Effect of Prior Statin Therapy on Outcomes in Large and Medium Vessel Occlusion Stroke with Endovascular Thrombectomy

Makara Inyu,
Sureerat Suwatcharangkoon

ABSTRACT

Introduction: The influence of prior statin therapy uses on the outcomes of patients with acute ischemic stroke treated with endovascular therapy is unclear. We compared procedural and clinical outcomes of endovascular therapy in patients on statin therapy or not before stroke onset.

Objectives: To assess effect of prior statin therapy on outcome in large and medium vessel occlusion stroke with endovascular thrombectomy

Methods: A retrospective observational study of 168 patients diagnosed with acute ischemic stroke within 7 days and received endovascular therapy with or without intravenous thrombolysis was conducted in Ramathibodi hospital between January 1, 2013 and December 31, 2022. Baseline characteristics, comorbidities, clinical and radiographic features, treatment were collected. Patients were divided into three groups according to statin therapy status category as patients without prior statin (no statin), patients with prior high intensity statin therapy (HIS) and patients with prior low or moderate intensity statin therapy (LIS). Multilevel mixed-effects logistic models including center as random effect were used to compare angiographic (rates of reperfusion at the end of procedure, procedural complications) and clinical outcomes according to statin subgroups. Comparisons were adjusted for prespecified confounders (age, admission National Institutes of Health Stroke Scale score, Alberta Stroke Program Early CT Score, intravenous thrombolysis, and time from onset to puncture), as well as for meaningful baseline between-group differences.

Results: A total of 168 patients were analyzed, of whom 97 patients (58%) had never taken any

Makara Inyu, Sureerat Suwatcharangkoon
Division of Neurology, Department of Internal Medicine, Faculty of Medicine, Ramathibodi Hospital, Department of Internal Medicine, Faculty of Medicine, Ramathibodi Hospital

Corresponding author:
Makara Inyu, MD
Division of Neurology, Department of Internal Medicine, Faculty of Medicine, Ramathibodi Hospital, Department of Internal Medicine, Faculty of Medicine, Ramathibodi Hospital
E-mail address: makarainyu@gmail.com

รับต้นฉบับ 31 มกราคม 2567, ปรับปรุงต้นฉบับ 1 พฤษภาคม 2567, ตอบรับต้นฉบับตีพิมพ์ 7 กรกฎาคม 2567

statin, 25 patients (15%) were on HIS and 46 patients (27%) were on LIS. No significant difference in recanalization rates, number of passes and periprocedural complication was found between patients with high intensity statin and without statin. Patients without statin therapy, HIS and LIS had similar discharge mRS and 90 days mRS, parenchymal hematoma. Symptomatic ICH is significantly higher in the high intensity statin group, compared with no statin group [OR 1.725 (95% CI, 3.5-11);P value = 0.003].

Conclusion: This study demonstrates the neutral effect of statin treatment with angiographic outcomes and clinical outcomes in acute ischemic stroke patient undergoing endovascular thrombectomy with or without intravenous thrombolysis.

Keyword: Stroke, Statin, Large vessel occlusion, Endovascular thrombectomy

Introduction

Acute ischemic stroke is a neurological emergency. Focal neurological disorders are observed immediately and last for up to 24 hours[1]. Statistically, stroke is the 4th leading cause of death and disability in the United States[2]. In Thailand, stroke is the leading cause of death and second most common cause of disability and disability[3,4].

Endovascular treatment alone or in combination with intravenous thrombolysis is the most effective treatment in treating acute ischemic stroke caused by large vessel occlusion in anterior circulation[5]. Successful recanalization in a timely manner is the most important factor that affects functional outcomes. However, more than a third of patients undergo successful recanalization unable to return to functional independent[6]. Stent retriever is widely used in the treatment of arterial catheter, which the stent is expanded to extract blood clots. This results in arterial intimal injury caused by friction between the inner artery wall and the stents[7]. Studies in patients and laboratory animals was found that the inner vessel wall was injured after treatment through an artery catheter with stent retriever resulting in vasospasm, intimal denudation, intimal hyperplasia, medial thickening and inflammatory reaction[8, 9].

