Thrombectomy outcomes of intracranial atherosclerosis-related occlusions: a systematic review and metaanalysis

Anderson Chun On Tsang, MBBS[1,2], Emanuele Orru, MD[2], Jesse M Klostranec, MD PhD[2], I-Hsiao Yang, MD[2], Kui Kai Lau, MBBS PhD[3], Frederick Chun Pong Tsang, MBBS[1], Wai Man Lui, MBBS[1], Vitor Mendes Pereira, MSc MD[2,4], Timo Krings, MD PhD[2]

Affiliations:

1. Division of Neurosurgery, Department of Surgery, The University of Hong Kong, Hong Kong
2. Division of Neuroradiology, Joint Department of Medical Imaging, Toronto Western Hospital, University of Toronto, Toronto, Canada
3. Division of Neurology, Department of Medicine, The University of Hong Kong, Hong Kong
4. Division of Neurosurgery, Department of Surgery, Toronto Western Hospital, University Health Network, University of Toronto, Toronto, Canada

Corresponding author:

Anderson Chun On Tsang, Address: Room 701, Administrative Block, Department of Neurosurgery, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong. Telephone: +852 22553368. Email: acotsang@hku.hk

Keywords

Intracranial stenosis, thrombectomy, angioplasty and stenting, endovascular recanalization

Abstract

Background and Purpose

Intracranial atherosclerosis (ICAS) is an important cause of large vessel occlusion (LVO) and poses unique challenges for emergent endovascular thrombectomy. The risk factor profile and therapeutic outcomes of patients with ICAS-related occlusions (ICAS-O) are unclear. We performed a systematic review and meta-analysis of studies reporting the clinical features and thrombectomy outcomes of LVO stroke secondary to underlying ICAS (ICAS-O) versus those of other etiologies (non-ICAS-O).

Methods

A literature search on thrombectomy for ICAS-O was performed. Random-effect meta-analysis was used to analyze the prevalence of stroke risk factors and outcomes of thrombectomy between ICAS-O and non-ICAS-O groups.

Results

A total of 1967 patients (496 ICAS-O and 1471 non-ICAS-O) were included. The ICAS-O group had significantly higher prevalence of hypertension (OR 1.46, 95% CI, 1.10-1.93), diabetes mellitus (OR 1.68, 95% CI, 1.29-2.20), dyslipidemia (OR 1.94, 95% CI, 1.04-3.62), smoking history (OR 2.11, 95% CI, 1.40-3.17), but less atrial fibrillation (OR 0.20, 95% CI, 0.13-0.31) than the non-ICAS-O group.

Regarding thrombectomy outcomes, ICAS-O had higher intraprocedural reocclusion rate (OR 23.7, 95% CI, 6.96-80.7), need for rescue balloon angioplasty (OR 9.49, 95% CI, 4.11-21.9), rescue intracranial stenting (OR 14.9, 95% CI, 7.64-29.2) and longer puncture-to-reperfusion time (80.8 vs 55.5 minutes, mean difference 21.3, 95% CI, 11.3-31.3). There was no statistical difference in the rate of final recanalization (mTICI2b/3) (OR 0.67, 95% CI, 0.36-1.27), symptomatic intracerebral hemorrhage

(OR 0.79, 95% CI, 0.50-1.24), good functional outcome (mRS 0-2) (OR 1.16, 95% CI, 0.85-1.58) and mortality (OR 0.94, 95% CI, 0.64-1.39) between ICAS-O and non-ICAS-O.

Conclusions

Patients with ICAS-O display a unique risk factor profile and technical challenges for endovascular reperfusion therapy. Intraprocedural re-occlusion occurs in one-third of ICAS-O patients. Intraarterial glycoprotein IIb/IIIa inhibitors infusion, balloon angioplasty and intracranial stenting may be viable rescue treatment to achieve revascularization, resulting in comparable outcomes to non-ICAS-O.

Introduction

Endovascular thrombectomy has become the standard of care for acute stroke due to large vessel occlusion (LVO).[1] Most LVOs are secondary to emboli of cardiac or carotid origin, and current techniques of stent-retriever and aspiration thrombectomy are highly effective in removing these emboli. On the other hand, these techniques are less efficacious in LVOs with underlying intracranial atherosclerosis (ICAS).[2, 3] Intraprocedural re-occlusion has been commonly reported and rescue treatment with intra-arterial thrombolysis, balloon angioplasty or stenting may be required for successful revascularization.[4] In addition, patients with ICAS-related occlusions (ICAS-O) demonstrate different risk factor profiles and unclear therapeutic outcomes. To understand the clinical features and thrombectomy outcomes of ICAS-O, we performed a systematic review and meta-analysis of studies comparing ICAS-O and non-ICAS-O treated with endovascular thrombectomy.

