The perioperative complications and short-term death in endovascular treatment for acute stroke induced by extracranial carotid occlusion: a systematic review and a meta-analysis

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Abstract. – **OBJECTIVE:** Endovascular treatment (EVT) has been demonstrated superior to pharmacological thrombolysis in acute ischemic stroke (AIS) induced by extracranial internal carotid artery occlusion. This paper aims to summarize clinical evidence about EVT and assess its efficacy and safety on acute extracranial carotid occlusion.

MATERIALS AND METHODS: We systematically reviewed all studies that reported endovascular therapy as carotid stenting, stent retriever, aspiration, and angioplasty for acute extracranial carotid occlusion. Literature retrieval was performed in PubMed, Embase, and Cochrane library, dated from January 1st, 2005 to December 31st, 2020. The primary endpoint was a favorable outcome rate. Major secondary endpoints were SICH incidence, 90-day mortality rate, and complications. Meta-analysis and subgroup analysis were conducted to identify predictors for prognosis. This systematic review has been registered in PROSPERO (CRD42020181154) on July 18, 2020.

RESULTS: 10 studies with 620 patients were included in total. Endovascular approach presented a favorable outcome rate of 0.47 (0.37, 0.56), an acceptable 90-day mortality rate of 0.16 (0.13, 0.19), and a mild SICH rate of 0.07 (0.05, 0.10). Age and NIHSS at admission were negatively associated with favorable outcome, with odds ratio of 0.95 (0.92, 0.98) and 0.74 (0.62, 0.88) respectively. Lower age (p=0.049) and aspiration thrombectomy (p=0.041) predicted less SICH events. In subgroup in which time window > 6 hours, endovascular therapy presented similar encouraging results, with favorable outcome rate of 0.59 (0.51, 0.66), 90-day mortality rate of 0.11 (0.07, 0.17), and SICH rate of 0.04 (0.02, 0.09).

CONCLUSIONS: EVT can effectively improve neurological function and reduce 90-day mortality for acute extracranial carotid occlusion patients without increasing the risk of symptomatic intracranial hemorrhage. Endovascular therapy is safe to perform from 6 to 24 hours after symptom onset.

Key Words:
   Acute stroke, Extracranial internal carotid occlusion, Symptomatic intracranial hemorrhage, 90-day mortality, Complications, Prognostic factor.

Abbreviations

SICH = symptomatic artery; NIHSS = National Institute of Health stroke scale; AF = atrial fibrillation; GP = glycoprotein; EVT = endovascular therapy; CEA = carotid endarterectomy; CAS = carotid artery stent; MCA = middle cerebral artery; CAD = coronary artery disease; ASPECTS = Alberta Stroke Program Early CT Score; IV = intravenous; IA = intraarterial; ACST = acute carotid stent thrombosis.

Introduction

A substantial proportion of internal carotid occlusion patients traditionally end with adverse outcome[1]. Among AIS (acute ischemic stroke) patients with carotid artery occlusion, 2-12% could functionally recover, 40-69% would live with severe disability, and 16-55% die from fatal stroke[2]. In terms of patients with AIS induced by intracranial arterial occlusion, approximately 10-20% were observed occlusion in the ipsilateral extracranial carotid artery[3].

IV thrombolysis is a traditional treatment strategy for large artery occlusion induced acute stroke. However, application of intravenous

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thrombolysis is limited with a short time window (4.5 hours), low recanalization rate (less than 20%)[4], and unsatisfied favorable outcome rate (depending on occlusion site). In 2006, the MERCI trial first described the safety and efficacy of mechanical thrombectomy in acute stroke[5]. Since then, endovascular therapy has gradually become a mainstream option for cerebrovascular occlusion. Kappelhof et al[6] proposed that once successfully performed, revascularization procedure can achieve a better vascular recanalization and profound functional recovery.

However, concerns about short-term death and perioperative complications have never stopped. Some severe complications include symptomatic intracranial hemorrhage (SICH), distal embolism, artery dissection, vasospasm, etc. could pose secondary risk. Also, in light of the fact that most studies focus on intracranial artery occlusion[7] and tandem occlusion[8], limited evidence support EVT for extracranial carotid occlusion. Besides, the efficacy of EVT for patients with onset to treatment time > 6 hours remains unclear. Therefore, we conducted this analysis to systematically review the safety and efficacy of EVT for extracranial carotid occlusion, especially when the time window is beyond 6 h. In addition, we intend to summarize factors influencing clinical outcome and complication.

Materials and Methods

The study was performed according to the PRISMA guidelines[9] and was registered in PROSPERO, an international prospective register of systematic reviews (https://www.crd.york.ac.uk/PROSPERO/), with the registration number of CRD42020181154.

