienced reocclusion within 7 days after successful EVT. Repeated EVT can be a safe and effective treatment for selected patients with reocclusion.

INTRODUCTION

Rationale and objectives

Several randomized controlled clinical trials have proved the efficacy of endovascular treatment (EVT) for selected patients with acute ischemic

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Early reocclusion is a possible complication in patients with acute ischemic stroke due to large vessel occlusion successfully treated with endovascular treatment (EVT). The prevalence and the risk factors for vessel reocclusion in this setting are not well elucidated. Also, the safety and effectiveness of repeated EVT for patients with reocclusion have not been systematically evaluated.

WHAT THIS STUDY ADDS

⇒ The incidence of reocclusion within the first 7 days after successful recanalization in cohorts of consecutively included patients receiving EVT for large vessel occlusion is 5%.
⇒ Ischemic stroke due to large artery atherosclerosis is associated with an increased risk of same-vessel reocclusion.
⇒ Repeated EVT in selected patients with early recurrent ischemic stroke appears to be a safe and successful procedure.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Patients with acute ischemic stroke successfully treated with EVT are at risk for early vessel reocclusion, especially when the event was due to large artery atherosclerosis.
⇒ Since selected patients with reocclusion may benefit from repeated EVT, careful clinical monitoring is necessary after successful EVT, and reassessment of the cerebral circulation should be considered in cases suspected of having reocclusion.
⇒ Future studies should assess specific treatment strategies in order to reduce the risk of vessel reocclusion in patients with acute ischemic stroke receiving EVT, as well as the criteria for patient selection in those with early reocclusion who are potentially eligible for repeated EVT.

stroke (AIS) due to large vessel occlusion (LVO).^{1–4} This treatment has been shown to be cost-effective⁵ and have high efficacy,^{2 6 7} maintained up to 24 hours after suspected symptom onset in patients with clinical or perfusion mismatch. EVT is also performed in most centers for basilar occlusions,^{8–11} and two randomized controlled trials, the Basilar Artery Occlusion Chinese Endovascular (BAOCHE) trial and the Endovascular Treatment for Acute Basilar Artery Occlusion (ATTENTION) study, recently confirmed the efficacy of EVT in this setting.

Although early recanalization increases the likelihood of achieving favorable neurological outcomes, several additional factors might have an impact on clinical prognosis.^{12 13} Despite successful recanalization, about half of patients do not achieve favorable functional outcome.¹ Many variables influence the clinical outcome, including patient-related factors (stroke severity, age, collateral status, and preclinical conditions), baseline infarct burden, and procedure-related factors (timing, number of passes, complications, and degree of reperfusion).¹⁴ Reocclusion may occur in the hours or days following successful initial reperfusion and lead to worse outcome.^{15 16} Predictors of vessel reocclusion have been suggested, such as stroke etiology, occlusion site, residual embolic fragments, cerebral microembolism, and procedure-related events.^{15 17 18} However, the prevalence and risk factors for reocclusion are not well elucidated.^{16 19 20} Moreover, the safety and effectiveness of treatment strategies for patients with reocclusion is not established and has not been systematically evaluated.^{21–23} In these cases, in which intravenous thrombolysis (IVT) is generally contraindicated due to the risk of hemorrhagic transformation related to recent stroke,^{2 24} repeated thrombectomy (rEVT) can be considered. However, particularly in the setting of recent ischemic stroke in the same territory, there may be an increased risk of complications, including vasospasm, disruption of the vascular endothelium, arterial dissection, reperfusion injury, or intracranial hemorrhage.^{25 26}

The aim of this review is to describe the available data on the prevalence, predictors, and functional outcome of patients with reocclusion following successful thrombectomy for AIS associated with LVO. We also sought to describe the characteristics, complications, and outcomes of patients with reocclusion treated with rEVT.

METHODS

For the purpose of this systematic review, we followed the MOOSE²⁷ (Meta-analysis Of Observational Studies in Epidemiology) proposal and the PRISMA²⁸ (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The data that support the findings of this study are available from the corresponding author on reasonable request. This review is registered at PROSPERO database (CRD 42020184655).

