Original Article

Complications in Acute Ischemic Stroke Patients during Endovascularization Therapy: A Retrospective Study

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Objective: The present study aimed to determine the preferential technique of anesthesia, and compare the peri-procedure or treatment complications in acute ischemic stroke patients who received endovascular recanalization therapy.

Materials and Methods: A retrospective descriptive cross-sectional study, data were collected from a list of patients who received endovascular recanalization therapy from January 2014 to December 2015. Data from all patients were retrieved from a database of the department of anesthesiology, Faculty of Medicine Siriraj Hospital. Baseline data were collected including age, sex, comorbidities, current medication, Glasgow Coma Scale [GCS] and stroke severity. Intra-procedural data and post-procedural complications were collected.

Results: Ninety-one patients were enrolled to the present study, 86% received general anesthesia [GA]. All baseline patients' characteristics were similar in both groups, except patients in local anesthesia [LA] group receiving anti-coagulants much more than GA group ($p = 0.004$). The overall procedure time and time record in stroke fast tract protocol were similar in both groups. In GA group found peri-procedural hypotension significantly greater than LA group ($p<0.001$). Hypertension and re-stroke were found in LA group, significantly greater than GA group ($p = 0.034$, $p = 0.048$).

Conclusion: GA was more preferable technique than LA in patients undergoing endovascular recanalization therapy. LA provided less hypotension than GA during procedure. The patients receiving LA suffered from hypertension and re-stroke more than GA in post-procedural period. Both GA and LA did not show greater improvement in neurological status at 24 hours after treatment.

Keywords: Complication, Acute ischemic stroke, Endovascular, recanalization, treatment, Retrospective

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Acute stroke is the second leading cause of death worldwide and the major sequalae is long-term disability[1]. Ischemic stroke accounts for 87% of strokes[1]. The pathophysiology of acute ischemic stroke is decreasing in blood flows to the brain, which is caused by either stenosis of the vessel to the brain (e.g. carotid artery) or occlusion of the vessel to the brain (e.g. embolus, thrombus)[1].

The goal of acute ischemic stroke treatment is to restore perfusion to the brain as fast as possible[1]. The acute stroke fast tract protocol was initiated in Siriraj Hospital in 2014 (Appendix 1). The acute stroke fast tract protocol is implemented in patients who develop stroke symptoms within 8 hours. This determines that all processes in the protocol cannot consume much more time frame. The main procedures to restore perfusion to brain are intra-venous thrombolysis with recombinant tissue plasminogen activator [rtPA] and endovascular recanalization therapy, including thrombectomy using stent retrievers[1-5]. The onset of stroke symptoms and severity of stroke symptom determine the acute ischemic stroke treatment (rtPA administration, endovascular recanalization therapy, or both.

According to the acute stroke fast tract protocol, the anesthesiologist plays a role in peri-endovascular recanalization therapy period. The anesthesiologist rapidly evaluates the patient, performs anesthesia during treatment, and transfers the patient to the stroke unit after the treatment is finished. There have recently been increased data about the

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relationship between types of anesthesia, which are general anesthesia [GA] and local anesthesia [LA], during endovascular therapy and the patient's outcome. Previous studies revealed the techniques of anesthesia used during endovascular recanalization may influence patient's outcome[6-11]. There is disagreement as to whether GA with intubation or LA is the best technique to treat these patients[10]. GA is most often used due to its perceived superior safety and efficacy[10]. GA can provide the immobility of the patient, adequate pain control, and airway protection[1]. The disadvantages of GA possibly are hemodynamic changes with intubation, delaying time to recanalization, increasi ng risk of pulmonary aspiration, and needing more anesthetic agents and anesthetic personnel[1]. LA allows surgeons to monitor the patient's neurological status during treatment and reduces time to procedure initiation[12]. Furthermore, LA may be associated with improved hemodynamic stability compared with GA[4-6,12]. However, LA also has the disadvantages such as lack of airway protection, movement of patient during treatment, inadequate pain control, agitation of the patient, and possibly causing prolonged procedure time[1]. The endovascular recanalization therapy is the new procedure itself, so the anesthesiologists and team have not enough experience in anesthetizing these kinds of patients. The other team members including neurologist and the interventionist (either neurosurgeon or radiologist) feel the same as anesthesiologist. GA is a familiar anesthetic technique during endovascular therapy at Siriraj Hospital. Nowadays, LA is becoming increasingly common as anesthesiologist and interventionist become more familiar with the treatment. Several recent reports have described higher incidence of unfavorable outcome when using GA, but most reports are retrospective studies[1-4,13]. Even prospective randomized controlled trial[3] is inconclusive about the effects of anesthetic techniques on the patient's outcome.