Methods

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Literature Search Strategy and Study Selection

A systematic search in the English literature with Ovid Medline, Pubmed, and Embase from January 2010 to December 2018 was performed. The following terms and their combinations were used as keywords or MeSH terms: intracranial atherosclerosis, stenosis, stenting, angioplasty, mechanical thrombectomy, endovascular and stroke. We also manually searched the reference lists of the 18 relevant articles to identify additional studies reporting on the clinical features and thrombectomy outcome of ICAS-O that were not included in the initial literature search.

The identified studies were then evaluated with the following inclusion criteria: (1) studies comparing clinical features and risk factors of ICAS-O and non-ICAS-O; (2) studies reporting separately the thrombectomy and clinical outcomes in ICAS-O and non-ICAS-O groups. The exclusion criteria were: (1) non-comparative studies reporting outcomes only on ICAS-O without a control group of non-ICAS-O, (2) case reports or studies with less than 5 patients in the ICAS-O group, (3) studies that reported ICAS treatment in a subacute, non-emergent setting. Both randomized and observational studies were included. This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. As this is a meta-analysis of published studies, formal approval by an ethics committee was not required.

Risk of bias assessment

The risk of bias of the included papers was assessed by two independent readers with the Newcastle Ottawa scale for cohort studies.[5] The scale assesses the selection, comparability, and ascertainment of outcomes of the study groups, with a higher score indicating lower risk of bias. Studies that used well-defined selection criteria, with comparable baseline stroke severity, clearly defined diagnostic criteria for ICAS-O, and those that had independent assessment of clinical and technical outcomes are considered to have a low risk of bias.

Outcome variables

Patients were divided into ICAS-O and non-ICAS-O groups. For the purpose of this study, patients were considered ICAS-O if they fulfilled the diagnosis criteria adopted by the authors of the respective paper. Patients with LVO who received thrombectomy in the same study period and not diagnosed as ICAS-O were considered non-ICAS-O.

The primary outcome was the rate of successful reperfusion, defined by a final modified Thrombolysis in Cerebral Infarction (mTICI) score of 2b/3. Secondary outcomes include: good functional outcome defined as modified Rankin Scale (mRS) 0-2 at 90 days, 90-day mortality, symptomatic intracererbal hemorrhage, baseline demographics and prevalence of cerebrovascular risk factors. Other technical outcomes studied include: intraprocedural re-occlusion, need for rescue endovascular treatment with balloon angioplasty or stent, the time from groin puncture to reperfusion, and time from symptom onset to reperfusion.

Statistical analysis

We extracted from each study a 2x2 table for binary outcomes and the mean group sample size and a variability measure for continuous outcomes. The pooled outcomes were meta-analyzed using a random-effects model.[6] Heterogeneity of the studies not attributable to chance was quantified with the I^2 statistic.[7] The 95% confidence intervals (CI) of the odds ratio (OR) for binary outcomes and weighted mean difference for continuous outcomes were reported. Outcomes with median and interquartile range were converted to a mean and standard deviation value based on the assumption of a lognormal distribution of the original measure.

Sensitivity analyses were performed by studying the comparative outcomes including only those studies that include predominantly (>85%) anterior circulation thrombectomy. Meta-analysis and statistical analysis was performed with OpenMeta-Analyst.[8]

Results

Literature search

The initial literature search yielded 125 articles. The titles and abstracts of these were read and 101 papers were excluded for irrelevance. Of the remaining 24 papers, 4 were excluded for being case reports or conference abstracts and 2 were excluded for being review or editorial articles. After review, 5 studies were excluded for not reporting separately outcomes of ICAS-O, and 2 papers were excluded for overlapping patient population. In total, 11 eligible studies were included for meta-analysis.[9-19] The PRISMA flow diagram is provided in Figure 1.

Study characteristics and the proportion of ICAS-O

A total of 1967 patients (496 ICAS-O and 1471 non-ICAS-O) in the 10 retrospective and 1 prospective observational studies were included. Ten studies were carried out in Asia (6 in Korea, 3 in China, 1 in Hong Kong), and 1 in the USA. Five studies reported on predominantly anterior circulation thrombectomy (>85%),[9, 12-14, 16] and three reported exclusively on posterior circulation thrombectomy[10, 11, 15]. ICAS-O accounted for 27.7% (95%CI 18.7%-36.7%) of all thrombectomies for LVO stroke. Five of the studies had low risk of bias, and six had moderate risk of bias. The included studies are summarized in Table 1.