Eligibility criteria

We considered studies reporting reocclusion following successful reperfusion achieved by EVT (Thrombolysis in Cerebral Infarction (TICI) scale score 2b/3) in patients with AIS due to LVO of the anterior or posterior circulation, and with systematic evaluation of vessel patency after successful EVT. We excluded single case reports and case series describing fewer than 50 patients receiving EVT for AIS, studies including pediatric patients (<18 years old) and patients treated using older generation thrombectomy devices such as Merci. Articles in English, Spanish, French, Italian, German, and Portuguese were reviewed.

Definitions

We used the following definitions of the main outcomes: (1) reocclusion was defined as recurrent occlusion of the target vessel (reocclusion of the same vessel), or other large artery occlusion (reocclusion of different vessel) after successful EVT (TICI \geq 2b), confirmed by imaging (CT angiography, MR angiography, or transcranial Doppler); (2) acute, early, and late reocclusion were defined as reocclusion occurring within 24 hours, 7 days or more than 7 days after successful recanalization, respectively; (3) repeated EVT was considered when a second EVT was performed for the same patient, due to recurrent AIS associated with LVO, occurring within the first 30 days after successful EVT; (4) good functional outcome was defined as modified Rankin Scale (mRS) score 0 to 2, whereas unfavorable functional outcome was defined as mRS score 3–6 at the last available follow-up.

Search strategy

A systematic search using combinations of keywords was performed in Medline/PubMed database, from January 1, 2012 to April 30, 2021. The search strategy combined the main terms ‘stroke, strokes, cerebrovascular accident, apoplexia, endovascular treatment, endoluminal repair, stent, angioplast*, re-oc*, reoc*, reocclusion or repeated endovascular treatment’ (details in online supplemental data). Potential eligible studies and selected study reference lists were crosschecked for additional studies. Additional data from international conferences abstracts and proceedings were analyzed for unpublished data.

Study selection

Identified studies were screened for potential eligibility by title and abstract analysis. The full text of potentially eligible studies was screened to meet the inclusion and exclusion criteria, by two independent reviewers (RO, MAC). Disagreements were resolved through discussion with a third or fourth reviewer (DAdS, LLN), where required.

Data extraction

Two independent authors (RO, MAC) extracted full-text data from included studies to a specially designed extraction tool. Disagreements were resolved through discussion with the assistance of a third or fourth reviewer (DAdS, LLN), where required. Corresponding authors of identified papers were contacted for additional data on critical variables.

Data items and outcomes

The primary outcome was reocclusion after successful EVT. For the selected studies, we extracted the following data: frequency of reocclusion categorized as acute (<24 hours); early (\leq 7 days); late (>7 days); same vessel/different vessel; use of intravenous thrombolysis; age, sex, vascular risk factors, location of the LVO (anterior vs posterior circulation); stroke etiology (TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification); functional outcome (mRS score) at 30 and 90 days.

Additional data were collected for patients with reocclusion treated with rEVT, including time from first recanalization to recurrent stroke onset; reocclusion of same vessel versus different vessel, neurological deficit (National Institutes of Health Stroke Scale (NIHSS) score, mRS score), baseline Alberta Stroke Program Early CT Score (ASPECTS) at recurrent NIHSS score, antithrombotic treatment at the time of recurrent stroke, TICI score, procedure-related complications (access-related,

embolization, and hemorrhagic complications), and functional outcome at 90 days after rEVT.

Assessment of study quality

Risk of bias for each eligible study was assessed with the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool by two authors (RO, MAC), using reocclusion as an intervention outcome. Potential conflicts were solved through discussion with assistance of a third and fourth reviewer (DAdS, LLN)

Statistical analysis

We calculated the pooled incidence of reocclusion per 100 patients with successful recanalization following EVT and 95% confidence intervals (CIs) using meta-analysis of proportions. A random-effects model with Freeman-Turkey double arcsine transformation was used for pooling the proportions. Heterogeneity between studies was assessed with I^2 statistics. Extracted incidences of reocclusion according to LVO etiology, and proportions of patients achieving favorable functional outcome in patients with and without vessel reocclusion were pooled using a random-effects model (DerSimonian Laird) owing to the presumed heterogeneity between individual study estimates and were compared using ORs. We performed a descriptive analysis of individual patient data on repeated EVT. We compared proportions of the outcome variable across groups using X^2 or Fisher's exact test as appropriate. As a secondary analysis, we also calculated the pooled proportion of favorable outcome in patients treated with rEVT and 95% confidence intervals (CIs) using study-aggregated data and meta-analysis of proportions.