Search Strategy and Selection Criteria

We retrieved studies published from January 1 in 2005 to December 31 in 2020 in PubMed/Medline database, Web of Science database, and Cochrane Central Register of Controlled Trials (CENTRAL). Search terms were set as "extracranial internal carotid artery," "occlusion," "endovascular therapy" and "stroke." Two authors independently reviewed and evaluated all the articles through titles, abstracts, and full texts. A study would be included if: (1) cervical carotid occlusion is the cause of acute stroke; (2) endovascular therapy was performed (e.g., carotid artery stent, stent-retriever thrombectomy, aspi-

ration thrombectomy, angioplasty); (3) favorable outcomes, mortality (90 days), SICH, and other complications were reported.

Cervical carotid artery occlusion was defined as total occlusion of internal carotid artery at cervical segment, which should be confirmed by at least one of DSA, MRA, CTA, or Doppler sonography. A favorable outcome is recognized as modified Rankin Scale score between 0 and 2. Endovascular therapy can be performed either alone or after the IV-thrombolysis failed. Other complications included various perioperative complications (e.g., in-stent thrombosis, artery dissection, artery perforation, hyperperfusion syndrome).

A study was excluded if (1) it enrolled patients with subacute or chronic carotid artery occlusion; (2) etiology of carotid artery occlusions was only dissection; (3) it enrolled patients with external carotid artery occlusion; (4) it enrolled patients whose NIHSS at admission < 4. Subacute or chronic carotid occlusion was defined as occlusion time beyond 7 days. Etiologies of carotid artery occlusion were composed of atherosclerosis, cardioembolism, and a small portion of artery dissection. Therefore, a study enrolled only carotid artery dissection resulted in selection bias.

Data Quality Assessment

Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information System (JBI-SUMARI) was used to evaluate the quality and bias of the included 10 studies. Critical appraisal checklists for Case series contain 10 questions. Four answers were given to each question (yes, no, nuclear, and not applicable), corresponding to different grades of quality. The discrepancy was resolved by two reviewers through discussion until consensus was reached.

Characteristics Screening

Essential information about studies were extracted from the following aspects: (i) Patient characteristics: gender, mean age, occlusion etiology, ASPECTS, NIHSS scores at admission; (ii) Disease history: hypertension, hyperlipidemia, diabetes, atrial fibrillation (AF), coronary artery disease (CAD); (iii) Details of treatment: revascularization approach, onset to reperfusion time, procedure duration; (iv) Clinical endpoints: the primary endpoint was favorable outcome (mRS 0-2), the secondary endpoints were mortality within 90 days, incidence of SICH and all periop-

erative complications; (v) Prognostic Predictors: predictors calculated by multivariate logistic regression model.

Statistical Analysis

We calculated the overall rate of favorable outcome, incidence of 90-day death, and SICH event, conducted meta-regression analysis and subgroup analysis of favorable prognostic factors. Cochran's Q test and I^2 test were used to quantify the heterogeneity among trials and subgroup differences. Cochran's Q test was used to verify subgroup differences. If $p \leq 0.05$, the between-subgroup differences were considered to be statistically significant. The random-effect model was used for data analysis when $I^2 > 75\%$; otherwise, the fixed-effect model was used. We carried out the Z-test to evaluate statistical significance in meta-regression analysis and checked publication bias through Begg's and Egger's regression asymmetry test. All statistical analysis and graphs were accomplished through R statistical software version 3.6.1.

Results

Characteristics of Included Studies

We included 10 studies with 620 patients in total[10-19] (Table I). Detailed literature screening process was displayed in the PRISMA flow dia-

gram[9] (Figure 1). Sample size of included studies ranged from 9 to 324. Mean age ranged from 57 to 77 years. Studies were published from 2005 to 2020. Surgeries were performed from 2002 to 2018. Major complications described include symptomatic ICH, artery dissection, and distal embolism. Rare complications include vessel perforation, neck hematoma, femoral hematoma. Less number of females were included than males (216 vs. 379).

Through JBI critical appraisal quality assessment of 10 studies, Jovin et al[13] meet 6 criteria out of 10; de Castro-Afonso et al[18] meet 7 criteria out of 10; while other studies meet 9 or 10 criteria out of 10. In all studies, participants' condition was measured and identified in a reliable and standard method. Demographic and clinical information was clearly reported for all studies. Quality evaluation results were summarized and presented in Table II.

Endpoints

With respect to primary endpoint, the proportion of favorable outcomes was 0.47 (0.37, 0.56) with a large heterogeneity ($I^2 = 74\%$) (Figure 2A). For secondary endpoints, the incidence of SICH was 0.07 (0.05, 0.10) with a moderate heterogeneity ($I^2 = 53\%$) (Figure 2B), and the incidence of deaths in 90 days was 0.16 (0.13, 0.19) with no heterogeneity ($I^2 = 0\%$) (Figure 2C).

Table I. Basic characteristics of included studies.