High intensity statin is one of the most effective treatments for good prognosis in patients with ischemic stroke[10]. In addition to the LDL-reducing effect, statins also result in improve endothelial function, Increase the durability of atherosclerotic plaque, reduce inflammation and inhibit clotting of blood[11]. Animal studies have shown that statins contribute to the prevention of vascular injury in endovascular thrombectomy procedures[12]. According to a study conducted by Seblani et al in patients who received statins prior to the procedure, showed that among those who received statins, there was higher in 30 days survival rate than the non-statin group[13].

However, studies on the effects of statins on the outcomes of endovascular thrombectomy treatment are still sparse, both abroad and especially in Thailand. The procedure is not yet widely popular, and past studies have had limitations, such as no angiographic outcome studies, Intensity type of statin and fasting LDL level, this makes such studies limited. Therefore, we are interested in studying the relationship of statin therapy with the outcomes of endovascular thrombectomy, so that the results of the research suggest the importance of statins. To reduce disability and death of acute ischemic stroke patients caused by large vessel occlusion.

Objective

To assess effect of prior statin therapy on outcome in large and medium vessel occlusion stroke with endovascular thrombectomy

Methods

Study Population

We compile a list of hospital numbers and data of patients diagnosed with acute cerebral ischemia from large vessel occlusion and treatment with endovascular thrombectomy from Ramathibodi Stroke registry from 1 January 2013 to 31 December 2022. We include patients whose duration from the onset of abnormal symptoms to hospital arrival occurs within 24 hours, aged over 15 years, detects a medium or large vessel occlusion and is treated through endovascular thrombectomy within a 24-hour period. After the onset of symptoms, patients treated with High intensity statin or low to moderate intensity for 3 months will be identified as a statin group. Exclusion criteria were the following: patients younger than 15 years of age, patients treated with Carotid endarterectomy or Carotid artery stenting within 24 hours of symptom onset, patients with a previous history of large vessel chronic occlusion, undefined statin therapy status and unknown initial and final modified Thrombolysis in Cerebral Infarction (mTICI).

Data recorded

The following variables were recorded: baseline characteristics such as age and sex, baseline mRS, cardiovascular risk factors (diabetes, hypertension, smoking, dyslipidemia), medical history (prior ischemic heart disease and atrial fibrillation), use of APT at the time of stroke onset, stroke severity assessed by the National Institutes of Health Stroke Scale score before EVT, arterial systolic and diastolic pressure, Trial of ORG 10172 in Acute Stroke Treatment etiologic classification of ischemic stroke, Alberta Stroke Program Early CT Score, occlusion site (divided into 5 groups: internal carotid artery, M1 and M2 portion of the middle cerebral artery, basilar artery and vertebral artery occlusion), as well as times from symptom onset to groin puncture and from symptom onset to revascularization. The full stroke diagnosis workup was up to the decision of the clinician included an ECG, a 48-hour cardiac rhythm recording in the acute stroke unit and a standard biological evaluation. All patients underwent non-contrast CT scan brain imaging within 24 hours post-treatment; additional non-contrast CT scan imaging could be performed at any time in case of neurological deterioration. Intracranial hemorrhages (ICHs) on post-treatment imaging were also studied. mTICI at the end of the procedure, the number of passes, and procedural complications were also recorded. Radiographic outcome measures were adjudicated by individual site investigators.