Patient characteristics and risk factors

Comparing ICAS-O and non-ICAS-O groups, there was statistically significant differences in the age (63.7 vs 67.2, mean difference -3.2, 95% CI, -4.68 to -1.67) and proportion of male patients (70.4% vs 51.8%, OR 1.84, 95% CI, 1.45-2.34).

The ICAS-O patients had significantly more hypertension (71.4% vs 63.1%, OR 1.46, 95% CI, 1.10-1.93), diabetes mellitus (31.9% vs 22.5%, OR 1.68, 95% CI, 1.29-

2.20), dyslipidemia (36.0% vs 28.6%, OR 1.94, 95% CI, 1.04-3.62), and smoking history (44.6% vs 21.8%, OR 2.11, 95% CI, 1.40-3.17), but less atrial fibrillation (16.4% vs 54.1%, OR 0.20, 95% CI, 0.13-0.31) and a lower National Institute of Health Stroke Scale score at presentation (14.5 vs 17.0, mean difference -2.23, 95% CI, -2.98 to -1.48). There was no difference in the prevalence of coronary artery disease (CAD), the location of occlusion, or the use of intravenous thromboysis. (Table 2)

Thrombectomy and clinical outcomes

The ICAS-O group had significantly higher intraprocedural reocclusion rate (36.9% vs 2.7%, OR 23.7, 95% CI, 6.96-80.7), need for rescue balloon angioplasty (9.0% vs 1.3%, OR 9.49, 95% CI, 4.11-21.9), and rescue intracranial stenting (37.8% vs 2.6%, OR 14.9, 95% CI, 7.64-29.16). The puncture-to-reperfusion time (80.8 vs 55.5 minutes, mean difference 21.3, 95% CI, 11.3-31.3) and onset-to-reperfusion time (401.5 vs 333.4 minutes, mean difference 56.4, 95% CI, 18.7-94.1) were also longer in the ICAS-O cohort.

There was no difference in the rate of final recanalization (TICI2b/3) and in the rate of symptomatic intracerebral hemorrhage between ICAS-O and non-ICAS-O. There was also no significant difference in the functional outcome (mRS0-2) and in the mortality rate at 90 days between groups. These results are summarized in Figure 2 and Table 3.

Study heterogeneity

There was low heterogeneity (I^2 <50%) for the following outcomes: proportion of male patients (I^2 =2.8%), hypertension (I^2 =21.3%), diabetes mellitus (I^2 =13%), atrial fibrillation (I^2 =48.6%), coronary heart disease (I^2 =49.1%), age (I^2 =25.4%), baseline NIHSS (I^2 =20.4%), need for rescue balloon angioplasty (I^2 =0%), need for rescue intracranial stenting (I^2 =36.3%), symptomatic intracranial hemorrhage rate (I^2 =0%), functional outcome (mRS 0-2) at 3 months (I^2 =44%) and mortality rate (I^2 =4.4%). There was moderate substantial heterogeneity (I^2 >50%) for the following outcomes: dyslipidemia (I^2 =69.5%), smoking (I^2 =58.6%), occlusion location (I^2 =58.3%), use of intravenous thrombolysis (I^2 =51.7%), intraprocedural re-occlusion (I^2 =78.2%), final rate of TICI2b/3 (I^2 =68.1%), puncture-to-reperfusion time (I^2=78.4%) and onset-to-reperfusion time (I^2 =53%).

Sensitivity analysis

Because of the notion that anterior and posterior circulation ICAS-O may have different prognosis, we performed a subgroup analysis to determine whether the outcomes were different in anterior circulation versus posterior circulation ICAS-O. In the 5 studies that include predominantly (>85%) anterior circulation ICAS-O, there was no statistically significant difference in final mTICI2b/3 rate (OR: 0.76; 95%CI, 0.52-1.11) and good functional outcome (mRS0-2) at 90 days (OR: 1.12; 95%CI, 0.74-1.69) between groups. In the 3 studies that exclusively include posterior circulation ICAS-O, there was also no statistically significant difference in final TICI2b/3 rate (OR: 0.47; 95%CI, 0.08-2.78) and good functional outcome (mRS0-2) at 90 days (OR: 0.99; 95%CI, 0.58-1.68)

Discussion

Intracranial atherosclerosis is an important cause of LVO stroke which poses unique challenges to endovascular thrombectomy. While it is more prevalent in Asia, it can affect patients of any ethnicity, and is also often found in the black and Hispanic populations.[20] The literature on endovascular thrombectomy in ICAS-O is mainly comprised of Asian studies, and our review suggests that ICAS-O accounts for up to a quarter of the LVO stroke burden in Asia. The exact proportion of ICAS-O in non-Asian populations has not been systematically studied but is likely lower, accounting for 5.5% and 8.3% of LVOs in single-center cohort studies from France and the USA, respectively.[17, 21] This disparity is likely due to the different risk factor profiles of patients with ICAS-O and non-ICAS-O, as highlighted by the current study.