Author	Surgery period	Num.	F:M	Mean age	NIHSS	Devices and procedures
Okumura et al[10] 2019	2015.01-2017.12	24	6:18	77	17	CAS; Penumbra/Solitaire
Jadhav et al[11] 2018	2003.11-2016.04	107	44:63	63	8	MERCI/Manual aspiration thrombectomy
Gliem et al[12] 2017	2010.12-2014.06	28	13:15	68	13	CAS; Stent retriever thrombectomy
Jovin et al[13] 2005	2002.01-2005.03	25	NA	62	14	CAS
Papanagiotou et al[14] 2011	2006-2010	22	5:17	64.6	17.2	CAS; Penumbra/Solitaire
Leker et al[15] 2013	2002-2012	33	12:21	57	20.2	MERCI/stent retriever devices Angioplasty; CAS
Paciaroni et al[16] (ICARO-3) 2014	2010.01-2013.08	324	119:205	62.9	15.8	Mechanical clot disruption; Stent retrieval/aspiration thrombectomy
Park et al[17] 2020	2011.01-2018.11	29	6:23	73.6	11.8	CAS;Penumbra/Solitaire
Mizowaki et al[19] 2020	2014.06-2017.12	19	7:12	77	20.5	Stent retriever thrombectomy; PTA; CAS
Castro-Afonso et al[18] 2020	2011.06-2017.06	9	4:5	77	11.8	Angioplasty; CAS

ICARO, Intravenous Thrombolysis or Endovascular Therapy for Acute Ischemic Stroke Associated with Cervical Internal Carotid Artery Occlusion study. CAS, carotid artery stent. NA, not available. F:M, Female: Male. PTA, percutaneous transluminal angioplasty.
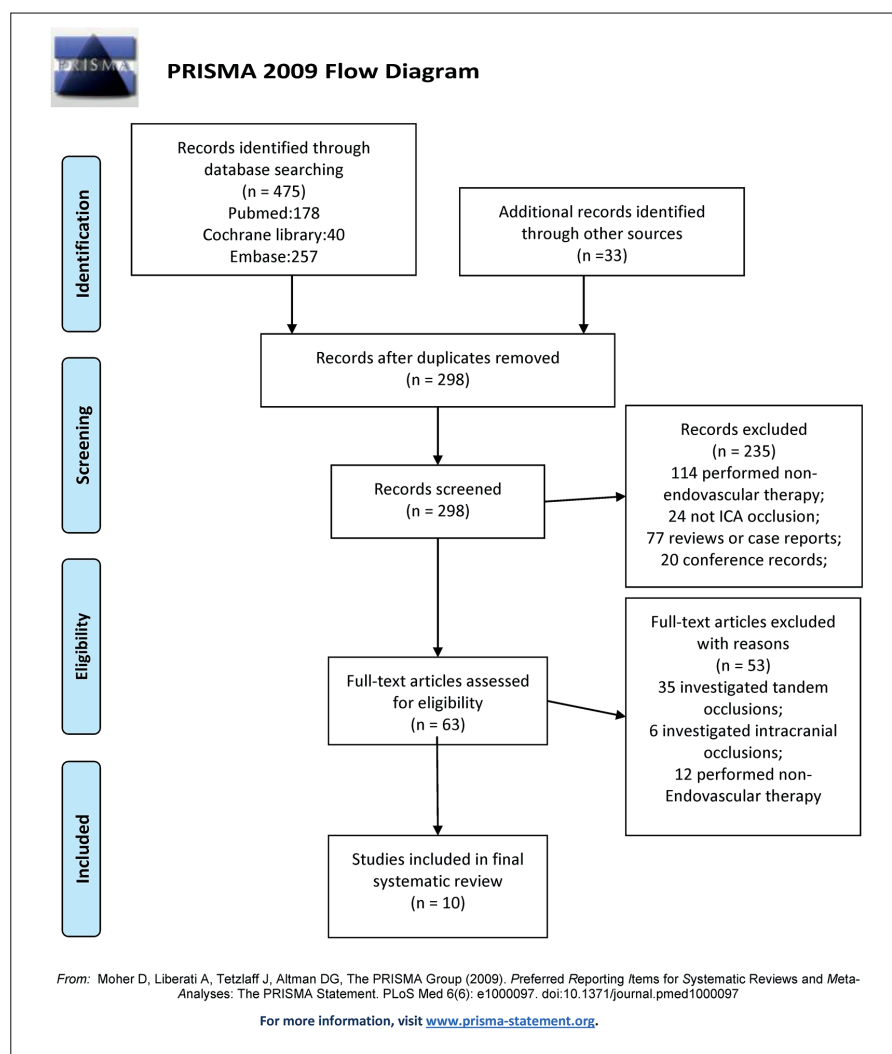
Figure 1. PRISMA 2009 flow diagram.

Table II. JBI critical appraisal quality assessment of the case series study.

