Journal of Neurology (2019) 266:609–615
https://doi.org/10.1007/s00415-018-09173-0

ORIGINAL COMMUNICATION

Incidence and mechanism of early neurological deterioration after endovascular thrombectomy

Jeong-Min Kim[1] · Jae-Han Bae[1] · Kwang-Yeol Park[1] · Woong Jae Lee[2] · Jun Soo Byun[2] · Suk-Won Ahn[1] · Hae-Won Shin[1] · Su-Hyun Han[1] · Il-Han Yoo[1]

Received: 31 October 2018 / Revised: 24 December 2018 / Accepted: 26 December 2018 / Published online: 10 January 2019
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

Abstract

Background We investigated the prevalence and mechanisms of neurological deterioration after endovascular thrombectomy.
Methods Between January 2011 and October 2017, acute ischemic stroke patients treated by endovascular thrombectomy in a tertiary university hospital were included. Early neurological deterioration (END) was defined as an increase of 2 or more National Institute of Health Stroke Scale (NIHSS) compared to the best neurological status after stroke within 7 days. The END mechanism was categorized into ischemia progression, symptomatic hemorrhage, and brain edema.
Results A total of 125 acute ischemic stroke patients received endovascular thrombectomy. Neurological deterioration was detected in 44 patients, and 38 cases (86.4% of END) occurred within 72 h. The END mechanism included 20 ischemia progression, 16 brain edema and 8 hemorrhagic transformation cases. Multivariable logistic regression analysis revealed that the patients who experienced END were more likely to have poor functional outcome defined as modified Rankin scale 3–6 at 90 days than neurologically stable patients (odds ratio (OR) = 4.06, confidence interval (CI) = 1.39–11.9). The risk factor of END due to ischemia progression was stroke subtype of large artery atherosclerosis (OR = 6.28, CI = 1.79–22.0). Successful recanalization (OR = 0.11, CI = 0.03–0.39) and NIHSS after endovascular thrombectomy (OR = 1.15 per one-point increase, CI = 1.06–1.24) were significantly associated with END due to hemorrhage or brain edema.
Conclusion Neurological deterioration frequently occurs after endovascular thrombectomy, and the risk factors of END differ according to the mechanism of END.

Keywords Stroke · Mechanical thrombectomy · Prognosis

Introduction

Recent clinical trials have shown that endovascular thrombectomy is an effective and safe recanalization modality for acute ischemic stroke patients [1–5]. Acute cerebral infarction patients were more likely to benefit in terms of functional independence, if treated with endovascular thrombectomy when symptom onset was within 6–8 h [6–8]. Meta-analysis results show that endovascular treatment is associated with a high ratio of successful recanalization rate and a low rate of symptomatic hemorrhage [6]. However, a number of patients still have functional dependence or die after endovascular treatment. Several studies report the incidence of futile recanalization, meaning poor clinical outcome despite successful recanalization among acute cerebral infarction patients, is as high as 20%, and its risk factors include age and initial poor collateral circulation status [9, 10].

It is desirable to know when and how the patients deteriorate beyond endovascular thrombectomy to ameliorate a functional outcome after recanalization treatment. However, the incidence, timing, and the mechanism of neurological deterioration have not been investigated among the cerebral infarction patients who were treated with endovascular thrombectomy. Therefore, we attempted to investigate the prevalence and mechanisms of neurological deterioration after endovascular thrombectomy. Specifically, we

✉ Kwang-Yeol Park
kwangyeol.park@gmail.com

[1] Department of Neurology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul, 224-1, Heukseok-dong, Dongjak-gu, Seoul 156-755, South Korea

[2] Department of Neuroradiology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul, South Korea

categorized the etiology of neurological deterioration into three groups, ischemia progression, symptomatic hemorrhage and brain edema, to study the etiology specific risk factors.