The present study aimed to determine the preferential technique of anesthesia, and compare the peri-procedure or treatment complications in acute ischemic stroke patients who received endovascular recanalization therapy.

Materials and Methods

When a patient with suspected acute ischemic stroke arrives at the emergency department [ED], a team consisting of a neurologist and interventionist is rapidly assembled. The acute stroke fast tract protocol in detail is shown in appendix 1. If the patient is experiencing an acute ischemic stroke, the ischemic stroke fast track protocol is implemented and the patient is transferred to radiology department for computed tomography scan (CT scan). If the patient requires thrombectomy, the interventionist notifies anesthesiologist and conducts the endovascular recanalization. The anesthesiologist anesthetizes the patient by either GA with intubation or LA. The choice of anesthetic technique is made collectively by the team depending on the location of disease (stroke), patient's cooperation, and the interventionist's preference. For some conditions, the anesthesiologist is able to retrieve a specific indication for GA including pre-procedure aspiration, airway obstruction and decreased level of consciousness. The patient considers to have received GA if endotracheal intubation with or without unconsciousness occurred at any time before the end of the procedure. LA is defined as patient who has not received anesthetic agents (inhalation agents and neuromuscular blocking agents).

Data collection

This retrospective descriptive cross-sectional study was conducted after the approval from Siriraj Institutional Review Board (Si. 274/2017). A list of patients, who activated the fast-track protocol from January 2014 to December 2015, was obtained from the Siriraj stroke unit. Anesthetic records and electronic medical records were retrieved from the database of anesthesiology department. Baseline data were collected including age, sex, comorbidities, current medication, Glasgow Coma Scale [GCS] and stroke severity. The stroke severity or neurological condition was calculated using the National Institutes of Health Stroke Scale [NIHSS] from 11 domains and ranging from 0 (no stroke) to 42 (most severe). The NIHSS detail is shown in appendix 2. The NIHSS is a common diagnostic tool for quickly evaluating the stroke severity and 4 scales difference indicates clinical difference[3]. The change in neurological condition was also collected.

Intra-procedure data including time record in stroke fast tract protocol, events (such as hypotension, hypertension, desaturation), and fluid administration were collected. Post-procedural data including delayed extubation, hypotension, hypertension, desaturation, re-stroke in admission, pneumonia in admission, length of intensive care unit [ICU]/hospital stay, ventilator use, and death in admission were also collected. The definitions of all events in this study were defined as being either intra-procedure or post-procedure events in appendix 3.

Statistical analysis

The prsent study examined the endovascular recanalization therapy which was the new treatment in AIS patients. The author collected the data since this treatment was initiated in Siriraj Hospital. Therefore, this study did not calculate for sample size.

Statistical analysis was performed with the SPSS 18 statistical software package (SPSS Inc). The categorical characteristic, neurological severity and events were reported in number of patients and percentage, mean and standard deviation, median and interquartile range. The categorical characteristic, neurological severity and events were compared using independent t-test, Chi-square test, Mann-Whitney U test, and Fisher exact test. A 2-side p-value of <0.05 is considered statistically significant.