Study	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
Okumura et al[10]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Jadhav et al[11]	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
Gliem et al[12]	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
Jovin et al[13]	N	Y	Y	Y	Y	N	N	Y	Y	N
Papanagiotou et al[14]	Y	Y	Y	Y	Y	Y	Y	Y	N	N
Leker et al[15]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Paciaroni et al[16] (ICARO-3)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Park et al[17]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Mizowaki et al[19]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Castro-Afonso et al[18]	N	Y	Y	Y	Y	Y	Y	Y	N	N

Note: (1) Were there clear criteria for inclusion in the case series?; (2) Was the condition measured in a standard, reliable way for all participants included in the case series?; (3) Were valid methods used for identification of the condition for all participants included in the case series?; (4) Did the case series have consecutive inclusion of participants?; (5) Did the case series have complete inclusion of participants?; (6) Was there clear reporting of the demographics of the participants in the study?; (7) Was there clear reporting of clinical information of the participants?; (8) Were the outcomes or follow up results of cases clearly reported?; (9) Was there clear reporting of the presenting site(s)/clinic(s) demographic information?; (10) Was statistical analysis appropriate? Y: Yes; N: No.
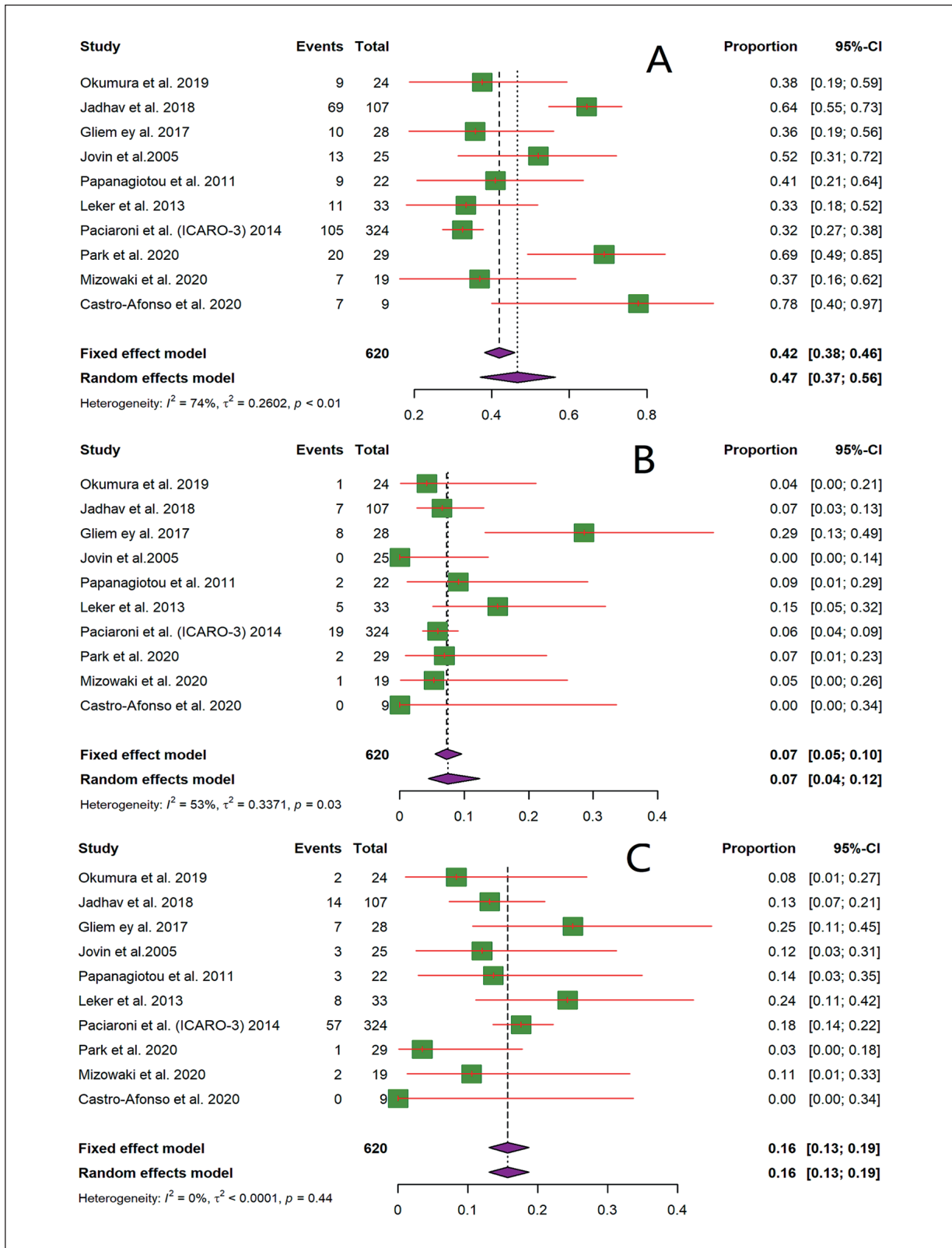
Figure 2. Forest plot of favorable outcome, SICH, and 90-day mortality. The favorable outcome rate is 0.47 (0.37, 0.56), with a huge heterogeneity (**A**). EVT showed an acceptable 90-day mortality rate of 0.16 (0.13, 0.19) (**B**), and a mild SICH rate of 0.07 (0.05, 0.10) (**C**).