Methods

Patient inclusion

This study was reviewed and approved by the institutional review board of the study institution and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Informed consent was exempted due to retrospective design. Between January 2011 and October 2017, acute ischemic stroke patients within 6–8 h after initial symptom onset treated with endovascular thrombectomy in a tertiary university hospital were included. All the patients underwent multidetector CT angiography to detect any occluded artery before endovascular treatment. Endovascular recanalization treatment using a stent retriever (SolitaireTM FR: ev3, Irvine, CA, USA) or aspiration thrombectomy (Penumbra system, Alameda, CA, USA) was performed. When symptom onset was within 3–4.5 h, the patients received intravenous alteplase infusion at a dose of 0.9 mg per kilogram before endovascular thrombectomy. All the patients were admitted to the stroke unit or intensive care unit after reperfusion treatment, where close neurological monitoring was maintained by the attending neurologists. The rating of National Institute of Health Stroke Scale (NIHSS) was recorded as a routine daily practice by a neurologist. Another brain imaging was performed at 24 h after endovascular thrombectomy before initiation of antithrombotics. Follow-up brain imaging was performed by brain MR imaging (MRI) including diffusion-weighted image, susceptibility weighted image, and time-of flight MR angiography when a patient had been neurologically stabilized. Additional brain imaging was performed by either brain CT or MRI when a patient deteriorated. Stroke subtype was determined by Trial of Org 10,172 in Acute Stroke Treatment classification [11]. Successful recanalization after endovascular treatment was defined as modified thrombolysis in cerebral infarction grade 2b or 3 [12].

Early neurological deterioration after endovascular thrombectomy

We reviewed a clinical record and laboratory data from the prospectively registered stroke registry. Early neurological deterioration (END) is defined as an increase of two or more NIHSS compared to the best neurological status after stroke within 7 days. The mechanism of neurological deterioration was categorized into ischemia progression, brain edema, and symptomatic hemorrhage according to the follow-up image as previously reported [13]. Symptomatic hemorrhagic transformation is defined as two or more NIHSS aggravations due to hemorrhagic lesions with mass effects, either within initial infarction site or distant area. Brain edema is identified when a patient deteriorates along with the progression of edema with noticeable mass effects of initial infarction without symptomatic hemorrhage. Ischemia progression or recurrence is defined as neurological worsening due to the progression of initial infarction or the development of additional lesions identified from brain imaging. Poor functional outcome was defined to include patients with modified Rankin scale (mRS) between 3 and 6 at 90 days, and good functional outcome was designated when mRS was between 0 and 2.

Statistical analysis

Categorical variables are expressed as the number of patients (%). Continuous variables are expressed as a mean (standard deviation) or a median (interquartile range). Student's t-tests were applied for continuous variables with normal distributions, and χ^2 tests were conducted for the categorical variables. First we constructed a multivariable logistic regression model to identify whether END is an independent predictor of poor functional outcome at 90 days by including variables with p values less than 0.05 based on the bivariate analysis. Second, we suspected that the risk factors of END might differ in terms of the etiology of END; especially, patients with ischemia progression may have different risk factors when predicting END than those with END due to brain edema or hemorrhage. Therefore we performed a bivariate analysis followed by multivariable logistic regression analyses to derive etiology specific risk factors predicting END by ischemia progression, and non-ischemic END (END due to brain edema or symptomatic hemorrhage). Each group was independently compared with the control group of patients who did not experience END. Six patients who died of non-neurological causes, three cases with septic shock, two cases with respiratory arrest, and one case with acute coronary artery disease were included in the control group.

Results

A total of 125 patients were identified within the study period with a mean age of 68.1 ± 13.5 years, 56 of which were female (Table 1). The most common occluded artery was the middle cerebral artery with 66 cases (52.8%), followed by 24 basilar artery (19.2%), 21 intracranial portion of internal carotid artery (ICA) (16.7%) and 13 extracranial ICA cases (10.4%). Stent retriever was the main endovascular treatment modality in 111 patients (88.8%). Successful