Outcomes

The primary study outcome was the percentage of patients who achieved a favorable after discharge outcome, defined as an mRS score of 0 to 2. Secondary outcomes included clinical outcomes (excellent 90-day outcome defined as an mRS score of 0–1, mRS score of 0-2, the degree of disability assessed by the overall distribution of 90-day mRS, any hemorrhagic complications, parenchymal hematoma, sICH and procedural outcomes [reperfusion rates at the end of endovascular procedure: successful reperfusion (mTICI

score 2b), complete reperfusion (mTICI score 3)], >1 passes, procedural complications [defined as arterial perforation, arterial dissection, embolization in a new territory, and subarachnoid hemorrhage]

Statistical analysis

Quantitative variables are expressed as mean (SD) in case of normal distribution or median (interquartile range) otherwise. Categorical variables are expressed as numbers (percentage). Patients were divided into 3 groups according to their medication (no statin, high intensity statin and low to moderate intensity statin groups) before EVT. Baseline characteristics were compared between the no statin and HIS study groups, as well as between the no statin and LIS study groups using the Student t test for gaussian continuous variables, the Mann-Whitney U test for nongaussian continuous variables, or the χ_2 test (or Fisher exact test when the expected cell frequency was <5) for categorical variables, as appropriate. Between-group imbalances in baseline characteristics were also assessed by calculating absolute standardized differences. Comparison in binary outcomes between groups was made using multilevel mixed-effects logistic models by including center as random effect, and odds ratios were calculated.

Results

Of the 258 patients analyzed, 45 were excluded because they did not have previous drug acquisition data, and 26 were excluded because they were not treated with the mechanical thrombectomy (only angiography) and 19 were excluded because there were no angiographic outcomes (Figure 1). A total of 168 patients were analyzed, of whom 25 (15%) were on high intensity statin (HIS) and 46 (27%) were on low to moderate intensity statin (LIS). Patients on HIS were male predominance, were more likely to have hypertension, hypercholesterolemia, diabetes, a history of ischemic stroke, ischemic heart disease, malignancy, antiplatelet treatment, lower mean NIHSS and less stent retriever in endovascular therapy (Table 1). Both populations showed differences in the location of occlusions while there were no differences in thrombectomy time metrics and stroke mechanisms.

Table 1 Baseline characteristics

Demographics	No Statin (n=97)	HIS (n=25)	LIS (n=46)	Total (n=168)	*P*-value
Age, y; mean (SD)	65.95	68.56	74.96	69.07	0.657
Female	50 (51%)	8 (32%)	30 (65%)	88	0.027*
Male	47 (48%)	17 (68%)	16 (35%)	80	
Hypertension	50 (51%)	20 (80%)	40 (87%)	110	0.000*
Hypercholesterolemia	23 (24%)	15 (60%)	40 (87%)	78	0.000*
Smoking	21 (22%)	2 (8%)	3 (6.6%)	26	0.002*
Diabetes	16 (16%)	15 (60%)	14 (30%)	45	0.000*
Ischemic heart disease	8 (8%)	8 (32%)	4 (8.7%)	20	0.003*
Prior stroke	5 (5%)	9 (36%)	14 (30%)	24	0.000*
Atrial fibrillation	37 (38%)	12 (48%)	26 (56%)	75	0.111
Malignancy	13 (13%)	22 (88%)	41 (89%)	76	0.910