Results

From January 2014 to December 2015, 91 patients were identified as having acute ischemic stroke according to criteria for endovascular therapy at the Siriraj Hospital. There were no missing data. Seventy-eight patients received GA and 13 received LA. Therefore, the preference of anesthetic technique with GA and LA were 86% and 14%, respectively. There were no differences in patients' characteristics except the lower number of patients receiving anti-coagulants in the GA group (10.3% vs. 46.2%, p = 0.004). The baseline serum glucose level was higher in patients having GA (120 mg/dL vs. 109 mg/dL). However, they were not significantly different (p = 0.053). The patients' ASA class III E was the majority number of patients in the present study (Table 1).

Table 2 demonstrates intra-procedural data and events. The time record in stroke fast tract protocol showed no significant difference between the two groups (p>0.05). The average time period from starting anesthesia to arterial puncture was 20 minutes on the GA group and 15.5 minutes for the LA group. The total average procedure time was 117 minutes in the GA group and 110 minutes in the LA group. Forty-three patients in GA group had hypotension, which showed significant difference compared with LA group (p<0.001). Intra-procedural fluid administration in GA group was 828.8+410.4 mL vs. LA group 488+166 mL, which was significantly different (p = 0.001).

The post-procedural data and events are shown in Table 3. For hypertension, there were 17.9% in the GA group, which was significantly lower than 46.2% in the LA group (p = 0.034). Moreover, re-strokes were found for 14.1% in the GA group and 38.5% in the LA group (p = 0.048). There were five patients in the LA group requiring intubation within 24 hours after procedure. The reasons of intubation were recurrent major stroke in two patients, congestive heart failure in two patients, and aspiration in one patient. However, the median duration of ventilator use was similar in both groups (p = 0.342). Finally, 12.8% of GA patients died and no patient died in LA group. However, there was no significant difference (p = 0.347).

Table 4 shows the neurological severity and the change in NIHSS scale between at admission and 24 hours after treatment. The neurological severity between both groups before treatment and 24 after hours treatment was similar (p = 0.479 and p = 0.474). The change in NIHSS scale was not significantly different between the two groups (p = 0.287).

Discussion

Previous studies showed that baseline NIHSS, GCS, American Society of Anesthesiologist [ASA] classification were the predictors to determine the postoperative morbidity and mortality in acute ischemic stroke patients[3,5,6,8-20]. GA was more popular than LA due to the endovascular recanalization therapy being a new treatment of choice in acute ischemic stroke, especially in the retrospective studies[1,2,5,6,8]. There was insufficient information and experiences in caring the patient undergoing this procedure. Our study revealed that in the year 2014, there was no patient receiving LA. LA was introduced in the year 2015. For the retrospective study, the authors categorized patients with acute ischemic stroke (anterior circulation, higher National Institutes of Health Stroke Scale [NIHSS] score (>10), and isolated/combined occlusion at any level of the internal carotid or middle cerebral artery) into two groups, GA and LA[3]. This study concluded that neither GA nor LA showed greater improvement in neurological status at 24 hours after treatment[3]. However, anesthesia technique selection during endovascular recanalization therapy depended on location of stroke, stroke severity, and patient's cooperation.

In present study, intra-procedural hypotension and intra-procedural fluid administration were also significantly greater in GA group than LA group. This implied that when hypotension occurred fluid resuscitation was applied as the treatment. Anesthetic agents caused hypotension and associated with a higher risk of cerebral hypo-perfusion and an increase in ischemic injury[1]. Davis et al found that patients with ischemic stroke receiving endovascular recanalization had higher rates of intra-procedural