Table 1 Basic clinical variables of the study population

Patient number	125
Age, years, mean (SD)	68.1 (13.5)
Gender, female patients, *n* (%)	56 (44.8)
Vascular risk factors, *n* (%)	
Hypertension	78 (62.4)
Diabetes mellitus	39 (31.2)
Atrial fibrillation	84 (67.2)
Previous stroke	24 (19.2)
Current smoker	24 (19.2)
Initial NIHSS, mean (SD)	16 (7)
Intravenous thrombolysis, number (%)	69 (55.2)
Occluded artery, number (%)	
Middle cerebral artery, M1	57 (45.6)
Middle cerebral artery, M2	9 (7.2)
Internal carotid artery, intracranial	21 (16.8)
Internal carotid artery, extracranial	13 (10.4)
Basilar artery	24 (19)
Anterior cerebral artery	1 (0.8)
Onset to treatment, minutes, mean (SD)	222 (128)
Stent retriever only, *n* (%)	97 (77.6)
Stent retriever + rescue treatment, *n* (%)	14 (11.2)
Successful recanalization, *n* (%)	101 (80.8)
Stroke subtype by TOAST criteria, *n* (%)	
Large artery atherosclerosis	17 (13.6)
Cardioembolism	99 (79.2)
Others or unknown	9 (7.2)
Good functional outcome, *n* (%)	50 (40.0)

SD stands for standard deviation, *TOAST* Trial of Org 10,172 in Acute Stroke Treatment

recanalization was achieved in 101 (80.8%) patients. The major stroke subtype was 99 cardioembolic cases (79.2%) followed by 17 large artery atherosclerosis cases (13.6%). Overall, a good functional outcome at 90 days after the index stroke was observed in 50 patients (40.0%). Eight patients received decompressive craniectomy, and 22 patients died during admission.

Neurological deterioration occurred in 44 patients (35.2%), which comprised 20 cases of ischemia progression, 16 cases of brain edema and eight cases of symptomatic hemorrhage. Regardless of its etiology, END most often occurred within 72 h after endovascular thrombectomy (38 out of 44 END cases, 86.4%). The END incidence and mechanism according to the occluded arteries are illustrated in Table 2. The rate of END tended to become less prevalent as the occluded arterial site was more distal in anterior circulation infarction patients ($p = 0.101$ by linear association test, Table 2). The incidence of END and the rate of poor functional outcome at 90 days among BA occlusion patients were similar to those of MCA occlusion patients. Regarding the functional status, the patients who experienced END were more likely to have a poor functional outcome at 90 days (Table 3), which remained significant after adjusting age, successful recanalization, NIHSS after endovascular treatment and blood glucose level [odds ratio (OR) = 4.06, confidence interval (CI) = 1.39–11.9, $p < 0.001$].

When clinical characteristics were compared between patients with END due to ischemia progression and neurologically stable patients, the patients with ischemia progression were more likely to be a female and more likely to have a higher platelet count and stroke subtype of large artery atherosclerosis (Table 4). Multivariable logistic regression analysis showed that large artery atherosclerosis (OR = 6.28, CI = 1.79–22.0, p = 0.004) is independently associated with END due to ischemia progression after endovascular treatment (Table 5). The detailed mechanisms of ischemia progression included eight patients with re-occlusion of initial relevant arteries, five patients with recanalization failure, and four patients with new infarctions from initially unaffected arterial territories, followed by three patients experiencing distal migration of thrombus during endovascular

Table 2 Geographical relationship of neurological outcome in terms of occluded artery

	M2 MCA	M1 MCA	Distal ICA	Proximal ICA	Basilar artery
Patient number	9	57	21	13	24
Successful recanalization, *n* (%)	9 (100.0)	45 (78.9)	16 (76.2)	8 (61.5)	22 (91.7)
Early neurological deterioration, *n* (%)	2 (22.2)	20 (35.1)	9 (42.9)	7 (53.8)	6 (25.0)
Ischemia progression	1 (11.1)	11 (19.3)	1 (4.8)	3 (23.1)	4 (16.7)
Symptomatic hemorrhage	0	1 (1.8)	3 (14.3)	2 (15.4)	2 (8.3)
Brain edema	1 (11.1)	8 (14.0)	5 (23.8)	2 (15.4)	0 (0)
Large artery atherosclerosis, @@*n* (%)	1 (11.1)	8 (14.0)	0 (0)	2 (15.4)	6 (25.0)
Cardioembolism, *n* (%)	8 (88.9)	47 (82.5)	20 (95.2)	10 (76.9)	13 (54.2)
Poor functional outcome, *n* (%)	4 (44.4)	37 (64.9)	18 (85.7)	7 (53.8)	14 (58.5)
Death, *n* (%)	1 (11.1)	6 (10.5)	7 (33.3)	4 (30.8)	4 (16.7)