Compared with LVOs of other etiologies, ICAS-O patients are more likely men and of a younger age. The prevalence of hypertension, diabetes mellitus, dyslipidemia and smoking is also higher compared with non-ICAS-O patients. This coincides with the different distribution and prevalence of cardiovascular risk factors between Asian and Caucasian populations demonstrated in the Global Burden of Disease study[22]. In particular, the prevalence of atrial fibrillation, a major culprit of LVO stroke, is lower in Asian populations when compared with other ethnicities.[23] It was estimated that 8% of the white elderly population has atrial fibrillation, while the prevalence is only 3.9% in the elderly population of Asian origin.[24] There was no difference in the coronary artery disease prevalence observed between ICAS-O and non-ICAS-O group, which could be due to under-diagnosis of asymptomatic CAD in these patients. Hoshino et al., systematically studied a cohort of ischemic stroke patients with no prior history of CAD with CT coronary angiogram, and identified asymptomatic CAD in 37.5% of patients.[25] Similar results were found by Wu et al., in a Taiwanese population.[26] In addition, ICAD in at least the Chinese population does not appear to be associated with the typical risk factors for CAD such as hypertension, DM and hyperlipidemia.[27] Knowledge and understanding of this unique risk factor profile is important for the clinician to consider the possibility of an underlying ICAS lesion when performing emergent thrombectomy for patients in this ethnic group.

There are both diagnostic and therapeutic challenges in the management of

ICAS-O. Currently, there is no reliable way to diagnose an ICAS-O using preoperative imaging in the setting of an acute LVO stroke.[4] Various imaging predictors had been suggested to be associated with ICAS-O, including the degree of calcification of the intracranial carotid arteries on CT, clot burden as assessed by gradient-echo MRI, and the pattern of ischemic lesions on MRI.[16, 28] While these factors may suggest an underlying ICAS, they are by no means definitive and may be present in other causes of arterial occlusion such as a fibrous embolus. In the absence of universally accepted diagnostic criteria, most centers consider an occlusion to be due to underlying ICAS when there is (1) residual stenosis of 50% or more after initial thrombectomy, or (2) intraprocedural restenosis or re-occlusion, or (3) evidence of hypoperfusion in territories downstream to the stenosis; and (4) other differential diagnosis such as vasospasm or vessel dissection have been ruled out. This is typically established by repeating the angiogram 10-20 minutes after a successful thrombectomy attempt. The inter-rater reliability using these criteria appeared to be good with a Kappa-value up to 0.9 in a Korean study[9], and similar criteria is adopted by most of the included papers in this review.

The major therapeutic difficulty of ICAS-O is the tendency of intra-procedural re-occlusion, which occurred in over one-third of patients compared with only 2.7% in the non-ICAS-O group. Previous autopsy studies on post-thrombectomy patients with underlying ICAS showed histological evidence of fibrous cap disruption, intra-plaque hemorrhage, and sub-intimal dissection of the involved vessel segment, which presumably led to early re-occlusion of the recanalized vessel.[29, 30] It is important and reassuring to note that endovascular rescue therapy with balloon angioplasty, local infusion of glycoprotein IIb/IIIa inhibitors, and ultimately stent deployment (or detachment of a stent-retriever) was successful in revascularizing the cerebral circulation in most cases. Indeed, despite the longer puncture-to-reperfusion time in the ICAS-O cohort, there was no difference in the rate of final TICI 2b/3 revascularization as well as good functional outcome between the two groups.

The optimal rescue therapy in case of early re-occlusion in ICAS-O remains unclear and different first line therapies were used. Among the studies included in this review, intra-arterial infusion of glycoprotein IIb/IIIa inhibitors such as Tirofiban or Abxicimab via the distal access catheter or the microcatheter was commonly employed as the first-line therapy or as an adjunct to intracranial angioplasty/ stenting, although detailed information regarding the dosage and duration was not available for analysis. Emergent intracranial stenting was necessary in one-third of the ICAS-O patients, and another 9% received balloon angioplasty without stenting. Kang et al., compared the outcomes of emergent angioplasty versus intraarterial glycoprotein IIb/IIIa inhibitor infusion in a recent two-center prospective study of 140 patients.[31] They showed that both approaches achieved a high revascularization rate of 95% with no difference in functional outcome and mortality. Additionally, the parenchymal and subarachnoid hemorrhage rate was non-significantly higher in the center which primarily used rescue balloon angioplasty and stenting, although most of these hemorrhage were asymptomatic.[31] Further comparative studies are needed to delineate the safety profile and efficacy of these endovascular rescue approaches.