Prognostic Factors

Two factors were identified to predict favorable outcomes: age and NIHSS score. Advanced age presented an OR of 0.95 (0.92, 0.98) with little heterogeneity (I^2=0%) (Figure 3). High NIHSS score presented OR of 0.74 (0.62, 0.88) with mild heterogeneity (I^2=25.8%). Thus, both advanced age and high NIHSS score indicate good prognosis. Other than above, male gender was not recognized as a prognostic factor since the OR is 2.68 (0.60, 12.01) (Figure 3).

Several prognostic factors were reported in only one study. Higher ASPECT score and distal embolism predicted poor clinical outcome, while cardioembolism etiology predicted more favorable outcome. As for mortality in 90 days, Jadhav et al[11] indicated age as a positive factor of death. However, more evidence is in demand to support their conclusions.

Subgroup-Analysis

Subgroup-analysis was performed based on age, NIHSS at admission, and aspiration throm-bectomy. Our results showed that higher NIHSS at admission is associated with less favorable outcomes. The overall proportion of favorable outcome is 0.58 (0.47, 0.69) in NIHSS at admission<15 subgroup, and 0.33 (0.29, 0.38) in NIHSS≥15 subgroup, which is consistent with previous prognostic factors analysis (Figure 4). Thus, NIHSS is reliable in predicting prognosis. Results of subgroup analysis showed that lower age (p=0.049) and aspiration thrombectomy (p=0.041) are in connection with lower SICH risk. Four studies performed thrombectomy through aspiration device, presenting an overall SICH incidence of 0.06 (0.04, 0.08). In contrast, among studies without aspiration thrombectomy, SICH incidence increased to 0.11(0.06, 0.17). Furthermore, SICH incidence of age ≥ 65 years is twice higher than age < 65 years [0.12 (0.07, 0.20) *vs.* 0.06 (0.04, 0.08)] (Figure 4). However, we identified no prognostic factor associated with 90-day mortality.

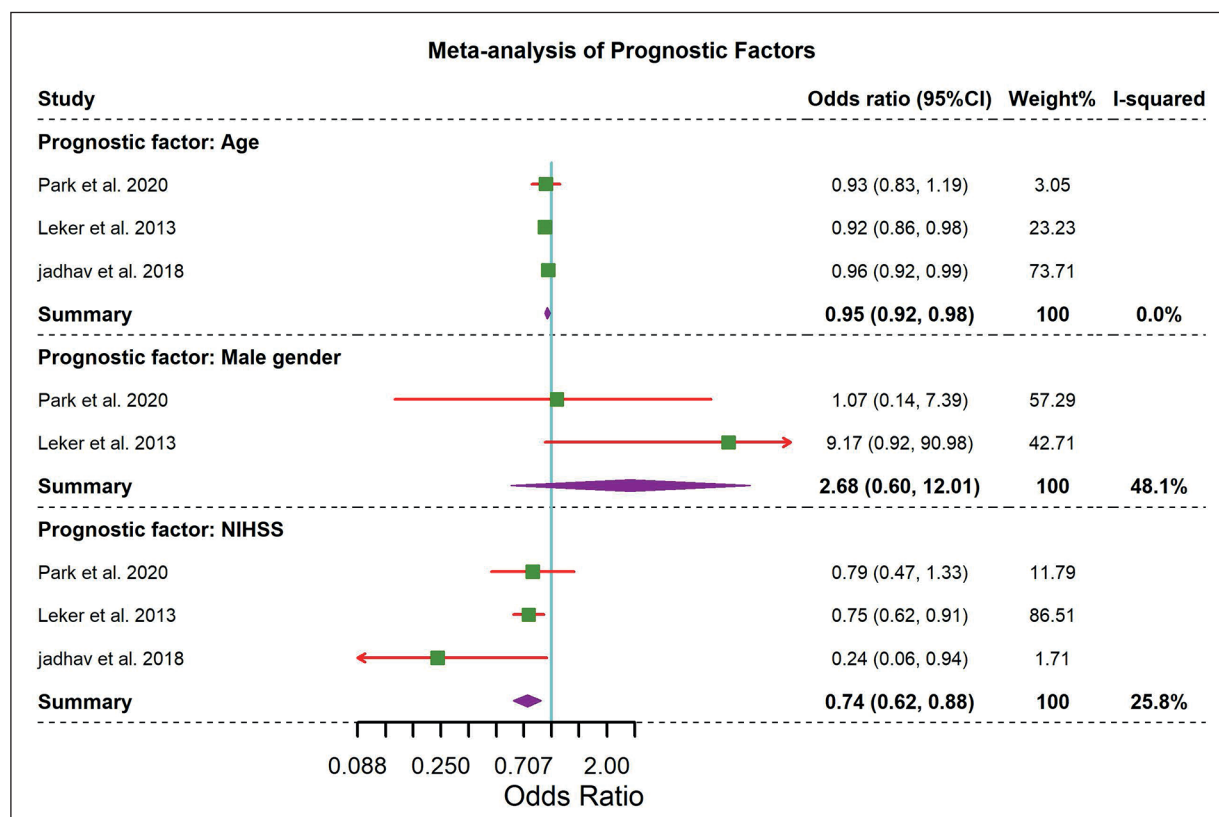To identify the safety and efficacy of EVT when the time window is beyond 6 hours, we syn-