One patient with anterior cerebral artery territorial infarction was excluded from the analysis

MCA middle cerebral artery, *ICA* internal carotid artery

Table 3 Factors associated with poor functional outcome at 3 months

	Patients with mRS 0–2	Patients with mRS > 2	*P*
Patient number	50	75	
Age, mean (SD)	64.6 (13.9)	70.5 (12.8)	0.02
Sex, female, *n* (%)	21 (42.0)	35 (46.7)	0.61
Hypertension, *n* (%)	27 (54.0)	51 (68.0)	0.11
Diabetes mellitus, *n* (%)	12 (24.0)	27 (365.0)	0.16
Smoking, *n* (%)	12 (24.0)	12 (16.0)	0.27
Atrial fibrillation, *n* (%)	32 (64.0)	52 (69.3)	0.53
Previous stroke, *n* (%)	7 (14.0)	17 (22.7)	0.23
Systolic blood pressure, mmHg, mean (SD)	146 (29)	141 (28)	0.37
NIHSS at admission, mean (SD)	14 (6)	17 (7)	0.006
NIHSS after thrombectomy, mean (SD)	10 (6)	18 (7)	< 0.001
Intravenous thrombolysis, *n* (%)	28 (56.0)	41 (54.7)	0.88
Onset to endovascular treatment, minutes, mean (SD)	212 (111)	229 (138)	0.47
Internal carotid artery occlusion, *n* (%)	11 (22.0)	23 (30.7)	0.29
Basilar artery occlusion, *n* (%)	11 (22.9)	14 (18.7)	0.65
Successful recanalization, *n* (%)	45 (90.0)	56 (74.7)	0.03
White blood cell count, x 10^9/L, mean (SD)	8.5 (5.7)	9.2 (3.7)	0.38
Platelet count, x 10^9/L, mean (SD)	221 (72)	212 (71)	0.47
Fasting blood sugar, mg/dL, mean (SD)	123 (26)	158 (57)	< 0.001
Total cholesterol, mg/dL, mean (SD)	166 (31)	160 (45)	0.43
Large artery atherosclerosis, *n* (%)	8 (16.0)	9 (12.0)	0.52
Cardioembolism, *n* (%)	40 (80.0)	59 (78.7)	0.86
Early neurological deterioration with two or more NIHSS increase, *n* (%)	7 (14.0)	37 (49.3)	< 0.001

mRS modified ranking score, *SD* standard deviation, *NIHSS* National Institute of Health Stroke Scale

thrombectomy. The patients with END due to hemorrhage or brain edema were more likely to have a higher NIHSS after endovascular thrombectomy and internal carotid artery occlusion, but were less likely to have successful recanalization (Table 4). Multivariable logistic regression analysis showed that NIHSS after endovascular thrombectomy (OR = 1.15 per one point of NIHSS increase, CI = 1.06–1.24, p = 0.001) and successful recanalization (OR = 0.11, CI = 0.03–0.39, p = 0.001) are independently associated with END due to symptomatic hemorrhage or brain edema (Table 5).

Discussion

The incidence of END after endovascular thrombectomy in acute cerebral infarction patients was 35.2% when END was defined as NIHSS increasing 2 or more increments within 7 days after interventional treatment. Patients who experienced END were more likely to have a poor functional outcome at 90 days after stroke, which remained significant after adjusting the clinical variables. The most common etiologies of END were ischemia progression, followed by brain edema and symptomatic hemorrhage. Large artery atherosclerosis stroke subtype is the risk factor of ischemia progression after endovascular treatment, whereas high NIHSS after endovascular thrombectomy and failure of successful recanalization are independently associated with neurological progression by brain edema or hemorrhage.