A P value of 0.05 was considered statistically significant. Analyses were conducted using Stata Statistical Software Release 14 (StataCorp, College Station, Texas, USA).

RESULTS

We identified 847 references using our search strategy and 13 additional studies were obtained from manually reviewing key references. After exclusion of duplicates and assessment of titles and abstracts using the predefined inclusion and exclusion criteria we retrieved 62 studies in full text for detailed evaluation and verification of overlaps in study populations. The list of excluded studies and reasons for exclusion are provided in the data supplement (online supplemental table 1). Finally, we selected 15 studies for qualitative analysis and seven studies for quantitative analysis²⁹ (figure 1).

Ten of these studies were included in the analysis of prevalence, predictive factors, and outcome of reocclusion after successful EVT, which reported a total of 2321 cases with successful recanalization after EVT (online supplemental table 2). Six of these studies had a moderate risk of bias (online supplemental table 3A). The type of EVT procedure was in all studies selected at the discretion of the treating physician, most using direct aspiration and stent retrieval as routine procedures. A detailed description of the procedures performed in each cohort is provided in online supplemental table 4). Five studies were included in the analysis of rEVT, of which three had moderate risk of bias (online supplemental table 3B).

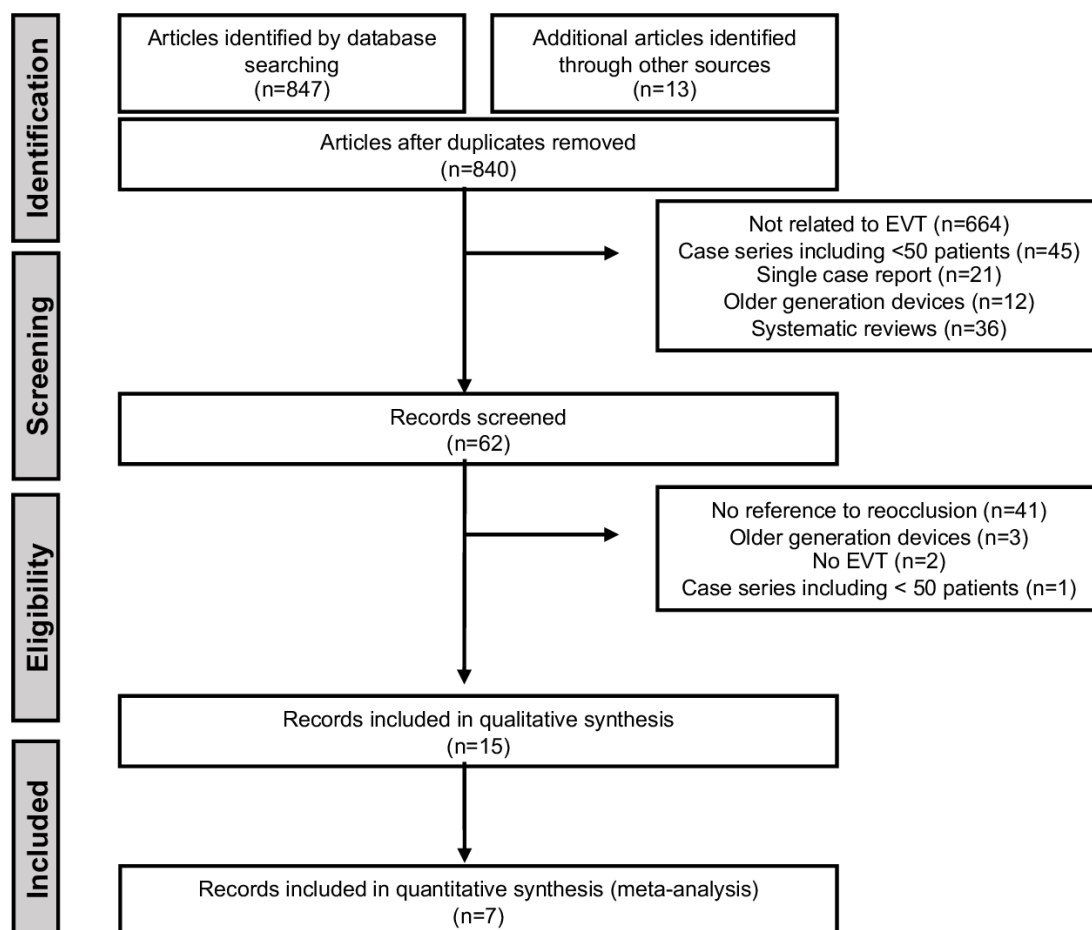


Figure 1 Flowchart summarizing literature search strategy. EVT, endovascular treatment.

