Research Project

Title

Target-controlled total intravenous anesthesia with propofol versus sevoflurane anesthesia for endovascular thrombectomy procedure in acute ischemic stroke patients: Comparison of the outcomes

Background knowledge and important issues in acute ischemic stroke

1. In 2019, cerebrovascular disease (i.e., stroke) was the second leading cause of death worldwide. (https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death)
2. The present guidelines for the early management of patients with acute ischemic stroke urge the in-time and early application of intravenous chemical thrombolysis and endovascular thrombectomy (EVT) due to better outcome and prognosis. "Timing is brain."
3. Patients with acute ischemic stroke, previous stroke, and severe stroke have high incidence of delirium, and the stroke-related delirium has been shown to correlate with higher morbidity and mortality.
4. Researches on the anesthetic management during EVT for acute ischemic stroke have shown that both general anesthesia and sedation anesthesia are safe and without difference in neurological outcome and long-term complications. However, general anesthesia might have higher rates in revascularization in EVT for acute ischemic stroke as compared with sedation anesthesia.
5. Anesthesia could produce postoperative cognitive dysfunction (POCD) or delirium (POD), and general anesthesia could produce higher rates of POCD and POD compared to general anesthesia and sedation anesthesia. Additionally, brain injury and acute ischemic stroke are independent risk factors for POCD and POD. Whether the anesthetic management for EVT would interfere with the acute ischemic stroke-produced POCD and/or POD or even delay the detection and treatment of stroke-related neurological impairment deserves investigation since EVT is the gold standard for acute ischemic stroke.

Cerebrovascular accident and acute ischemic stroke

Stroke is a disease that affects the arteries leading to and within the brain. It is the second leading cause of death worldwide, the fifth leading cause of death and a leading cause of disability in the United States, and the fourth leading cause of death in Taiwan in 2019. [American Stroke

Association 2020; 衛生福利部統計處 108 年度死因統計] Meanwhile, ischemic strokes was accounted for 87% of all strokes after analysis from a report of the American Heart Association in 2014. [Go et al., 2014]

Endovascular thrombectomy (EVT) for acute ischemic stroke with large vessel occlusion

The time elapsed since onset of symptoms of stroke (time window) play important roles in clinical outcome of the acute ischemic stroke. In 2015, the encouraging results of the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke), ESCAPE (Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times), EXTEND-IA (Extending the Time for Thrombolysis in Emergency Neurological Deficits-Intraarterial), and SWIFT PRIME (Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment) trials all demonstrated the superiority of intra-arterial EVT therapy over intravenous tissue plasminogen activator (IV-tPA) alone in patients with acute ischemic stroke due to large vessel occlusion in the anterior circulation. [Berkhemer et al., 2015; Campbell et al., 2015; Goyal et al., 2015; Saver et al., 2015] Therefore, the American Heart Association/American Stroke Association (AHA/ASA) published the updated guidelines on EVT for the early management of patients with acute ischemic stroke in 2018 [Powers et al., 2018; Tang et al., 2019]. The criteria (Class I; Level of Evidence A) for EVT therapy in patients of acute ischemic stroke include (1) age ≥ 18 years, (1) pre-stroke functionally independent with modified Rankin Scale (mRS) score of 0 to 1 and have post-stroke neurological deficit assessed with a National Institute of Health Stroke Scale (NIHSS) score ≥ 6, (3) causative occlusion of the internal carotid artery or proximal middle cerebral artery (MCA-M1 branch), (4) the volume of the ischemic core estimated with the Alberta Stroke Program Early CT score (ASPECTS) is not large and should be ≥ 6, and (5) the treatment can be initiated (time to groin puncture) within 6 hours of symptom onset. In addition, EVT should be offered regardless of whether the patient received IV-tPA therapy. [Powers et al., 2018]

Anesthesia for EVT

Several randomized clinical trials, i.e. MR CLEAN, SWIFT PRIME, EXTEND-IA, ESCAPE, REVASCAT, and THRACE, have demonstrated strong efficacy with improved disability and better outcome of EVT either with or without the combined intravenous thrombolysis therapy with tissue plasminogen activator for patients with acute ischemic stroke from large vessel (including internal carotid artery or middle cerebral artery segment M1) occlusion. [Berkhemer et al., 2015, Bracard

et al., 2016, Campbell et al., 2015, Goyal et al., 2015, Jovin et al., 2015, Saver et al., 2015] Therefore, the American Heart Association/American Stroke Association 2018 guidelines for the early management of patients with acute ischemic stroke strongly recommends to perform EVT earlier (within 6 hours of onset of symptoms) and on-time (Powers et al., 2018).