Five pivotal randomized trials of endovascular thrombectomy after ischemic stroke demonstrated revolutionary therapeutic improvements of acute ischemic stroke patients [6]. However, these studies also showed that a considerable portion of patients were left with poor functional outcome, ranging from 28.6 to 67.4% according to study designs [6]. The reasons for the poor functional outcome must be heterogeneous and it is necessary to implement differential approaches according to the etiology of neurological progression to mitigate secondary neuronal damage after recanalization treatment. This study emphasizes close neurological monitoring after intra-arterial recanalization treatment because END concentrated during acute period, especially within 72 h after thrombectomy, and was associated with poor functional outcome after discharge. Since more than half of the patients with internal carotid artery occlusion experienced END, they are an especially susceptible

Table 4 Comparison of clinical characteristics of the patients with early neurological deterioration in terms of its etiology

	Control (A) $N=81$	IS (B) $N=20$	Non-IS (C) $N=24$	P value A vs. B	P value A vs. C
Age, years, mean (SD)	67.8 (14.7)	69.5 (9.9)	68.1 (12.2)	0.64	0.94
Sex, female, *n* (%)	32 (39.5)	13 (65.0)	11 (45.8)	0.04	0.58
Hypertension, *n* (%)	50 (61.7)	13 (65.0)	15 (62.5)	0.79	0.95
Diabetes mellitus, *n* (%)	22 (27.2)	8 (40.0)	9 (37.5)	0.26	0.33
Smoking, *n* (%)	16 (19.8)	4 (20.0)	4 (16.7)	0.98	0.99
Atrial fibrillation, *n* (%)	56 (69.1)	11 (55.0)	17 (70.8)	0.23	0.87
Previous stroke, *n* (%)	14 (17.3)	4 (20.0)	6 (25.0)	0.78	0.39
Systolic blood pressure, mmHg, mean (SD)	144 (29)	151 (34)	143 (23)	0.55	0.94
NIHSS at admission, mean (SD)	15 (7)	15 (8)	19 (7)	0.97	0.006
NIHSS after thrombectomy, mean (SD)	13 (8)	14 (7)	20 (7)	0.39	< 0.001
Intravenous thrombolysis, *n* (%)	41 (50.6)	13 (65.0)	15 (62.5)	0.25	0.31
Onset to endovascular treatment, minutes, mean (SD)	231 (128)	225 (162)	188 (85)	0.84	0.12
Onset to recanalization, minutes, mean (SD)	336 (123)	360 (149)	343 (86)	0.46	0.81
Internal carotid artery occlusion, *n* (%)	18 (22.2)	4 (20.0)	12 (50.0)	0.99	0.008
Basilar artery occlusion, *n* (%)	18 (22.2)	5 (25.0)	2 (8.3)	0.77	0.15
Successful recanalization, *n* (%)	73 (90.1)	15 (75.0)	13 (54.2)	0.13	< 0.001
White blood cell count, x 10^9/L, mean (SD)	8.6 (4.9)	9.9 (2.9)	9.1 (4.7)	0.25	0.62
Platelet, x 10^9/L, mean (SD)	214 (69)	247 (63)	194 (76)	0.05	0.23
Fasting blood sugar, mg/dL, mean (SD)	140 (49)	145 (51)	156 (52)	0.73	0.17
Total cholesterol, mg/dL, mean (SD)	161 (39)	178 (46)	152 (37)	0.11	0.31
Large artery atherosclerosis, *n* (%)	8 (9.9)	8 (40.0)	1 (4.2)	0.001	0.68
Cardioembolism, *n* (%)	68 (84.0)	11 (55.0)	20 (83.3)	0.01	0.99

Six patients who deteriorated by non-neurological causes were included in the control group

IS stands for neurological deterioration due to ischemia progression, *Non-IS* neurological deterioration due to brain edema or hemorrhage

Table 5 Factors associated with neurological deterioration due to ischemia progression and non-ischemic causes (brain edema and hemorrhage)

	Odds ratio	Confidence interval	P value
Ischemia progression			
Sex, female	3.02	1.00–9.27	0.05
Platelet count	1.01	0.99–1.002	0.25
Large artery atherosclerosis	6.28	1.79–22.0	0.004
Brain edema or hemorrhage			
NIHSS after endovascular therapy	1.15	1.06–1.24	0.001
Successful recanalization	0.11	0.03–0.39	0.001
Internal carotid artery occlusion	2.64	0.84–8.31	0.10

NIHSS National Institute of Health Stroke Scale

population to secondary neuronal injury after endovascular thrombectomy.