Table 1. Demographic data

	General anesthesia (n = 78)	Local anesthesia (n = 13)	*p*-value
Gender: Female	38 (48.7)	7 (53.8)	0.732
Age (year)	65.5±15.2	72.2±13	0.142
Weight (kilogram)	58.7±11.6	60.7±14.5	0.579
ASA classification			0.741
II E	3 (3.8)	0 (0)	
III E	69 (88.5)	13 (100)	
IV E	6 (7.7)	0 (0)	
Glasgow Coma Score	10.8±3.1	12.5±2.1	0.066
Comorbidities			
Hypertension	61 (78.2)	9 (69.2)	0.488
Atrial fibrillation	37 (47.4)	9 (69.2)	0.231
Hyperlipidemia	37 (47.4)	3 (23.1)	0.135
Heart failure	3 (3.8)	1 (7.7)	0.466
Diabetes mellitus	24 (34.8)	5 (38.5)	0.749
Peripheral arterial disease	17 (21.8)	5 (38.5)	0.291
Smoking	11 (14.1)	4 (30.8)	0.217
Current medication			
Anti-platelets	23 (29.5)	3 (23.1)	0.751
Anti-coagulants	8 (10.3)	6 (46.2)	0.004*
Statins	38 (48.7)	5 (38.5)	0.560
Baseline serum glucose (mg/dL)	120 (104,146)	107 (94,128)	0.053

The data are presented as mean ± standard deviation, n (%) or median (P_{25}, P_{75})
ASA = American Society of Anesthesiologists; E = emergency

Table 2. Intra-procedural data and events

	General anesthesia (n = 78)	Local anesthesia (n = 13)	*p*-value
Time record in stroke fast track protocol			
CT to arterial puncture (min)	94.6±47.4	106.5±48.4	0.194
Start anesthesia to arterial puncture (min)	20±11	15.5±2.1	0.383
Procedure time (min)	117±55	110±31	0.892
Events			
Hypotension	43 (51.1)	0 (0)	<0.001*
Hypertension	15 (19.2)	4 (30.8)	0.459
Desaturation	1 (1.3)	0 (0)	1.000
Hypocarbia	46 (59.0)	N/A	-
Hypercarbia	6 (7.7)	N/A	-
Perforation with ICH and/or SAH	4 (5.1)	0 (0)	1.000
Fluid administration (mL)	828.8±410.4	488.5±166	0.001*

The data are presented as mean ± standard deviation or n (%)
CT = Computerized Tomography; ICH = Intracerebral hemorrhage; SAH = Subarachnoid hemorrhage; N/A = Not applicable

hypotension with general anesthesia than with conscious sedation[9]. Induction and recovery phases of general anesthesia often associated with significant hemodynamic changes (hypotension and rapid blood pressure fluctuations) that could exacerbate ischemic injury[1]. Other reports found that hypotension and

Table 3. Post-procedural data and events

	General anesthesia (n = 78)	Local anesthesia (n = 13)	*p*-value
Delayed extubation	52 (66.7)	NA	-
Hypotension	21 (26.9)	5 (38.5)	0.508
Hypertension	14 (17.9)	6 (46.2)	0.034*
Desaturation	4 (5.1)	0 (0)	1.000
Re-stroke (in admission)	11 (14.1)	5 (38.5)	0.048*
Pneumonia (in admission)	25 (32.1)	5 (38.5)	0.752
Length of hospital stay (d)	15.5 (9.8, 27)	16 (9, 36)	0.695
Length of ICU stay (d)	10.5 (6, 16)	13 (5.5, 27.0)	0.440
Ventilator use (d)	5 (2.8, 10.00)	5 (5, 10.0)	0.342
Death (in admission)	10 (12.8)	0 (0)	0.347

The data are presented as mean ± standard deviation, n (%), or median (P_{25}, P_{75})
ICU = Intensive care unit

Table 4. Stroke severity

	General anesthesia	Local anesthesia	*p*-value
NIHSS at admission	17±6	15±3	0.479
NIHSS after 24 hours	12±6	14±6	0.474
Change in NIHSS	2 (0, 8)	3.00 (-4, 6.5)	0.287

NIHSS = The National Institutes of Health Stroke Scale; Change in NIHSS = NIHSS at admission-NIHSS after 24 hours

higher rate of fluid administration contribute to the higher morbidity and mortality rates observed with general anesthesia[5-8].