Intracranial stenting and angioplasty for ICAS in acutely symptomatic patients with stroke is controversial due to the high complication rate demonstrated in previous randomized trials.[32, 33] Although the recent WEAVE trial showed a low periprocedural complication rate if intracranial stenting was performed 8 days or more from the last stroke, stenting during emergent thrombectomy as a rescue procedure may carry a higher risk.[34] Similarly, intensive antiplatelet therapy after acute cerebral ischemia may increase the hemorrhagic risk.[35] Nevertheless, the risk-benefit profile has to be reconsidered in the context of LVO stroke with an underlying ICAS lesion that has a high re-occlusion rate, as the degree of reperfusion is a strong predictor of functional outcome.[36] This is supported by a recent study by Baracchini et al., that showed ICAS patients who received urgent intracranial stenting to rescue a failed LVO thrombectomy had superior functional outcome and survival than those whose artery was left occluded.[37] Likewise, the present meta-analysis shows that a high revascularization rate in ICAS-O can be achieved with judicious use of rescue endovascular therapies and that complication rates were not increased. Indeed, as shown in Table 3, there was no significant difference in the symptomatic hemorrhage rate between the ICAS-O group and non-ICAS-O group, and the rate of functional independence or mortality were similar. There is at present no consensus regarding the anti-platelet management in the acute phase after rescue strategies such as stenting and angioplasty. In the authors' center, a CT scan is routinely performed immediately to exclude intracranial hemorrhage after rescue stenting, and intravenous glycoprotein IIb/IIIa inhibitor infusion is commenced. This is then switched to standard oral anti-platelet agents after 24 hours if no major hemorrhagic transformation occurs.

This study has limitations. First, most of the included studies were performed in Asia, and the outcomes and clinical profile of Western ICAS-O patients may be different. A recent case series of rescue stent angioplasty in LVO patients with early re-occlusion in Germany found less favourable outcomes and a higher rate of symptomatic intracranial hemorrhage was found.[38] It is possible that the collateral perfusion status of ICAS-O patients may be different and contributed to the favorable clinical outcome despite the longer revascularization time. However, the lack of collateral status data in the included papers precludes detail analysis of this factor. The heterogeneity of thrombectomy techniques and rescue therapeutic approaches preclude detail comparison. Finally, the long term outcomes of re-stenosis or recurrent strokes after thrombectomy in the ICAS group were not reported in most of the studies included.

Conclusion:

ICAS-O is an important and challenging entity and can account for up to a quarter of LVO strokes receiving endovascular treatment. Patients with ICAS-O display a unique risk factor profile compared to non-ICAS-O. There are technical difficulties in endovascular thrombectomy of ICAS-O as evidenced by the longer puncture-to-reperfusion time and high intraprocedural re-occlusion rate. Although the optimal rescue treatment remains to be defined, successful revascularization may be achieved by intraarterial glycoprotein IIb/IIIa inhibitors infusion, balloon angioplasty, or intracranial stenting. The final successful reperfusion, favourable functional outcome and mortality rates were comparable between ICAS-O and non-ICAS-O.

Source of Funding

This study was supported by the Health and Medical Research Fund of Hong Kong (01150027).

Conflicting interest

There is no conflicting interest to declare.

Figure legends:

Figure 1: Literature search flowchart.

Figure 2: Forest plot of meta-analysis results: a) Final successful reperfusion mTICI 2b/3, b) rate of symptomatic intracranial hemorrhage after endovascular therapy, c) good functional outcome mRS 0-2 at 90 days, and d) mortality rate at 90 days.

Table 1. Patient population and study design of included papers.

Author	Year	No. of ICAS-O	No. of Non-ICAS-O	% of ICAS-O among all LVO	Population	% of anterior circulation	Study design	Risk of bias (NOS)
Kang et al.[13]	2014	40	92	30.3%	Korea	90%	Retrospective, single center	7
Lee JS et al.[18]	2015	24	134	15.2%	Korea	63%	Retrospective, single center	6
Yoon et al.[19]	2015	40	132	23.3%	Korea	81%	Retrospective, single center	5
Al Kasab et al.[17]	2016	36	165	8.3%	USA	67%	Retrospective, single center	6
Jia et al.[12]	2017	47	93	33.6%	China	100%	Prospective, multi-center	7
Lee YY et al.[15]	2017	15	47	24.2%	Korea	0%	Retrospective, single center	7
Baek et al.[9]	2018	56	262	17.6%	Korea	100%	Retrospective, single center	8
Fan et al.[11],	2018	35	32	52.2%	China	0%	Retrospective, single center	5
Lee JS et al.[14]	2018	99	421	19.0%	Korea	100%	Retrospective, multi-center	8
Tsang et al.[16]	2018	9	55	14.1%	Hong Kong	89%	Retrospective, single center	6
Zhang et al.[10]	2018	95	38	71.4%	China	0%	Retrospective, single center	5

ICAS-O, Intracranial atherosclerosis related occlusion; NOS, Newcastle Ottawa Scale; LVO, Large vessel occlusion

Table 2. Clinical features and risk factors of ICAS-O versus non-ICAS-O.