Figure 3. Meta-analysis of prognostic factors for favorable outcome. Older age predicts fewer favorable outcome [OR: 0.95(0.92, 0.98)]; Gender has no effect on favorable outcome [OR: 2.68 (0.60, 12.01)]; Higher NIHSS score predicts fewer favorable outcome [OR: 0.74 (0.62, 0.88)].
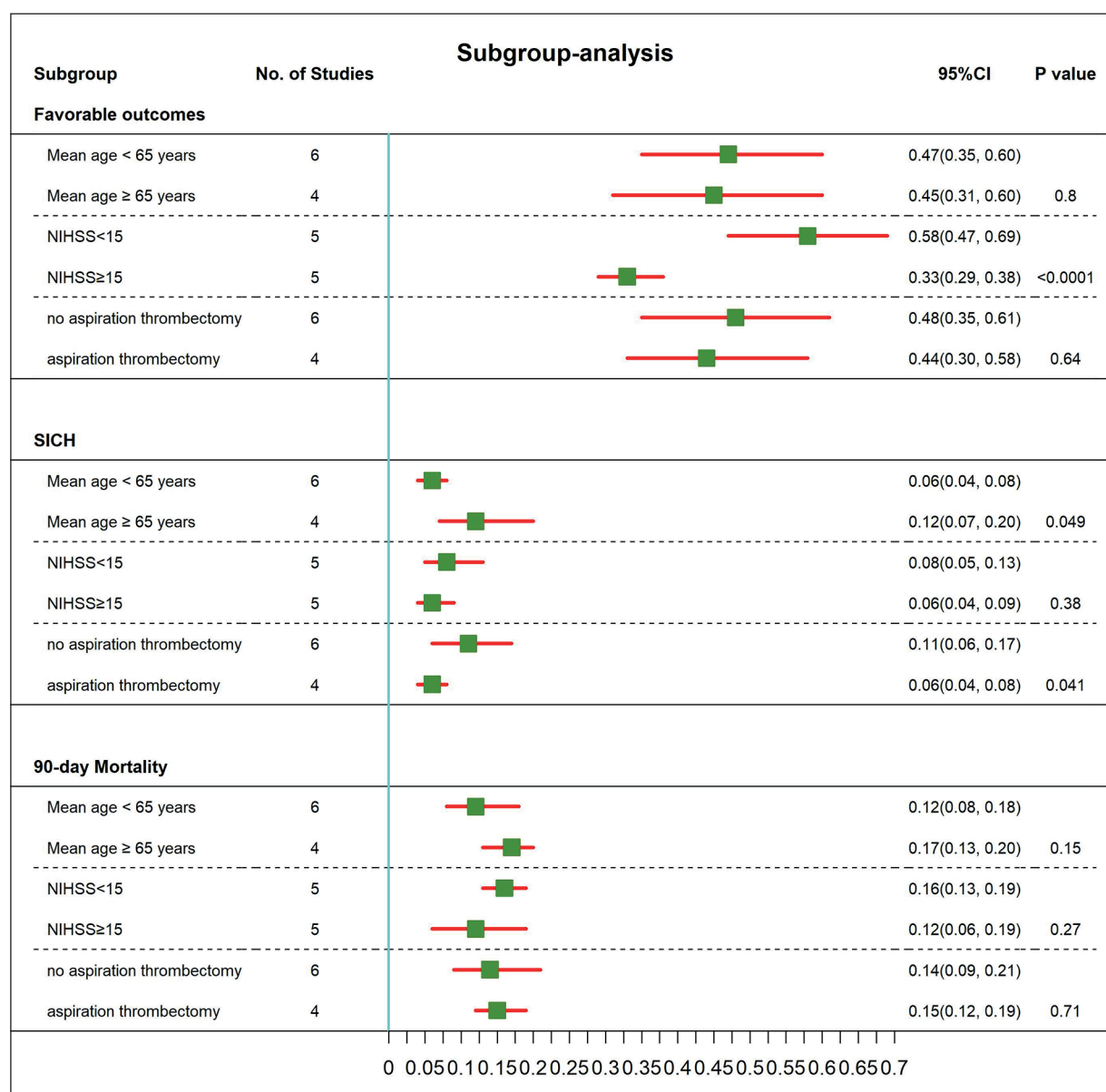
Subgroup-analysis