Patients undergoing EVT can be managed either with conscious sedation anesthesia in spontaneous breathing or general anesthesia (GA) with volatile anesthetics or total intravenous anesthesia (TIVA). There are debates about the advantages between these anesthetic managements: GA provides muscular paralysis to facilitate intracranial arterial stenting in difficult cases and avoid the possible EVT-related complications, endotracheal intubation to prevent aspiration, and improved patient comfort, while conscious sedation anesthesia shortens the time to intervention (i.e., delay to groin puncture and reperfusion) without delay waiting for anesthesia team and avoids the GA-related detrimental side effects. Furthermore, GA-induced profound decrease in blood pressure and mechanical hyperventilation-produced hypocapnia and cerebral vasoconstriction might worsen the neurological outcomes in the acute ischemic stroke patients which raise concerns not favoring GA for the anesthetic management of EVT. [Takahashi et al., 2014] However, 3 randomized controlled trials including SIESTA (Sedation versus Intubation for Endovascular Stroke Treatment), AnStroke (Anesthesia During Stroke), and GOLIATH (General or Local Anesthesia in Intra Arterial Therapy) revealed no significant difference between GA and conscious sedation in neurological outcome as assessed by post-EVT National Institute of Health Stroke Scale, modified Rankin score, and infarct volume demonstrated on MRI diffusion-weighted imaging study in patients with acute ischemic stroke undergoing EVT, but with higher rates of successful reperfusion and better clinical outcome in general anesthesia group. [Hendén et al., 2017; Schönenberger et al., 2016; Simonsen et al., 2018] Therefore, GA is considered safe for the anesthetic management of EVT procedure.

General anesthesia and postoperative cognitive dysfunction or delirium

Delirium is characterized by disturbances of attention and cognition that cause functional decline and complications. The predisposing factors of delirium are age, male gender, systemic or metabolic disorders, dementia, and stroke. [Alvarez-Perez and Paiva, 2017; Caeiro et al., 2004] Postoperative neurocognitive disorders including postoperative dementia (POD) and postoperative cognitive dysfunction (POCD) not only affect cognitive function but also increase the risk for significant complications such as dementia and death. [Avelino-Silva et al., 2017; Rudolph and Marcantonio, 2011] Patient's characteristics including carotid and intracranial arterial

atherosclerosis, prior stroke and transient ischemic attack, intraoperative factors such as general anesthesia and inhaled anesthetics, and postoperative factors might precipitate to the development of POD and POCD with prolonged in-hospital stay and costs. [Ravi et al., 2019; Rutdolph and Marcantonio, 2011] The incidence of POCD/POD has been estimated to develop in 46% of patients undergoing cardiac surgery, with delirium lasting 1 to 2 days in 65% of these patients and 3 or more days in 35%; 9.1% of patients undergoing fast-track hip and knee surgery at 1 to 2 weeks and 8.0% at 3 months; 19.4%-22% in patients undergoing vascular surgery. [Ellard et al., 2014; Krenk et al., 2014; Saczynski et al., 2012; Katznelson et al., 2009]

Cognitive dysfunction after ischemic stroke

Ischemic stroke could injure the brain with both neurological dysfunction (including cognitive impairment) and physical disability in patients. It has been shown in the Framingham study that hemiparesis was most common neurological deficit (50%), followed by the cognitive deficits (46.2%), after ischemic brain stroke in elderly. [Kelly-Hayes et al., 2003] In addition, 22.2% to 39.6% patients with ischemic stroke were significantly more disabled from all domains including dependence on activity of daily living, poor health, incontinence, depression, social disability, and need institutionalization. [Kelly-Hayes et al., 2003] In MEDIAS (the Management Effort for Delirium and Insomnia in Acute Ischemic Stroke) study, delirium occurred in 25.8% of acute ischemic stroke patients (i.e., within 7 days after stroke onset) and these delirium patients were older and had significantly worse modified Rankin scale (mRS) scores both at discharge and 1 year after stroke onset. [Matsuzono et al., 2020] Furthermore, these acute ischemic stroke patients with delirium received delirium management including physical restraint alone (45.3%), combined physical restraint and major tranquilizers (36.8%), and major tranquilizers alone (17.8%). The authors raised the concern that physical restraint may be required to ensure patient safety but inversely have potential harmful consequences including death in these acute ischemic stroke patients with delirium. [Matsuzono et al., 2020]