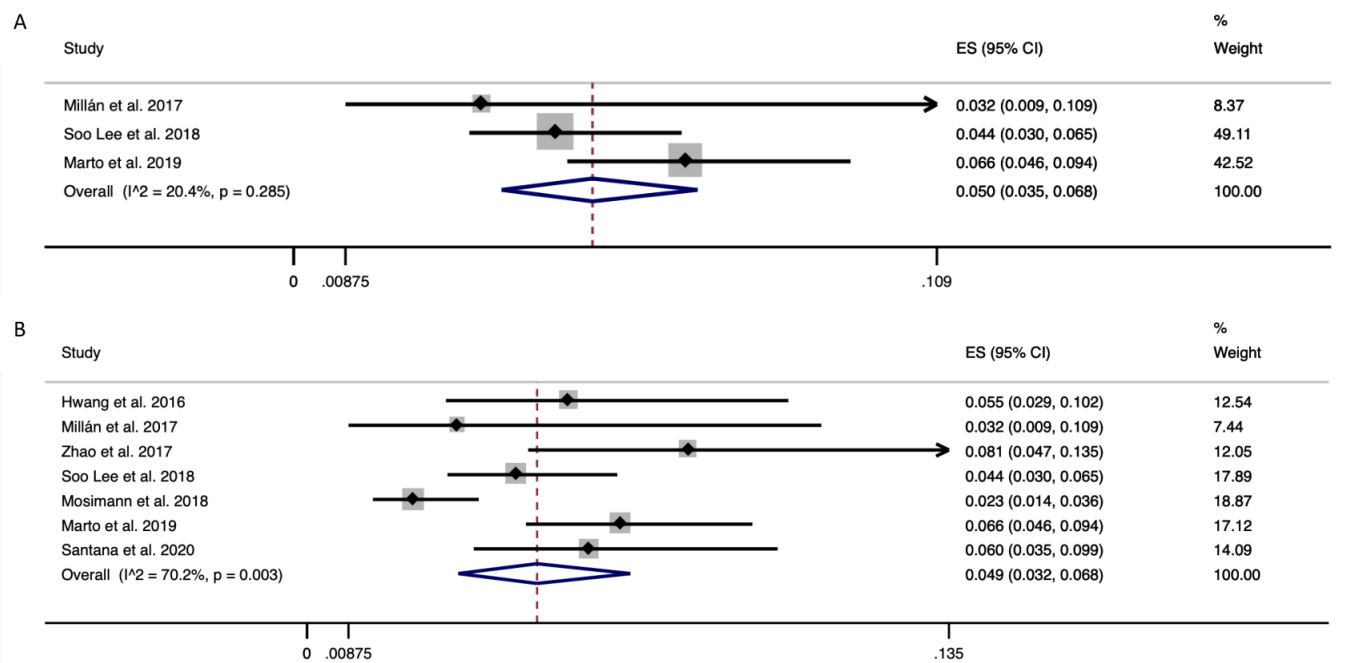


Figure 2 Rate of reocclusion (A) within the first 24 hours, and (B) within the first 7 days after endovascular treatment.

Incidence, predictive factors, and outcome of large vessel reocclusion after successful EVT

Incidence of large vessel reocclusion

For this analysis we excluded studies reporting reocclusion in populations considered not to be representative of the overall population of patients treated with EVT—namely, studies focusing only on patients with intracranial atherosclerosis,^{30 31} emergency carotid artery stenting,³² severe AIS and hypertension.³³

The mean age of the patients experiencing reocclusion in the included cohorts^{15 16 20 33–36} ranged from 63 to 72 years. Most patients had an occlusion in the anterior circulation (75/82 patients, 91.5%) and large artery atherosclerosis was the most frequently identified stroke mechanism (33/58 patients, 56.9%). Fifty-two percent received concomitant IVT treatment (33/63 patients).