Subgroup	No. of Studies		95%CI	P value
Favorable outcomes				
Mean age < 65 years	6		0.47(0.35, 0.60)	
Mean age ≥ 65 years	4		0.45(0.31, 0.60)	0.8
NIHSS<15	5		0.58(0.47, 0.69)	
NIHSS≥15	5		0.33(0.29, 0.38)	<0.0001
no aspiration thrombectomy	6		0.48(0.35, 0.61)	
aspiration thrombectomy	4		0.44(0.30, 0.58)	0.64
SICH				
Mean age < 65 years	6		0.06(0.04, 0.08)	
Mean age ≥ 65 years	4		0.12(0.07, 0.20)	0.049
NIHSS<15	5		0.08(0.05, 0.13)	
NIHSS≥15	5		0.06(0.04, 0.09)	0.38
no aspiration thrombectomy	6		0.11(0.06, 0.17)	
aspiration thrombectomy	4		0.06(0.04, 0.08)	0.041
90-day Mortality				
Mean age < 65 years	6		0.12(0.08, 0.18)	
Mean age ≥ 65 years	4		0.17(0.13, 0.20)	0.15
NIHSS<15	5		0.16(0.13, 0.19)	
NIHSS≥15	5		0.12(0.06, 0.19)	0.27
no aspiration thrombectomy	6		0.14(0.09, 0.21)	
aspiration thrombectomy	4		0.15(0.12, 0.19)	0.71

0 0.05 0.1 0.15 0.2 0.25 0.3 0.35 0.4 0.45 0.5 0.55 0.6 0.65 0.7

Figure 4. Results of subgroup analysis. NIHSS < 15 is associated with higher favorable outcome rate; age < 65 years and aspiration thrombectomy are associated with less SICH rate.

thesized studies in which the onset meantime was between 6 and 24 hours. The results displayed overall favorable outcome rate as 0.59 (0.51, 0.66), overall mortality as 0.11 (0.07, 0.17), overall SICH rate as 0.04 (0.02, 0.09), with all endpoints are considerably satisfactory.

Other Rare Complications

Except for SICH, other complications were reported as well. Four artery dissection cases were reported by Jadhav et al[11], three by Paciaroni et al[16], two by Park et al[17] and one by Jovin et al[13].

Besides SICH, distal embolisms were also reported by Jadhav et al[11] (28 cases) and Paciaroni et al[16] (3 cases). Furthermore, hyperperfusion syndrome was reported by Park et al[17] (3 cases) and Jadhav et al[11] (2 cases). It is also noting that in-stent occlusion was not reported.

Publication Bias

The test for funnel plot asymmetry is not significant. Thus, the publication bias was ignored (*p*=0.26 for Egger's test, *p*=0.32 for Begg's test).

Discussion

Though the overall proportion of favorable outcome (0.47) is promising, the high heterogeneity among included studies is a great concern. We believe this could attribute to the different selection criteria of patients. Notably, Papanagiotou et al[14] set enrollment criterion as NIHSS≥10, while Leker et al[15] set as NIHSS≥4, Mizowaki et al[19] set as NIHSS≥6. Inter-study diversity of mean NIHSS score ranged from 8 to 20.5 and partially explained the heterogeneity. In addition, age and multiple endovascular devices were assumed as two other contributing/causing factors. With odds ratio near to one, age has also been documented as a prognostic factor. The proportion of favorable outcome ranges widely from 0.32 to 0.78, which could be the consequence of different criteria for selection of patients.

Mokin et al[20] conducted a systematic review and compared pharmacological thrombolysis with endovascular therapy. Although, in their results, EVT achieved a better outcome (43.5% *vs.* 26.3%, *p*<0.0001) and displayed a higher risk of SICH (11.4% *vs.* 3.9%, *p*=0.001). We believe this could attribute to the IA thrombolysis involvement in EVT treatment. Therefore, we excluded EVT studies involving IA thrombolysis in our analysis and calculated out a milder SICH rate.

ICARO-3[16], a non-randomized multicenter prospective paired study, compared intraarterial procedure with intravenous thrombolysis in acute ICA occlusion. In IA procedure group, combination of mechanical thrombectomy and IA/IV thrombolysis presented non-significantly but more encouraging favorable outcome, lower mortality, but higher SICH incidence. One limitation of ICARO-3 is partial patients were given all of IV thrombolysis (tPA), IA thrombolysis (urokinase/tPA), and mechanical thrombectomy, which may sharply increase the risk of intracranial hemorrhage (IA procedure group *vs.* IV group: 37% *vs.* 17.3%, *p*=0.0001). Besides, the therapeutic time window was different in two groups: 4.5 hours for IV thrombolysis group and 6 hours for EVT group. Currently, the time window for IV thrombolysis is strictly limited to 4.5 hours. Several attempts to open up this window has failed. Nevertheless, feasibility of EVT for time window beyond 6 hours have been encouragingly confirmed. The DEFUSE 3 trial[20], as a multicenter randomized trial, investigated the efficacy and safety of thrombectomy in acute stroke from 6 to 16 hours after onset of symptom. The results showed that dramatic improvement on outcome (45% *vs.* 17%, *p*<0.001) and significant reduction of 90-day mortality (14% *vs.* 26%, *p*=0.05) were achieved by thrombectomy compared with IV thrombolysis. However, DEFUSE 3 trial focused on proximal middle cerebral artery and internal carotid artery occlusion. Whether thrombectomy is feasible for extracranial internal carotid artery occlusion in time window beyond 6 hours warrants further investigation.