Demographics	No Statin (n=97)	HIS (n=25)	LIS (n=46)	Total (n=168)	*P*-value
Antiplatelets	12 (12%)	13 (52%)	19 (41%)	34	0.000*
Oral anticoagulants	5 (5%)	2 (8%)	2 (4.3%)	9	0.073
Fibrate	2 (2%)	2 (8%)	0 (0%)	4	0.102
Ezetimibe	2 (2%)	1 (4%)	2 (4.3%)	5	0.715
Baseline mRS					
0	90 (92%)	20 (80%)	39 (85%)	149	
1	5 (5%)	5 (20%)	3 (6.5%)	13	
2	0 (0%)	0 (0%)	3 (6.5%)	3	0.048*
4	1 (1%)	0 (0%)	1 (2.2%)	2	
5	1 (1%)	0 (0%)	0 (0%)	1	
Initial systolic BP,mean (SD)	152.64	155.39	153.89	146.74	0.309
Initial diastolic BP,mean (SD)	83.36	85.46	83.46	80.38	0.564
Glycemia, mean (SD)	135.32	167.63	134.89	132.11	0.076
Hemoglobin A1c	5.78	6.73	6.01	5.83	0.180
LDL level (mean)	123.33	82.54	94.41	106.84	0.393
NIHSS (mean)	15	13.32	17.98	15.51	0.024*
ASPECTS (mean)	7.99	8.48	8.39	8.16	0.876
Collateral score	3.92	3.76	4.09	3.92	0.334
Cardioembolic, etiology (yes), n(%)	52 (53%)	15 (60%)	34 (74%)	101	0.068
Occlusion site					
Right MCA					
M1	30 (31%)	8 (32%)	14 (30%)	52	0.990
M2	12 (12%)	0 (0%)	2 (4%)	14	0.071
Left MCA					
M1	25 (26%)	9 (36%)	13 (28%)	47	0.596
M2	7 (7%)	1 (4%)	8 (17%)	16	0.091
Right ICA	8 (8%)	3 (12%)	9 (19.5%)	20	0.149
Left ICA	16 (16%)	3 (12%)	2 (4.3%)	21	0.121
Basilar artery	7 (7%)	2 (8%)	3 (6.5%)	12	0.973
Right VA	0 (0%)	0 (0%)	0	0	0
Left VA	1 (1%)	0 (0%)	0	1	0.699
Procedural data					
Thrombolytic agents	37 (38%)	7 (28%)	17 (37%)	61	0.639
General anesthesia	62 (64%)	14 (56%)	20 (43%)	96	0.048*
First line thrombectomy strategy					
Stent retriever	49 (51%)	7 (28%)	30 (65%)	86	0.011*
Aspiration	59 (61%)	20 (80%)	26 (56%)	105	0.299
Stent retriever and aspiration	11 (11%)	0 (0)	2 (4.3%)	13	0.100

Demographics	No Statin (n=97)	HIS (n=25)	LIS (n=46)	Total (n=168)	*P*-value
Other	13 (13%)	2 (8%)	2 (4.3%)	17	0.228
Stenting					
No stenting	93 (96%)	25 (100%)	43	43	0.422
Cervical	1 (1%)	0 (0%)	2	2	0.288
Intracranial	2 (2.1%)	0 (0%)	1	1	0.765
Time from onset to puncture, min, median (IQR)	504.44	416.52	429.73	469.43	0.358
Time from puncture to recanalization, min, median (IQR)	56.12	44.5	53.62	53.39	0.064
Time from onset to recanalization, min, median (IQR)	574.41	452.54	480.52	526.42	0.140

HIS indicates High intensity statin; LIS indicated Low to moderate intensity statin; ASPECT, Alberta Stroke Program Early CT Score; BP, blood pressure; ICA, intracranial carotid artery; IQR, interquartile range; M1, M1 segment of the middle cerebral artery; M2, M2 segment of the middle cerebral artery; VA, vertebral artery