The included studies described 91 same-vessel reocclusions within the first 7 days after EVT among 2067 patients, with a rate of same-vessel reocclusion up to 7 days after treatment of 4.9% (95% CI 3.2% to 6.8%, I²=70.2%). A sensitivity analysis considering reocclusion occurring within the first 24 hours (three studies, 1006 patients, 53 reocclusions) yielded a rate of same-vessel reocclusion of 5.0% (95% CI 3.5% to 6.8%, I²=20.4%, figure 2). With regard to studies focusing on specific stroke populations, Kim *et al* reported a reocclusion rate of 13.0% in patients with underlying intracranial atherosclerotic disease who received emergent intracranial angioplasty.³⁰ In a cohort of hypertensive patients with severe AIS, defined as NIHSS score ≥ 17 , the reocclusion rate after EVT was 15.7%.³³

Predictors of large vessel reocclusion

We explored the following risk factors of reocclusion: stroke etiology (four studies, 53 patients with reocclusion of 1441 patients)^{15 16 35 36}; and treatment with IVT (four studies, 63 patients with reocclusion of 1398 patients).^{15 16 35 36}

Patients with reocclusion were three times more likely to have large artery atherosclerosis as the indicated stroke etiology (OR=3.44, 95% CI 1.12 to 10.61, I²=50%), whereas

cardioembolic etiology was protective (OR=0.24, 95% CI 0.12 to 0.50, I²=0%). Data on the specific involvement of the intracranial arteries in patients with atherosclerotic disease was scarce.

There was no association between treatment with IVT and reocclusion (OR=0.83, 95% CI 0.48 to 1.43, I²=3.9%) (figure 3).

Some single studies described an association between other baseline characteristics and higher risk of reocclusion, such as proximal intracranial occlusion involving the internal carotid artery,¹⁵ M2 occlusions,¹⁶ higher platelet count on admission ($>220 \times 10^9/L$),¹⁶ or diabetes,³¹ but a quantitative synthesis was not possible. Risk factors specifically related to the technical procedure included higher number of device passes,¹⁵ residual thrombus/stenosis after EVT,¹⁶ and transient reocclusion during EVT.^{15 35} Acute carotid stenting or balloon angioplasty was associated with increased risk of reocclusion in one of the two included cohorts providing information on reocclusion rates stratified according to this procedure.^{15 36} Acute intracranial permanent stenting was not associated with a different rate of reocclusion,¹⁵ but information was scarce.

Functional outcome in patients with large vessel reocclusion

Reocclusion was associated with a fourfold higher likelihood of unfavorable functional outcome (mRS score 3–6) at 3 months compared with patients without reocclusion (three studies, OR=4.27, 95% CI 2.38 to 7.65, I²=0%)^{15 16 36} (online supplemental figure 1).

Repeated endovascular treatment in patients with large vessel reocclusion

We included five studies that identified patients with acute stroke receiving recurrent EVT within 30 days after a successful EVT (online supplemental table 5).^{19 37–40} Ninety patients were included (51 with same-vessel reocclusion and 39 with different-vessel reocclusion).