Jovin et al[13] divided patients into two groups: acute stroke group with mean time to angiography of 5 hours, and subacute group with mean time to angiography of 30 hours. 24 hours after carotid stent, subacute group patients achieved higher mean NIHSS score improvement (*p*=0.01) and better overall outcome 30 days after carotid stent (*p*=0.05), which might be due to the careful patient selection for subacute group. In Jadhav et al[11], 36% (n=39) patients had 24-72 hours from symptom onset to revascularization, and 29% (n=31) beyond 72 hours. Okumura et al[10] enrolled patients with time window between 6 and 24 hours. Compared to the aforementioned studies, our results showed promising favorable outcome rate, mild mortality rate and less SICH rate, which is relatively acceptable. After analyzing studies beyond 6-hour time window, we concluded that the safety of EVT considerably deserves to be discussed in a wider/larger time window.

Jadhav et al[11] reported 22% distal embolism in 65% dEPD (distal embolic protection device) patients. The authors employed IA thrombolysis to dissolve small distal occlusion (i.e., M3) and performed thrombectomy (stent-retriever/aspiration) for proximal occlusion. The post-hoc sensitivity analysis in Jadhav et al[11] showed that dEPD could not significantly prevent cerebrovascular embolism events (*p*=0.51). The authors assumed that proximal EPD might be more effective. In PROFI (Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection During Carotid Artery Stenting) Study[21], authors proved that proximal EPD has better effect on cerebral embolization prevention. Lee et al[22] had similar conclusions. Stabile et al[23] compared Filter Cerebral Protection and Proximal Balloon Occlusion in their meta-analysis and confirmed the superiority of proximal EPD over distal EPD in preventing CAS-related cerebral embolization. In a case-control study, Maegerlein

et al[24] also indicated a significant association between proximal EPD and shorter procedure time, higher successful recanalization rate, and higher complete reperfusion rate.

Acute carotid stent thrombosis (ACST) is a rare but devastating post elective CAS complication. One of its characteristics is failure to enjoy rapid flow normalization. In Yoon et al[25], aspirin and clopidogrel were given *via* nasogastric tube to prevent ACST. Whereas intravenous loading of glycoprotein IIb/IIIa inhibitor is faster for producing antiplatelet effects, which would be more effective for ACST prevention.

GP IIb/IIIa receptor antagonists as an antiplatelet drug can serve as a method of preventing ACST after CAS. At present, the safety of GP IIb/IIIa antagonists remains controversial. Heck et al[26] suggested that abciximab could increase the risk of SICH. Stampfl et al[3] reported four cases of SICH and three of them received tirofiban. Kellert et al[27] showed that tirofiban could significantly increase risk of fatal bleeding for patients who received mechanical thrombectomy. Ciccone et al[28] presented the association between abciximab and risk of intracranial hemorrhage in acute ischemic stroke in their review. Our previous systematic review[29] demonstrated that low-dose application of tirofiban can be guaranteed in AIS, especially for those patients at a lower age and NIHSS score.

In addition to pharmacological thrombolysis and EVT, emergent carotid endarterectomy (CEA) seems to become another option for acute carotid occlusion. Schubert et al[30] performed CEA in 12 cases, five of which used Fogarty embolectomy catheters. The final results presented a 58% favorable outcome rate and zero 90-day mortality. Currently, there is still a lack of studies comparing CEA and EVT for acute ICA occlusion, but we suggest EVT as a potential therapeutic strategy for acute ICA occlusion. Currently, there is no study comparing CEA and EVT for acute ICA occlusion, but EVT should be considered when combined with intracranial distal occlusion, and CEA is more invasive.

Park et al[17] made a comparison between isolated cervical ICA occlusion and tandem occlusion. With insignificant difference between their 3-month outcome (68.9% *vs.* 63.0%, *p*=0.476), isolated cervical ICA occlusion achieved higher successful recanalization rate (96.6% *vs.* 76.1%, *p*=0.019). Besides, patients who received IV-thrombolysis were not given aspirin and clopidogrel; and those who did not receive IV-throm-

bolysis were not given aspirin or clopidogrel. There was no difference in favorable outcome between them (67.3% *vs.* 65.2%, *p*=0.598).

This review has a few limitations. First, most included studies are retrospective, which could lead to certain selection bias and reporting bias. Second, most of included studies are single arm (case series), we cannot compare EVT with pharmacological thrombolysis or other kinds of therapy strategies. Third, the type of endovascular device varied among studies, resulting in heterogeneity.

Conclusions

Our meta-analysis indicated the efficacy and safety of EVT in acute extracranial carotid occlusion beyond 6-hour time window. NIHSS at admission, age, and aspiration thrombectomy are prognostic factors for favorable outcomes or SICH.

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