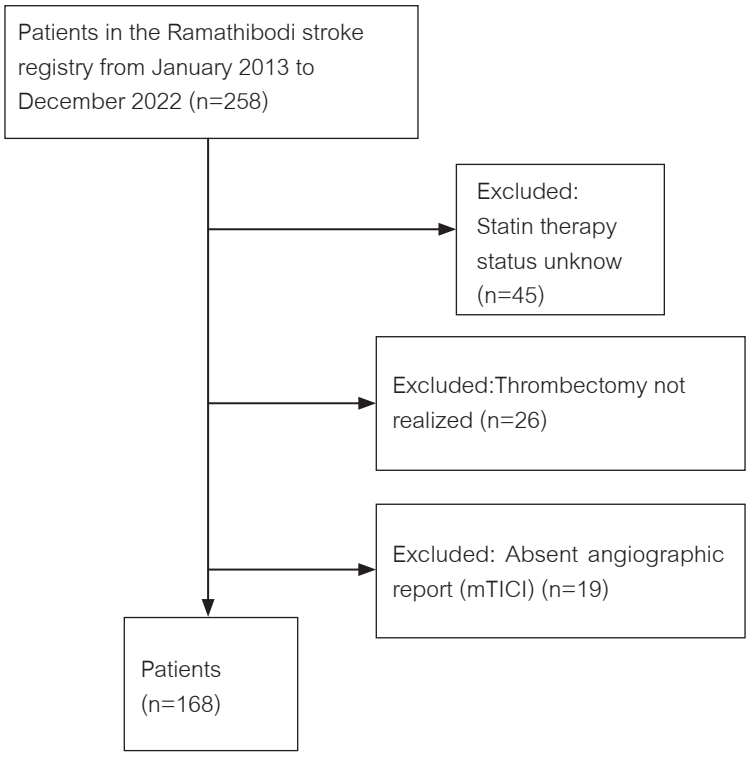

Figure 1 Flow chart

Angiographic Outcomes

As shown in Table 2, on multivariate analysis no significant difference in recanalization rates, number of passes and periprocedural complication was found between patients with high intensity statin and without statin. No difference in reperfusion rates was observed in the Endovascular treatment group. Prior statin therapy was not associated with complete recanalization.

Table 2 Comparison of outcome between patients treated with no statin and high intensity statin

	No Statin (n=97)	HIS (n=25)	OR (95% CI)	*P*-value	OR (95% CI) after adjustment†	*P*-value
Angiographic outcomes						
First-pass recanalization	17 (18%)	11 (44%)	3.395	0.005*	0.500	0.125
mTICI score 0	15 (15%)	1 (4%)	0.241	0.141	0.887	0.466
mTICI score 1	2 (2%)	0	0.980	0.474	0.955	0.404
mTICI score 2a	10 (10%)	0	0.919	0.141	0.889	0.725
mTICI score 2b	35 (36%)	6 (24%)	0.665	0.389	0.750	0.386
mTICI score 3	37 (38%)	17 (68%)	3.334	0.007*	0.500	0.083
Total pass >1	50 (51%)	13 (52%)	1.013	0.976	0.750	0.386
Complication	13 (13%)	3 (12%)	0.777	0.747	0.333	0.248
Clinical outcomes						
END	20 (21%)	6 (24%)	1.202	0.718	0.778	0.598
PH	25 (26%)	7 (28%)	0.950	0.914	0.667	0.386
	No Statin (n=97)	HIS (n=25)	OR (95% CI)	*P*-value	OR (95% CI) after adjustment†	*P*-value
sICH	3 (3%)	2 (8%)	1.752	0.496	1.752	0.003*
mRS score after discharge						
score 0-2	23 (24%)	5 (20%)	0.992	0.988	0.556	0.083
score 3-5	48 (49%)	10 (40%)	0.575	0.205	0.778	0.386
score 6	11 (11%)	1 (4%)	0.346	0.294	0.833	0.157
mRS score after 90 days						
score 0-2	39 (40%)	12 (48%)	1.561	0.304	0.333	0.248
score 3-5	31 (32%)	8 (32%)	0.869	0.761	0.500	0.386
score 6	9 (9%)	1 (4%)	0.399	0.37	0.800	0.524

END ,early neurological deterioration;

†Calculated using the no antithrombotic group as reference after adjustment for center, age, hypertension, hypercholesterolemia, diabetes, previous stroke, ischemic heart disease, glycemia, admission NIHSS score, admission ASPECT score, intravenous thrombolysis, stroke etiology, time from symptom onset to puncture

Clinical Outcomes

On fully adjusted shift analysis and multivariate analysis of binary outcome variables after imputation, patients without statin therapy, HIS and LIS had similar discharge mRS and 90 days mRS, parenchymal hematoma (Table 2). Symptomatic ICH occurred significantly more in the high intensity statin group than in the no statin group [OR 1.725 (95% CI, 3.5-11);P value = 0.003].