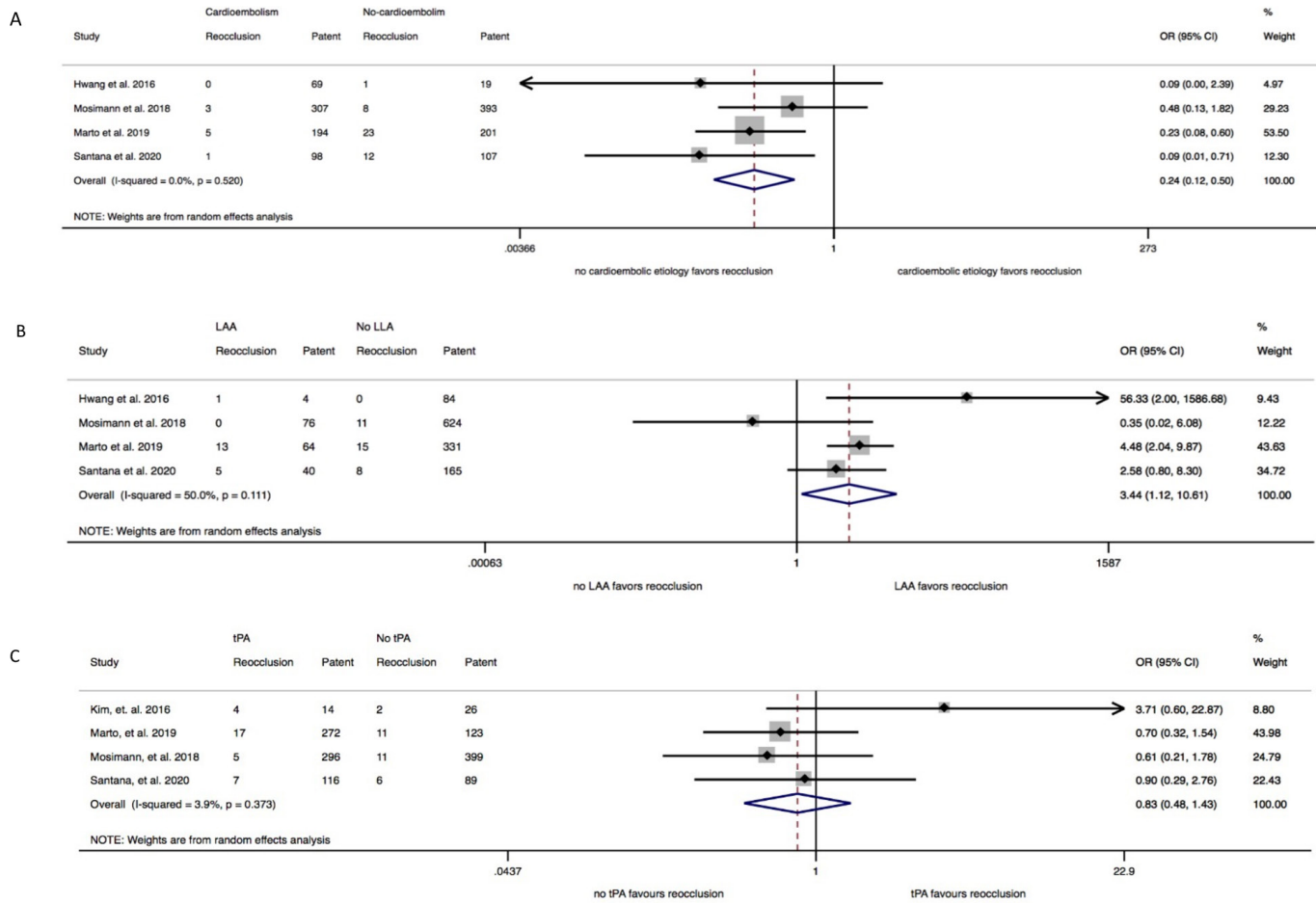


Figure 3 Rate of vessel reocclusion after successful endovascular treatment according to specific factors: (A) cardioembolic etiology, (B) large artery atherosclerosis, (C) treatment with intravenous thrombolysis. LAA, large artery atherosclerosis; tPA tissue plasminogen activator.

Four corresponding authors were contacted for additional data sharing. Unpublished deidentified individual patient data from the cohort described by Mohamed *et al*,⁴⁰ was used in accordance with a standing data sharing agreement. Their study described 43 patients who had repeated EVT for recurrent LVO within a 30-day window at several US centers. Fifty-five percent of those patients were male, with a mean age of 61.7 ± 15.8 years. At the time of recurrent stroke most patients were taking antiplatelet medication (53.5%) or anticoagulants (14%). In this cohort, most cases were reocclusions of the same vessel (65.1%), related to cardioembolism (46.5%), occurring in the first 7 days after the first EVT (83.7%).

Repeated EVT was a relatively rare procedure in the stroke centers contributing to the included cohorts, corresponding to 0.7–2.0% of the total volume of EVT procedures in patients with AIS performed in these hospitals, in the reported period.^{19 37 38 40} Using individual patient data, we describe the baseline characteristics, treatment details, and outcomes of 90 patients. The median time between first EVT and rEVT was 3 days, with 66 patients (73.3%) being treated within 7 days. Twenty percent of the treated reocclusions occurred within the first 24 hours after the index EVT. The proportion of cases with same-vessel reocclusion was 69.4% for patients with early reocclusion (within the first 24 hours) and 48.1% when considering reocclusion occurring after the first 24 hours (online supplemental table 6). The average age of the described patients was 63.6 ± 16.1 years, 51% were male. The median NIHSS score after the index ischemic stroke (assessed at 24 hours or at discharge, depending

on the studies) was 8 (IQR 2–17).^{37 39 40} Regarding clinical and radiological severity at the recurrent ischemic event for treated patients, the median NIHSS score immediately prior to rEVT was 14 (IQR 10–18.8) and the median ASPECTS was 9 (IQR 8–10). Most patients (79%, 64/81 patients) were receiving secondary stroke prevention at the time of the recurrent stroke due to LVO. Specifically, almost two thirds were taking antiplatelet drugs (44.4% single antiplatelets and 18.5% dual antiplatelets), and 18.3% were receiving anticoagulation treatment (8.6% vitamin K antagonists and 8.6% direct oral anticoagulants).