Since the mechanism of END in acute ischemic stroke is heterogeneous, the etiology specific management strategy may be necessary to maximize neurological outcome after recanalization treatment [13]. This study demonstrated the etiology specific risk factors of END after endovascular therapy. Ischemia progression could be predicted when a patient had stroke subtype of large artery atherosclerosis. Atherosclerotic stroke patients with vulnerable plaque are known to experience frequent stroke recurrence, which is concentrated in the acute phase [14]. A previous study performed on ischemic stroke patients treated by intravenous thrombolysis with the same definition and categorization of END also showed that the stroke subtype of large artery atherosclerosis was an independent predictor of END due to ischemia progression [13]. Since END due to hemorrhagic transformation is a minority, while the most common mechanism of ischemic END is re-occlusion of initial relevant arteries in this study, whether early initiation of

antithrombotic treatment and/or high intensity statin could reduce ischemia progression for the selected patient with high risk of ischemia progression and low risk of hemorrhage needs to be investigated in a prospective interventional study.

Patients experiencing non-ischemic END (brain edema or symptomatic hemorrhage) were more likely to have a higher level of NIHSS after endovascular treatment and were less likely to have successful recanalization compared to neurologically stable patients. Recanalization failure might result in large infarct volume with widespread blood brain barrier disruption, thereby increasing the risk of brain edema and/or symptomatic hemorrhage. A recent study showed that early hemicraniectomy increased the proportion of patients with survival without severe disability after malignant middle cerebral artery infarction [15]. Several studies suggested a promising effect of therapeutic hypothermia among stroke patients with increased intracranial pressure [16, 17]. Although these invasive treatment modalities may not be implemented for all the stroke patients, patients who are at high risk of deterioration due to brain edema or hemorrhage may be an appropriate target population. Intravenous glyburide reduced brain swelling by the blockade of the inducible sulfonylurea receptor 1-transient receptor potential melastatin 4 channel in neuron, astrocyte, and endothelium from a preclinical study, and was also well tolerated with non-significant mortality reduction in patients with large hemispheric stroke from a clinical trial [18]. This novel and relatively less invasive treatment might be considered after thrombectomy for patients with a possible risk of brain edema.

This study has several limitations. First, this study was conducted from a single center and cardioembolic stroke was the major stroke etiology (79.2%). This is higher than the rates of atrial fibrillation from major randomized clinical trials investigating the efficacy and safety of endovascular thrombectomy among stroke patients, which is about 26–40% [1–5]. We speculated that the detection rate of cardioembolic source was high in our institution because all the patients had been monitored in the stroke unit or intensive care for at least 24 h after admission and 24-h Holter monitoring and transthoracic echocardiography were mandatory studies among stroke survivors. The number of stroke patients with large artery atherosclerosis subtype is rather small compared to cardioembolic stroke patients. Future studies with larger sample size or prospective design with a stringent definition of END mechanism are necessary to confirm the relationship between END mechanisms and stroke subtype. Second, the endovascular treatment modality was not homogeneous although the majority was accomplished by stent retriever-based treatment. Third, the incidence of END was assessed by chart review which might have resulted in selection bias. Although NIHSS is known to be a reliable indicator of stroke severity, agreement between raters can vary, especially for individual elements of the NIHSS [19]. Finally, pretreatment infarct burden was not assessed. The Alberta Stroke Program Early CT Score is a useful tool to estimate initial ischemic injury, but we could not apply it because occluded arteries were rather heterogeneous including 24 cases of basilar artery occlusion. A prospective study with standardized imaging protocol including diffusion-weighted image can disclose the relationship between initial infarct burden and END after recanalization therapy.