Target-monitored GA to reduce the risk of intraoperative awareness and unfavorable hypotension

The goals of GA are to provide unconsciousness, amnesia, analgesia, and blunting of sympathetic stress responses; however, the incidence of intraoperative awareness during general anesthesia has been estimated to around 0.1-0.2% among general anesthesia. [Myles et al., 2004] Intraoperative awareness can cause significant psychological trauma to the patient which results in

post-traumatic stress disorder (PDSD) in 70% of patients who experience it [Avidan et al., 2011], and light anesthesia is responsible for the most common cause contributing to the development of intraoperative awareness. [Ghoneim et al., 2009] Therefore, awareness or sedation monitor has been developed to reduce the risk of intraoperative awareness. The electroencephalogram (EEG)-based monitor with the bispectral index (BIS) and patient state index (PSI) are both numerical scales that measure brain activity derived from EEG signal processing techniques, with the BIS index range from 0 to 100 represents a continuum value of 0 (isoelectric EEG), < 40 (a deep hypnosis), 40-60 (range of general anesthesia), 60-80 (light or moderate sedation), and 80-100 (awake), and PSI range < 25 (deep anesthetic state), 25-50 (optimal hypnotic state for general anesthesia), and > 50 (light hypnotic state for general anesthesia). [Avidan et al., 2011; Chen et al., 2002]

Although there are concerns about the GA-related time delay from symptom onset to EVT initiation and blood pressure fluctuation with potential cerebral hypoperfusion in patients with acute anterior circulation ischemic stroke caused by large vessel occlusion, it has been shown that GA will not worsen neurological functional outcome and mortality when compared to conscious sedation [Ilyas et al., 2018; Simonsen et al., 2018; Wang et al., 2017], yet GA-reduced every 10 mmHg reduction in mean blood pressure (MAP) as compared to baseline MAP before recanalization by EVT is associated with a 4.1 mL increase in infarct volume and 22% increase of worse functional outcome [Petersen et al., 2019; Treurniet et al., 2018] It is mandatory not to arbitrarily reduce blood pressure before recanalization during EVT procedure unless extreme hypertension with hazard of subarachnoid or intracranial hemorrhage, and target-controlled blood pressure with continuous invasive arterial BP monitoring is indicated during EVT procedure.

Hypothesis

We hypothesize that GA with either volatile anesthetics (intubated) or total intravenous anesthesia (non-intubated) is both effective anesthetic modality for EVT. Meanwhile, these two general anesthetic modalities, monitored with both the target-controlled sedation depth and blood pressure control, do not have significant difference among the functional recovery and incidence of postoperative delirium or cognitive dysfunction for patients with acute ischemic stroke undergoing EVT. Based on that, we conduct this prospective, randomized controlled trial to examine our hypothesis.

Aim of the present study

The study compares the effect of two general anesthetic modalities, the one with volatile anesthetic sevoflurane (intubated) and the other integrating TIVA with propofol (non-intubated), on post-procedural delirium and cognitive dysfunction after EVT in patients with acute ischemic stroke. To assess the outcome of both modalities, the sedation depth of GA will be regulated with processed electroencephalogram monitor to reduce the incidence of postoperative delirium and the peri-procedural blood pressure will be controlled according to the guideline. [Tang et al., 2019; MacKenzie et al., 2018] Based on that, we try to find a better general anesthetic modality for acute ischemic stroke patients undergoing EVT.

Importance and impact of the study

A proportion of patients with acute ischemic stroke will develop post-stroke cognitive dysfunction and/or delirium, and this cognitive dysfunction/delirium has great impact on morbidity and mortality. EVT therapy has become a promising interventional therapy for patients with acute ischemic stroke with large vessel occlusion, and it should be performed in time within the limited time window. General anesthesia would induce post-operative cognitive dysfunction and/or postoperative delirium among patients undergoing surgery, especially in pre-stroke patients. Similarly, GA performed in patients of acute ischemic stroke with large vessel occlusion receiving EVT therapy has the potential to induce or increase the risk of post-stroke cognitive dysfunction in these brain-injured and inflamed patients. An EEG-guided anesthetic depth monitoring and a targeted blood pressure management during the peri-EVT period will be initiated in our present clinical study among patients of acute ischemic stroke. Therefore, it is important and mandatory for us to find an optimal and safe protocol of general anesthesia management for patients of acute ischemic stroke with large vessel occlusion undergoing EVT therapy.