For post-procedure period, the patients in LA group had significantly greater hypertension and re-stroke in admission than GA group and increased the length of hospital and ICU stay in LA group. Conversely, Jumaa et al[5] showed good outcome and decreased length of hospital stay in LA group. As described before, there were five patients in the LA group requiring intubation within 24 hours after procedure. The reasons for intubation were recurrent major stroke in two patients, congestive heart failure in two patients, and aspiration in one patient. With a small number in LA group, patients who suffered severe complication could make the results in the length of hospital and ICU stay, and the ventilator use similar with GA group. Post-procedure pneumonia was found equally in both LA and GA groups. It was proposed that insufficient airway protection in non-intubated patients with acute ischemic stroke may lead to higher aspiration rate and subsequently pneumonia in these patients in post-procedure period[4,5]. The benefit from LA was no intra-procedural hypotension, but patients could suffer from post procedural hypertension and re-stroke.

Parameters related to post-procedural complication included time to intra-arterial therapy and procedure time[13]. The overall procedure time was no significant difference in both groups. The time from starting anesthesia to intra-arterial therapy was not so similar in both groups. Previous studies[1-3,5,6] reported no significant difference, the same as our study. This could be explained concerning GA. Anesthesiologist performed rapid sequence induction which did not take much time for ordinary patients. On the other hand, anesthesiologist and team informed, confirmed, and made sure that the patient could tolerate the treatment, and these processes could take time.

For stroke severity, baseline NIHSS scale was not significantly different between the two groups. After procedure, stroke severity improved in both GA and LA groups (NIHSS scale 24 hours after treatment <NIHSS scale at admission). Unfortunately, the improvement of stroke severity was not significantly different between the two groups. As described in

Schonenberger S. study, 4 difference scales indicate clinical differences[3]. In present study, the change in NIHSS scale was 2 in GA group and 3 in LA group and did not show improvement in clinical outcome. Schonenberger S[3] study revealed neither GA nor LA provided greater improvement in neurological status at 24 hours, and for the neurological outcome, required longer period for follow-up.

The mortality rate in admission of LA group is zero but in GA group is 12.8% (p = 0.347). Even stroke severity was not significantly different between two groups (NIHSS (GA group 16.6$\pm$5.7, LA group 15.4$\pm$3.4, p = 0.479), and GCS (GA group 10.8$\pm$3.1, LA group 12.5$\pm$2.1, p = 0.066 in GA group). Consistent with SIESTA trial (a single center randomized, appareled-group, and open-label treatment trial), it was reported that GA did not increase morbidity and mortality compared with LA[3].

The present study had several limitations. This study was retrospective, not randomized, and a small convenient sample. The possibility of uncontrolled selection bias and unmeasured confounding variables limit our ability to draw meaningful conclusion. For example, it is possible that patients with more severe strokes received general anesthesia or were intubated before the procedure due to inability to preserve airway patency. According to the number of patients in LA group (13 patients), it was insufficient to compare the entire outcome statistically between two groups. This study did not stratify outcome on the basis of stroke location (anterior/posterior circulation) or initial ASPECTS score from CT scan (Alberta stroke programmed early CT score [ASPECTS] is a 10-point quantitative topographic CT scan score, assessment of the MCA vascular territory. One point is deducted from the initial score of 10 for every region involved)[11]. The site of vascular occlusion was another determinant of outcome and a potential confounder in this study.

Therefore, a prospective randomized controlled trial is needed to determine if general anesthesia is associated with higher rates of complications and poor neurologic outcome in patients receiving endovascular therapy for acute ischemic stroke.

Conclusion

The present study revealed GA was a more preferable technique than LA in patients undergoing endovascular recanalization therapy. LA provided less hypotension than GA during this procedure. However, patients receiving LA suffered from hypertension and re-stroke more than GA in post-procedural period. Both GA and LA did not show greater improvement in neurological status at 24 hours after treatment.

What is already known on this topic?

Acute ischemic stroke is the emergency condition which requires immediate treatment consisting of endovascular recanalization therapy plus standard treatment (intravenous rtPA). Both GA and LA are anesthetic techniques of choice for this procedure. There is insufficient information indicating the relative benefit on neurological outcome between the two techniques.