	ICAS-O	**Non-ICAS-O**	**OR (95%CI)**	**p-value**	**I^2 (p-value)**
Male*	70.4%	51.8%	1.84 (1.45-2.34)	<0.001	2.8% (0.42)
Hypertension*	71.4%	63.1%	1.46 (1.10-1.93)	0.009	21.3% (0.24)
Diabetes mellitus*	31.9%	22.5%	1.68 (1.29-2.20)	<0.001	13.0% (0.32)
Atrial fibrillation*	16.4%	54.1%	0.20 (0.13-0.31)	<0.001	48.6% (0.041)
Coronary artery disease	12.1%	14.7%	0.46 (0.42-1.49)	0.46	49.1% (0.081)
Dyslipidemia*	36.0%	28.6%	1.94 (1.04-3.62)	0.037	69.5% (<0.001)
Smoking*	44.6%	21.8%	2.11 (1.40-3.17)	<0.001	58.6% (0.009)
ICA occlusion	27.3%	35.4%	0.72 (0.44-1.17)	0.19	58.3% (0.048)
MCA occlusion	67.7%	61.8%	1.17 (0.67-2.04)	0.59	71.8% (0.007)
IV thrombolysis	30.7%	43.9%	0.89 (0.56-1.42)	0.49	51.7% (0.043)
	ICAS-O (mean)	**Non-ICAS-O (mean)**	**Mean difference (95%CI)**	**p-value**	**I^2 (p-value)**
Age (years)*	63.7	67.2	-3.17 (-4.68 to -1.66)	<0.001	25.4% (0.202)
Baseline NIHSS*	14.5	17.0	-2.23 (-2.98 to -1.48)	<0.001	20.4% (0.249)

ICAS-O, Intracranial atherosclerosis related occlusion; ICA; Internal carotid artery; IV, Intravenous; MCA. Middle cerebral artery; NIHSS, National Institute of Health Stroke Severity Scale. *p<0.05

Table 3. Summary of meta-analysis outcomes of thrombectomy in ICAS-O versus non-ICAS-O.

	ICAS-O	**non-ICAS-O**	**OR (95% CI)**	**p-value**	**I^2 (p-value)**
Intraprocedural re-occlusion*	36.9%	2.7%	23.7 (6.96-80.7)	<0.001	78.2% (0.01)
Rescue with balloon angioplasty alone*	9.0%	1.3%	9.49 (4.11-21.9)	<0.001	0% (0.6)
Rescue with intracranial stenting*	37.8%	2.6%	14.9 (7.64-29.2)	<0.001	36.3% (0.15)
Final mTICI2b/3	81.5%	84.3%	0.67 (0.36-1.27)	0.22	68.1% (<0.001)
Symptomatic intracranial hemorrhage	5.5%	8.1%	0.79 (0.50-1.25)	0.31	0% (0.72)
mRS0-2 at 90 days	49.8%	47.9%	1.16 (0.85-1.58)	0.34	44.0% (0.057)
Mortality at 90 days	20.2%	18.0%	0.94 (0.64-1.39)	0.76	4.4% (0.40)
	ICAS-O (mean)	**non-ICAS-O (mean)**	**Mean difference (95%CI)**	**p-value**	**I^2 (p-value)**
Puncture-to-reperfusion (minutes)*	80.8	55.5	+21.3 (11.3-31.3)	<0.001	78.4% (<0.001)
Onset-to-reperfusion (minutes)*	401.5	333.4	+56.4 (18.7-94.1)	0.003	53.0% (0.059)

ICAS, Intracranial atherosclerosis related occlusion; mRS, modified Rankin Scale; TICI, Thrombolysis in cerebral infarction scale. *$p<0.05$