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Materials and methods

This study is a prospective, single-centered, double-blind, randomized control trial at Taipei Veterans General Hospital. Patients who are scheduled to undergo emergent EVT for acute ischemic stroke with large vessel occlusion will be randomly assigned to either of the two intra-procedural general anesthetic regimens that include a volatile anesthesia with sevoflurane (Sev-GA) or to a total intravenous anesthesia with propofol (TIVA-propofol).

Subjects

All patients scheduled for EVT are screened for eligibility. Patients are eligible to enter the study must fulfill the indications for EVT in acute ischemic stroke according to the American Heart Association/American Stroke Association 2018 Guidelines for the early management of patients with acute ischemic stroke and 2019 Taiwan stroke society guideline for EVT in acute ischemic stroke patients and agree to receive the EVT for reperfusion at Taipei Veterans General Hospital. [Powers et al., 2018; Tang et al., 2019] Exclusion criteria are allergy to the anesthetics used in this clinical study and refusal for enrolling in study. Written informed consent will be obtained from all patients or delegates.

Patients who meet the enrollment criteria and who provide written informed consent will be randomly assigned to either of the intubated Sev-GA or non-intubated TIVA-propofol groups according to either the discretion of anesthesiologist in charge or random allocation. If the patient

was in critical situation, uncooperative, or with uncontrolled movement, the anesthesiologist would choose the intubated Sev-GA instead of the scheduled randomization. However, if patient is cooperative and not critical, the patient would be randomly assigned according to the randomization list created with the use of computer-generated, permuted-block sequences. Only the anesthesiologist and physicians involved in EVT ae aware of the anesthesia assignment. On the contrary, patients, personnel who collect data, fill out questionnaire and scale measurement, and personnel who assess outcomes are unaware of the group assignments.

The case number is determined according to previous studies. [Ellard et al., 2014; Katznelson et al., 2009; Matsuzono et al., 2020] Under the null hypothesis of there is no mean difference between two groups and no patients lost follow-up. The type I error is set as 0.05 with power of 0.8. A total of 298 patients is required to detect a difference of 12.8% in POCD incidence in acute ischemic stroke patients receiving EVT therapy within 7 days after stroke. Considering the potential 10% attrition rate, a sample size of 328 participants will be recruited into the present clinical trial.

General anesthesia protocol

American Society of Anesthesiologists standard monitors (including pulse oximeter, ECG, and non-invasive blood pressure), invasive arterial blood pressure monitoring, end-tidal agent monitor (including CO_2 and anesthetic concentrations), hypnotic level monitor (either BIS or PSI), and cerebral oximeter using near-infrared spectroscopy are applied to all patients peri-procedurally.

Non-intubated TIVA-propofol group:

With the application of Optiflow nasal high flow set at a flow rate of 20 L/min and 60% FiO2, total intravenous anesthesia is induced with target-controlled infusion of propofol (effect site (Ce) concentration around 1.5-2 μ g/ml) and remifentanil (Ce value around 1.0-1.5 ng/ml), and adjusted as required.

Intubated Sev-GA group:

After preoxygenation for 3 minutes with 100% oxygen, anesthesia is induced with intravenous injection of propofol (1.5-2 mg/kg), remifentanil infusion (Ce value around 1-1.5 ng/kg), and cisatracurium (0.15-0.2 mg/kg), and followed by endotracheal intubation. General anesthesia is maintained with cisatracuirum (0.03 mg/kg every 45-50 min), remifentanil (Ce value around 1-1.5 ng/kg) and sevoflurane inhalation. Sevoflurane concentration will be adjusted to keep BIS value within the range of 40-60. Mechanical ventilation will be processed at volume-controlled mode with fraction of inspired oxygen (FiO2) 60%, tidal volume 6 ml/kg, and respiratory rate 9-12/min

to keep normocapnia and avoid desaturation during the EVT procedure.