This study illustrates the incidence and mechanism of neurological worsening after endovascular thrombectomy among acute cerebral infarction patients with major cerebral artery occlusion. The etiology of neurological deterioration needs to be categorized to derive its risk factor and tailored treatment strategy. The risk factor predicting ischemia progression was stroke subtype of large artery atherosclerosis. The neurological severity by NIHSS after endovascular thrombectomy and recanalization failure predicted neurological deterioration due to brain edema or symptomatic hemorrhage.

Acknowledgements The work was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2016R1D1A1B03933891). The funding has no role in the design, collection, analysis, or interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Compliance with ethical standards

Conflicts of interest All the authors declare that they have no conflict of interest.

References

1. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ et al (2015) A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 372:11–20
2. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J et al (2015) Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 372:1019–1030
3. Saver JL, Goyal M, Bonafe A, Diener HC, Levy EI, Pereira VM et al (2015) Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med 372:2285–2295
4. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N et al (2015) Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 372:1009–1018
5. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A et al (2015) Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 372:2296–2306
6. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM et al (2016) Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 387:1723–1731

7. Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC et al (2015) 2015 American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 46:3020–3035
8. Hong KS, Ko SB, Yu KH, Jung C, Park SQ, Kim BM et al (2016) Update of the Korean Clinical Practice Guidelines for Endovascular Recanalization Therapy in Patients with Acute Ischemic Stroke. J Stroke 18:102–113
9. Espinosa de Rueda M, Parrilla G, Manzano-Fernández S, García-Villalba B, Zamarro J, Hernández-Fernández F et al (2015) Combined multimodal computed tomography score correlates with futile recanalization after thrombectomy in patients with acute stroke. Stroke 46:2517–2522
10. Hussein HM, Georgiadis AL, Vazquez G, Miley JT, Memon MZ, Mohammad YM et al (2010) Occurrence and predictors of futile recanalization following endovascular treatment among patients with acute ischemic stroke: a multicenter study. Am J Neuroradiol 31:454–458
11. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL et al (1993) Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke 24:35–41
12. Suh SH, Cloft HJ, Fugate JE, Rabinstein AA, Liebeskind DS, Kallmes DF (2013) Clarifying differences among thrombolysis in cerebral infarction scale variants: is the artery half open or half closed? Stroke 44:1166–1168
13. Kim JM, Moon J, Ahn SW, Shin HW, Jung KH, Park KY (2016) The etiologies of early neurological deterioration after thrombolysis and risk factors of ischemia progression. J Stroke Cerebrovasc Dis 25:383–388
14. Kim JM, Jung KH, Sohn CH, Moon J, Han MH, Roh JK (2016) Intracranial plaque enhancement from high resolution vessel wall magnetic resonance imaging predicts stroke recurrence. Int J Stroke 11:171–179
15. Jüttler E, Unterberg A, Woitzik J, Bösel J, Amiri H, Sakowitz OW et al (2014) Hemicraniectomy in older patients with extensive middle-cerebral-artery stroke. N Engl J Med 370:1091–1100
16. Jeon SB, Koh Y, Choi HA, Lee K (2014) Critical care for patients with massive ischemic stroke. J Stroke 16:146–160
17. Su Y, Fan L, Zhang Y, Zhang Y, Ye H, Gao D et al (2016) Improved neurological outcome with mild hypothermia in surviving patients with massive cerebral hemispheric infarction. Stroke 47:457–463
18. Sheth KN, Elm JJ, Molyneaux BJ, Hinson H, Beslow LA, Sze GK et al (2016) Safety and efficacy of intravenous glyburide on brain swelling after large hemispheric infarction (GAMES-RP): a randomised, double-blind, placebo-controlled phase 2 trial. Lancet Neurol 15:1160–1169
19. Josephson SA, Hills NK, Johnston SC (2006) NIH Stroke Scale reliability in ratings from a large sample of clinicians. Cerebrovasc Dis 22:389–395