References

1. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: A guideline for healthcare professionals from the american heart association/american stroke association. *Stroke*. 2018;49(3):e46-4110
2. Tsang COA, Cheung IHW, Lau KK, Brinjikji W, Kallmes DF, Krings T. Outcomes of stent retriever versus aspiration-first thrombectomy in ischemic stroke: A systematic review and meta-analysis. *AJNR Am J Neuroradiol*. 2018;39:2070-2076
3. Lee JS, Hong JM, Lee KS, Suh HI, Choi JW, Kim SY. Primary stent retrieval for acute intracranial large artery occlusion due to atherosclerotic disease. *Journal of stroke*. 2016;18:96-101
4. Lee JS, Hong JM, Kim JS. Diagnostic and therapeutic strategies for acute intracranial atherosclerosis-related occlusions. *Journal of stroke*. 2017;19:143-151
5. Wells G SB, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. . The newcastle-ottawa scale (nos) for assessing the quality of nonrandomised studies in meta-analyses. 2013 available online http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp Accessed December 15, 2018
6. DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. *Contemporary clinical trials*. 2015;45:139-145
7. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ (Clinical research ed.)*. 2003;327:557-560
8. Wallace BC, Dahabreh IJ, Trikalinos TA, Lau J, Trow P, Schmid CH. Closing the gap between methodologists and end-users: R as a computational back-end. *2012*. 2012;49:15
9. Baek JH, Kim BM, Heo JH, Kim DJ, Nam HS, Kim YD. Outcomes of endovascular treatment for acute intracranial atherosclerosis-related large vessel occlusion. *Stroke*. 2018;49:2699-2705
10. Zhang X, Luo G, Jia B, Mo D, Ma N, Gao F, et al. Differences in characteristics and outcomes after endovascular therapy: A single-center analysis of patients with vertebrobasilar occlusion due to underlying intracranial atherosclerosis disease and embolism. [published online December 4, 2018] *Interv Neuroradiol*. 2018 https://journals.sagepub.com/doi/abs/10.1177/1591019918811800 Accessed

December 22, 2018
11. Fan Y, Li Y, Zhang T, Li X, Yang J, Wang B, et al. Endovascular therapy for acute vertebrobasilar occlusion underlying atherosclerosis: A single institution experience. *Clinical neurology and neurosurgery*. 2018;176:78-82
12. Jia B, Feng L, Liebeskind DS, Huo X, Gao F, Ma N, et al. Mechanical thrombectomy and rescue therapy for intracranial large artery occlusion with underlying atherosclerosis. *J Neurointerv Surg*. 2018;10:746-750
13. Kang DH, Kim YW, Hwang YH, Park SP, Kim YS, Baik SK. Instant reocclusion following mechanical thrombectomy of in situ thromboocclusion and the role of low-dose intra-arterial tirofiban. *Cerebrovascular diseases (Basel, Switzerland)*. 2014;37:350-355
14. Lee JS, Lee SJ, Yoo JS, Hong JH, Kim CH, Kim YW, et al. Prognosis of acute intracranial atherosclerosis-related occlusion after endovascular treatment. *Journal of stroke*. 2018;20:394-403
15. Lee YY, Yoon W, Kim SK, Baek BH, Kim GS, Kim JT, et al. Acute basilar artery occlusion: Differences in characteristics and outcomes after endovascular therapy between patients with and without underlying severe atherosclerotic stenosis. *AJNR Am J Neuroradiol*. 2017;38:1600-1604
16. Tsang ACO, Lau KK, Tsang FCP, Tse MMY, Lee R, Lui WM. Severity of intracranial carotid artery calcification in intracranial atherosclerosis-related occlusion treated with endovascular thrombectomy. *Clinical neurology and neurosurgery*. 2018;174:214-216
17. Al Kasab S, Almadidy Z, Spiotta AM, Turk AS, Chaudry MI, Hungerford JP, et al. Endovascular treatment for ais with underlying icad. *J Neurointerv Surg*. 2017;9:948-951
18. Lee JS, Hong JM, Lee KS, Suh HI, Demchuk AM, Hwang YH, et al. Endovascular therapy of cerebral arterial occlusions: Intracranial atherosclerosis versus embolism. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*. 2015;24:2074-2080
19. Yoon W, Kim SK, Park MS, Kim BC, Kang HK. Endovascular treatment and the outcomes of atherosclerotic intracranial stenosis in patients with hyperacute stroke. *Neurosurgery*. 2015;76:680-686; discussion 686
20. Banerjee C, Chimowitz MI. Stroke caused by atherosclerosis of the major intracranial arteries. *Circulation research*. 2017;120:502-513
21. Gascou G, Lobotesis K, Machi P, Maldonado I, Vendrell JF, Riquelme C, et al. Stent retrievers in acute ischemic stroke: Complications and failures during the perioperative period. *AJNR Am J Neuroradiol*. 2014;35:734-740