Discussion

This retrospective cohort study assessing the effect of prior statin treatment with endovascular thrombectomy. Emphasized 3 main results: (1) there are major baseline differences in the population of patients with prior statin therapy versus no prior statin therapy, (2) after adjusting for those differences, the apparent difference in rates of recanalization, and 30-day functional outcomes becomes nonsignificant and (3) Symptomatic ICH occurred significantly more in the high intensity statin group than in the no statin group.

Previous studies demonstrated the effectiveness of statins on functional outcomes and reduced ICH incidence after catheterization. the study had a large number of people participating in the study. This makes the effect of treatment clearly visible[13].

The limitations of this study are multifactorial. (1) There were fewer people in the statin group who did not see the clear results of this study. (2). There was a clear confounding factor in the statin population, such as DM and HT hypercholesterolemia, than in the population who did not receive statins and (3) We cannot concluded that statin exposure causes symptomatic ICH because the event is low and the population is small. However, univariated analysis showed tha High intensity statin has an effect on first pass effect and good angiographic outcome.

Conclusion

In conclusion, this study demonstrates the neutral effect of statin treatment with angiographic outcomes and clinical outcomes with endovascular thrombectomy. Due to such limitation, future studies on the effects of statins and vascular catheterization should have a larger population or have randomized controlled trials.

References

1. Sacco RL, Kasner SE, Broderick JP, et al. An updated definition of stroke for the 21st century. Stroke 2013; 44: 2064-89.
2. Minino AM, Murphy SL, XU J, Kochanek KD, et al. Deaths: final data for 2008. Natl Vital Stat Rep 2011;59: 1- 126
3. สำนักวิจัยนโยบายสร้างเสริมสุขภาพ สำนักงานพัฒนานโยบายสุขภาพระหว่างประเทศ (IHPP). รายงานภาระโรคและการบาดเจ็บ ของประชากรพ.ศ.2557.2018;1-78
4. Hoy DG, Rao C, Hoa NP, et al. Stroke mortality variations in South-East Asia: empirical evidence from the field. Int J Stroke 2012; 8:21-7.
5. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, Dávalos A, Majoie CB, van der Lugt A, de Miquel MA, et al; HERMES Col- laborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 2016; 387:1723–31.
6. Saver JL, Goyal M, van der Lugt A, Menon BK, Majoie CB, Dippel DW, Campbell BC, Nogueira RG, Demchuk AM, Tomasello A, et al; HERMES Collaborators. Time to treatment with endovascular thrombectomy and outcomes From ischemic stroke: a meta-analysis. JAMA 2016; 316:1279–88.
7. Arai D, Ishii A, Chihara H, Ikeda H, Miyamoto S. Histological examination of vascular damage caused by stent retriever thrombectomy devices. J Neurointerv Surg 2016; 8:992–5.
8. Brekenfeld C, Schroth G, El-Koussy M, Nedeltchev K, Reinert M, Slotboom J, et al. Mechanical thromboem-

bolectomy for acute ischemic stroke: comparison of the catch thrombectomy device and the Merci Retriever in vivo. Stroke 2008; 39:1213–9.

9. 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; 35:734–40.
10. Amarenco P, Labreuche J. Lipid management in the prevention of stroke: review and updated meta-analysis of statins for stroke prevention. Lancet Neurol 2009; 8:453–63.
11. Liao JK, Laufs U. Pleiotropic effects of statins. Annu Rev Pharmacol Toxicol 2005; 45:89–118.
12. Lee SH, Shin HS, Oh I. The protective effects of statins towards vessel wall injury caused by a stent retrieving mechanical thrombectomy device: A histological analysis of the Rabbit Carotid Artery Model. Korean Neurosurg Soc 2021;64:693–704.
13. Seblani NE, Nagaraja N. Outcomes of statins post-endovascular thrombectomy in ischemic stroke. Stroke: Vascular and Interventional Neurolog 2023;3: e12823_241.