What this study adds?

GA was a more familiar technique than LA in patients undergoing endovascular recanalization therapy in Siriraj hospital during 2014 to 2015. LA showed less hypotension than GA during treatment, but patients receiving LA had hypertension and re-stroke more often than patients receiving GA in post-procedural period. The improvement in neurological status at 24 hours after treatment was similar in both GA and LA.

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Trial registration

Clinical Trials.gov registration as NCT 03426917.

Potential conflicts of interest

The authors declare no conflict of interest.

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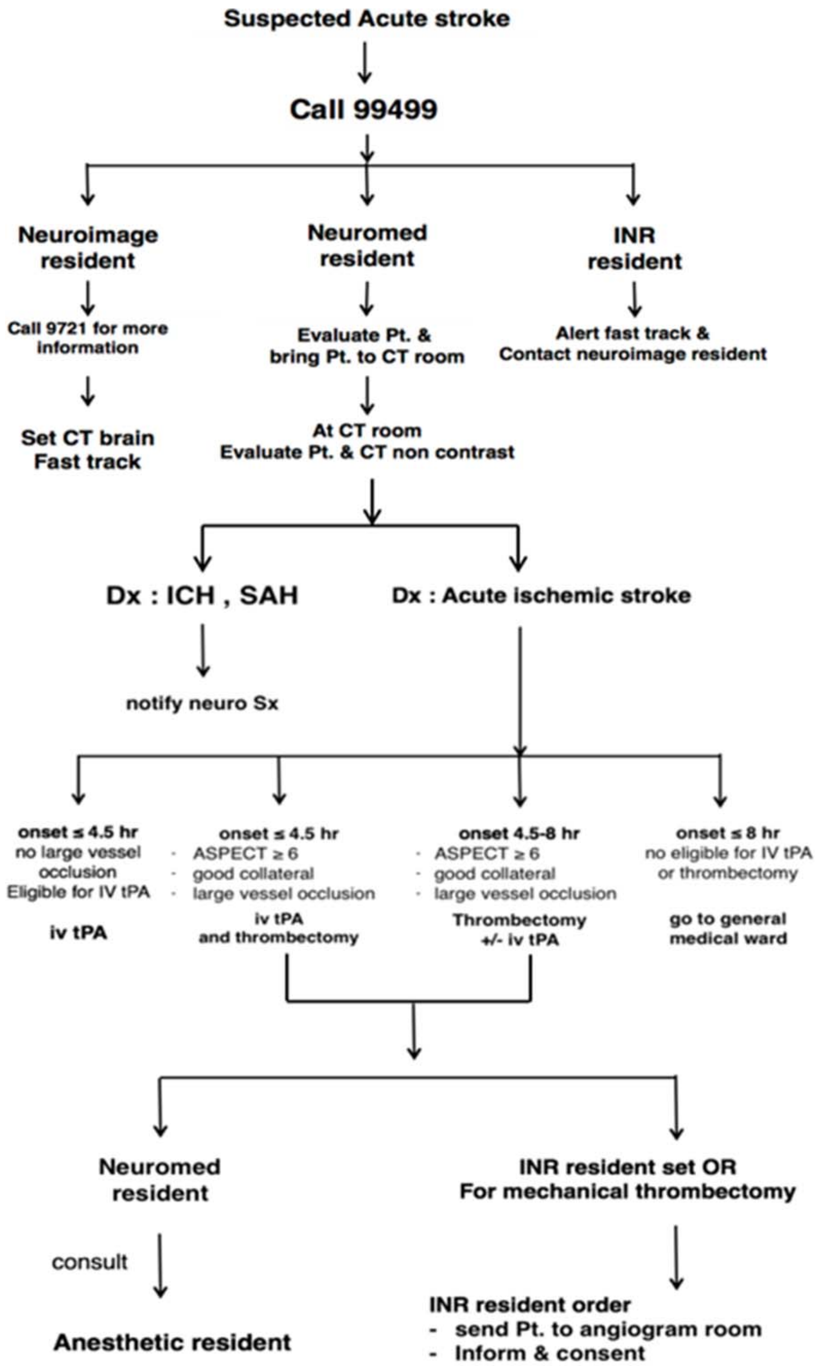
Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. Stroke 2007;38:1655-711.