22. Feigin VL, Roth GA, Naghavi M, Parmar P, Krishnamurthi R, Chugh S, et al. Global burden of stroke and risk factors in 188 countries, during 1990-2013: A systematic analysis for the global burden of disease study 2013. *Lancet Neurol*. 2016;15:913-924
23. Rahman F, Kwan GF, Benjamin EJ. Global epidemiology of atrial fibrillation. *Nature reviews. Cardiology*. 2014;11:639-654
24. Shen AY, Contreras R, Sobnosky S, Shah AI, Ichiuji AM, Jorgensen MB, et al. Racial/ethnic differences in the prevalence of atrial fibrillation among older adults--a cross-sectional study. *Journal of the National Medical Association*. 2010;102:906-913
25. Hoshino A, Nakamura T, Enomoto S, Kawahito H, Kurata H, Nakahara Y, et al. Prevalence of coronary artery disease in japanese patients with cerebral infarction: Impact of metabolic syndrome and intracranial large artery atherosclerosis. *Circulation journal : official journal of the Japanese Circulation Society*. 2008;72:404-408
26. Wu YW, Lin MS, Lin YH, Chao CL, Kao HL. Prevalence of concomitant atherosclerotic arterial diseases in patients with significant cervical carotid artery stenosis in taiwan. *The international journal of cardiovascular imaging*. 2007;23:433-439
27. Stevens J, Truesdale KP, Katz EG, Cai J. Impact of body mass index on incident hypertension and diabetes in chinese asians, american whites, and american blacks: The people's republic of china study and the atherosclerosis risk in communities study. *American journal of epidemiology*. 2008;167:1365-1374
28. Suh HI, Hong JM, Lee KS, Han M, Choi JW, Kim JS, et al. Imaging predictors for atherosclerosis-related intracranial large artery occlusions in acute anterior circulation stroke. *Journal of stroke*. 2016;18:352-354
29. Yang WJ, Wong KS, Chen XY. Intracranial atherosclerosis: From microscopy to high-resolution magnetic resonance imaging. *Journal of stroke*. 2017;19:249-260
30. Yin NS, Benavides S, Starkman S, Liebeskind DS, Saver JA, Salamon N, et al. Autopsy findings after intracranial thrombectomy for acute ischemic stroke: A clinicopathologic study of 5 patients. *Stroke*. 2010;41:938-947
31. Endovascular treatment for emergent large vessel occlusion due to severe intracranial atherosclerotic stenosis. *J Neurosurg*. 2018:1-8
32. Chimowitz MI, Lynn MJ, Derdeyn CP, Turan TN, Fiorella D, Lane BF, et al. Stenting versus aggressive medical therapy for intracranial arterial stenosis. *The New England journal of medicine*. 2011;365:993-1003

33. Zaidat OO, Fitzsimmons BF, Woodward BK, Wang Z, Killer-Oberpfalzer M, Wakhloo A, et al. Effect of a balloon-expandable intracranial stent vs medical therapy on risk of stroke in patients with symptomatic intracranial stenosis: The vissit randomized clinical trial. *Jama*. 2015;313:1240-1248
34. Alexander MJ, Zauner A, Chaloupka J. C., Baxter B, Callison R. C., Gupta R., Song S. S., Yu W., et al.,. Weave trial final results in 152 on-label patients. *Stroke*. 2019;50:889-894
35. Bath PM, Woodhouse LJ, Appleton JP, Beridze M, Christensen H, Dineen RA, et al. Antiplatelet therapy with aspirin, clopidogrel, and dipyridamole versus clopidogrel alone or aspirin and dipyridamole in patients with acute cerebral ischaemia (tardis): A randomised, open-label, phase 3 superiority trial. *Lancet (London, England)*. 2018;391:850-859
36. Tung EL, McTaggart RA, Baird GL, Yaghi S, Hemendinger M, Dibiasio EL, et al. Rethinking thrombolysis in cerebral infarction 2b: Which thrombolysis in cerebral infarction scales best define near complete recanalization in the modern thrombectomy era? *Stroke*. 2017;48(9):2488-2493
37. Baracchini C, Farina F, Soso M, Viaro F, Favaretto S, Palmieri A, et al. Stentriever thrombectomy failure: A challenge in stroke management. *World Neurosurg*. 2017;103:57-64
38. Forbrig R, Lockau H, Flottmann F, Boeckh-Behrens T, Kabbasch C, Patzig M, et al. Intracranial rescue stent angioplasty after stent-retriever thrombectomy : Multicenter experience. [published online May 14, 2018] *Clinical neuroradiology*. 2018 https://link.springer.com/article/10.1007%2Fs00062-018-0690-4 Accessed December 29, 2018