Cardioembolism was the assumed etiology for recurrent stroke in 50 cases (55.6%). However, stroke etiology was considerably different depending on the timing of reocclusion, with large artery atherosclerosis being more common in the first 24 hours after EVT (25%) than between 24 hours to 7 days (7%) (online supplemental table 7). Successful reperfusion was achieved after repeated EVT in 61/68 patients (89.7%). Two studies reported on the use of intracranial angioplasty or permanent stenting during rEVT.^{19 40} Intracranial stenting was performed in eight out of 51 patients (15.7%), more frequently in same-vessel reocclusions than in different-vessel reocclusions (75.0% vs 57.9%). Patients receiving intracranial stenting during rEVT more often had an mRS score >2 at 3 months (87.5% vs 55.3%).

The overall rate of procedural and postprocedural complications was 18% (11/61 patients), mostly related to intracranial bleeding (nine cases, 14.8%), which was symptomatic in five (8.2%).

Data on the criteria for patient selection were limited. Reasons indicated for withholding rEVT included extensive infarction in the reoccluded territory, risk of hemorrhagic transformation, and further distal clot location. The absolute number of patients achieving favorable functional outcome at 90 days was 39.7% (25/63 patients). A secondary analysis pooling the rates of favorable functional outcome at 90 days using meta-analysis, gave similar results (44%; 95% CI 25% to 64%, $I^2=44%$, (online supplemental figure 2). The mortality rate at 3 months was 18.8% (16/85 patients).

Information on the functional outcome after rEVT according to specific patient and procedural features is provided in online supplemental table 8). Anticoagulation at the time of recurrent stroke due to LVO was associated with favorable outcome at 90 days in patients receiving rEVT (OR=0.28, 95% CI 0.08 to 0.98, $I^2=0%$).

DISCUSSION

In this systematic review, we documented an incidence of reocclusion of 4.9% within the first 7 days after endovascular treatment for AIS due to LVO among 2067 patients with successful recanalization. A similar rate was documented in the sensitivity analysis including only studies with data on reocclusion within the first 24 hours after the procedure, suggesting that most events occur within the first hours. Patients experiencing reocclusion had a fourfold increased risk of unfavorable functional outcome, supporting the importance of maintaining vessel patency to achieve a good functional outcome.²⁰

In the analysis exploring predictors of reocclusion, large artery atherosclerosis as suspected etiology was associated with higher risk of reocclusion, while patients with cardioembolic etiology showed a lower risk of early reocclusion. Intravenous thrombolysis was not associated with a significantly lower risk of reocclusion.

AIS due to LVO is an heterogeneous disease that, broadly, can be associated with either embolic etiology or arteriopathy. We confirmed in this review that the presumed etiological mechanism of the index AIS is associated with the risk of postprocedural reocclusion. Indeed, atherosclerotic vessel disease has been associated with worse outcomes after mechanical thrombectomy, with higher rates of immediate reocclusion and in situ thrombo-occlusion.^{31–35} Our review suggests that having atherosclerotic vessel disease as the presumed etiology is also a risk factor for postprocedural reocclusion after a successful recanalization in a first procedure. Different mechanisms can be correlated with this increased risk, including artery–artery embolism, hemodynamic impairment, and in situ thrombo-occlusion. Also, especially in patients with intracranial atherosclerotic disease, endothelial damage, longer procedure times, more device passes, and residual stenosis may all occur more often after EVT and contribute to the increased risk of reocclusion.^{34–36} However, identifying the cause of LVO in the hyperacute phase remains challenging and the most likely stroke etiology is often established only several days or even weeks after the event.^{41–42} Certain imaging findings, such as hyperdense middle cerebral artery sign on head CT, have been associated with cardioembolic stroke, and new techniques such as vessel wall imaging show promise in the identification of atherosclerotic lesions of the intracranial arteries.⁴³ We could not find an association between the use of intravenous thrombolysis and vessel reocclusion in these patients, although the pooled proportion was slightly lower in treated patients. Protective mechanisms could include lysis of residual thrombi or fewer number of passes, but data to test these hypotheses were lacking.⁴⁴