Appendix 1. Siriraj stroke fast track protocol.



Pt = Patient; ICH = intracerebral hemorrhage; SAH = subarachnoid hemorrhage; CTA = computed tomography angiography; CTP = computed tomography perfusion; IV tPA = intravenous tissue plasminogen activator; INR = interventional radiology.

Appendix 2. National Institutes of Health Stroke Scale

Tested Item	Title	Responses and Scores
1A	Level of consciousness	0 = alert 1 = drowsy 2 = obtunded 3 = coma/unresponsive
1B	Orientation questions (2)	0 = answers both correctly 1 = answers one correctly 2 = answers neither correctly
1C	Response to commands (2)	0 = performs both tasks correctly 1 = performs one task correctly 2 = performs neither
2	Gaze	0 = normal horizontal movements 1 = partial gaze palsy 2 = complete gaze palsy
3	Visual fields	0 = no visual field defect 1 = partial hemianopia 2 = complete hemianopia 3 = bilateral hemianopia
4	Facial movement	0 = normal 1 = minor facial weakness 2 = partial facial weakness 3 = complete unilateral palsy
5	Motor function (arm) A) Left B) Right	0 = no drift 1 = drift before 5 seconds 2 = falls before 10 seconds 3 = no effort against gravity 4 = no movement
6	Motor function (leg) A) Left B) Right	0 = no drift 1 = drift before 5 seconds 2 = falls before 5 seconds 3 = no effort against gravity 4 = no movement
7	Limb ataxia	0 = no ataxia 1 = ataxia in 1 limb 2 = ataxia in 2 limbs
8	Sensory	0 = no sensory loss 1 = mild sensory loss 2 = severe sensory loss
9	Language	0 = normal 1 = mild aphasia 2 = severe aphasia 3 = mute or global aphasia
10	Articulation	0 = normal 1 = mild dysarthria 2 = severe dysarthria
11	Extinction or inattention	0 = absent 1 = mild (loss 1 sensory modality) 2 = severe (loss 2 modalities)

From: Harold PA, Gregory Z, Mark JA, Deepak LB, Lawrence B, et al. Guidelines for the early management of adults with ischemic stroke. Stroke 2007;38:1655-711[21]

Appendix 3. Definitions used in this study

Complication	Definitions
Critical hypertension	Systolic blood pressure >180 mm.Hg
Critical hypotension	Systolic blood pressure <120 mm.Hg
Critical oxygenation disturbance	O_2 saturation < 90%
Critical ventilation disturbance	End tidal CO_2 <30 mm.Hg or > 40 mm.Hg)[1]
Aspiration	Seen gastric fluid or content in oropharynx or endotracheal tube
Procedural complications	Vessel perforation
Delayed extubation	Exceeding 2 hours after cessation of sedation and analgesia
Re-stroke	Second attack of stroke including ischemic and hemorrhagic
Pneumonia	Intrahospital pneumonia with other causes
Early neurological improvement indicated by change of NIHSS score 24 hours after admission	NIHSS on admission – NIHSS after 24hour
Intrahospital mortality	Death in admission with other causes
Length of stay in hospital	Days from admission to discharge
Length of stay on ICU	Days from ICU admission to transfer from ICU
Duration of ventilator use	Hours from start to extubation

From: Schonenberger S, Uhlmann L, Hacke W, Schieber S, Mundiyanapurath S, Purrucker JC, et al. Effect of conscious sedation vs. general anesthesia on early neurological improvement among patients with ischemic stroke undergoing endovascular thrombectomy: a randomized clinical trial. JAMA 2016;316:1986-96[3]