Analysis of reocclusion rates according to specific periprocedural antithrombotic prophylaxis regimens was not possible in this review, due to inconsistency of the management protocols and scarce reported data. Of note, the administration of periprocedural antiplatelet therapy was not associated with a lower risk of acute reocclusion in the study by Kim *et al*,³⁰ an approach also not supported by the MR-CLEAN-MED trial.⁴⁵ Use of glycoprotein IIb/IIIa antagonists, such as low dose tirofiban, or the use of a direct thrombin inhibitor, such as argatroban, have been reported in selected cases,^{46–48} but there is an overall lack of data on the efficacy and safety of specific strategies targeted at reducing the risk of reocclusion in patients at higher risk. Our results suggest that future studies assessing the benefit of specific strategies targeting early reocclusion should consider the possible interaction with LVO etiology.

Another aim of this review was to describe the available evidence on the safety and outcomes of rEVT in patients with reocclusion occurring within 30 days from the index event. Overall, rEVT was performed in a small percentage of patients with a stroke (0.7–2.0%). The fact that the number of patients reported in these series is much lower than the 5.0% rate of reocclusion found in cohorts of patients with AIS and LVO treated with EVT in a similar setting suggests that this is a highly selected subset of patients.

Although a systematic analysis of the untreated patients is not possible, reasons for withholding rEVT were indicated in some of these studies and included extensive infarction in the reoccluded territory and perceived high risk of hemorrhagic transformation.¹⁶ Moreover, cardioembolic etiology was more frequent in rEVT cases, which may also suggest a selection bias, as clinicians can be more prone to perform rEVT in patients with presumed cardioembolic stroke. Also, almost all patients who received rEVT had ASPECTS equal or above 8, which again reflects the bias towards the ideal rEVT candidates. Anticoagulation at the time of recurrent LVO was associated with better functional outcome after rEVT, which may suggest a better prognosis in patients with recurrent LVO associated with embolic etiology.

The rate of procedure-related complications in patients treated with rEVT was higher than the 4% complication rate of EVT for AIS reported in major EVT trials.²⁶ Although data were limited, we found an overall rate of intracranial hemorrhage of 15% (8.2% symptomatic). However, it should be considered that about three-quarters of patients were treated within 7 days after the index event. Moreover, the proportion of patients treated with rEVT who had a favorable functional outcome was close to that described in patients treated with EVT for AIS due to LVO in general. Overall, this suggests that the procedure can be effective in selected patients with early reocclusion.

Our review has some limitations. First, there was heterogeneity between the studies regarding the location of LVO, endovascular treatment criteria, techniques, and exclusion criteria. We also acknowledge potential heterogeneity both on the report and definition of acute stroke and treatment complications. Third, patient management protocols, experience of the interventionalists, learning curve with new devices, and the specific devices in use varied across time. Fourth, the estimated rate of acute reocclusion was based on studies reporting same-vessel reocclusion, thus hampering the generalizability of these findings to cases of different-vessel reocclusion. Moreover, information on other specific stroke etiologies, such as arterial dissection, prior use of antithrombotic therapy, or whether large artery atherosclerotic disease specifically affected the reoccluded intracranial artery, was often not available. Finally, data available for the specific

analysis concerning rEVT were limited, although our review was strengthened by additional unpublished data. Additional limitations are related to the retrospective design of these studies and the concerns related to selection bias, including publication bias. We need prospective studies and, eventually, clinical trials to establish the most appropriate selection criteria for treatment in patients with rEVT.

In conclusion, this systematic review estimates an incidence of reocclusion up to 7 days after successful EVT for AIS due to LVO of 4.9%. Large artery atherosclerosis was associated with a higher risk of reocclusion. A favorable functional outcome at 90 days was achieved in 40% of the highly selected cases treated with rEVT at experienced centers. Acute clinical worsening after a successful EVT should prompt exclusion of reocclusion and, if confirmed, consideration of repeated thrombectomy in selected cases. We need studies assessing whether specific strategies might reduce the risk of reocclusion in patients at risk.

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