Peri-EVT procedural anesthetic monitoring

1. Standard monitoring: continuous ECG, non-invasive blood pressure (NIBP), pulse oximeter (SpO_2)
2. Invasive arterial blood pressure (ABP)
3. Anesthetic agent monitor: to monitor sevoflurane concentration
4. Cerebral oximeter (ScO_2): for regional brain oxygenation monitor
5. End-tidal CO_2 ($ETCO_2$) monitor
6. Processed electroencephalogram (EEG) monitoring: either with Medtronic BIS™ brain monitoring system with bispectral index (BIS) or Masimo SedLine Brain function monitoring with Patient State Index (PSI)

Physiologic target during peri-EVT procedure

1. Propofol target effect-site concentration (Ce): 1.5 ~ 2.0 μ g/ml.
2. Remifentanil Ce: 1.0 ~ 1.5 ng/ml
3. Partial pressure of arterial blood CO_2 ($PaCO_2$): kept around 30-40 mmHg
4. $ETCO_2$: kept around 35-45 mmHg
5. Target-controlled sedation level: PSI maintained between 25 and 50 or BIS maintained between 40 and 60 by adjusting the infusion rate of propofol or the inhaled concentration of sevoflurane
6. Systolic blood pressure (target-controlled): before completion of thrombectomy (110-180 mmHg), and after completion of thrombectomy (110 -140 mmHg).

Post-procedural care

After completion of the EVT procedure, patient will be transferred to the Stroke Care Unit for post-procedural intensive care. The endotracheal tube will be removed once weaning from mechanical ventilation, ability to spontaneous respiration, and recovery of both muscle power and respiratory mechanics.

Outcomes:

<u>Cognitive function and delirium evaluation</u>

Cognitive functions (including delirium) will be assessed pre-procedure (baseline) and emergency department (before EVT), on days 1 and 7 after EVT procedure, using the confusion assessment method (CAM).

Neurological functional assessment

National Institute of Health Stroke Scale (NIHSS) and modified Rankin scale (mRS) will be assessed before (baseline but after stroke) and after EVT on days 1 and 7 after procedure up to 3 months follow-up.

Data collection and analysis

The primary outcome is to compare the incidence and severity of postoperative delirium between intubated GA-sevoflurane and non-intubated TIVA-propofol, which is assessed using CAM. The secondary outcomes are neurological and clinical outcomes by assessing the NIHSS and mRS, and activity of daily living. All analyses are based on the intention-to-treat principle. The normally distributed data will be expressed as mean ± SD, while non-normally distributed data will be presented as median and interquartile ranges (IQR). Binary outcomes will be analyzed with logistic regression. The Chi-Square test is used to compare categorical data. The Mann-Whitney test and Kruskal-Wallis test are used to compare non-normally distributed data within the trial. Modified Rankin score is analyzed with an ordinal logistic regression. Safety outcomes are assessed with Chi-Square test for categorical variables and Student's t test for continuous variables. *P* values less than 0.05 are considered statistically significant. All data analysis will be performed using the Statistical Package for the Social Sciences (SPSS) version 17.0 for Windows (SPSS Inc., Chicago, IL, USA).

Questionnaire

1. **Modified Rankin Scale**: assessed before procedure and the day at discharge, respectively.

Score	Degree of disability or dependence in the daily activities
0	No symptoms
1	No significant disability: able to carry out all usual activities, despite some symptoms
2	Slight disability: able to look after own affairs without assistance, but unable to carry out all previous activities
3	Moderate disability: requires some help, but able to walk unassisted
4	Moderately severe disability: unable to attend to own bodily needs without assistance, and unable to walk unassisted
5	Severe disability: requires constant nursing care and attention, bedridden, incontinent
6	Dead

2. **National Institutes of Health Stroke Scale (NIHSS)**: assessed before procedure and day 1 after EVT, and the day at discharge, respectively.

Time point	**Before EVT**	**D1 after EVT**	**Day at discharge**

1a. Level of consciousness, Responsiveness	**0: Alert; responsive** **1: Not alert; Verbally arousable or aroused by minor stimulation to obey, answer, or respond** **2: Not alert; Only responsive to repeated or strong and painful stimuli** **3: Totally unresponsive; Responds only with reflexes or is areflexic**			
1b. Level of consciousness, Questions	**0: Correctly answers both questions** **1: Correctly answers one question** **2: Does not correctly answer either question**			
1c. Level of consciousness, Commands	**0: Correctly performs both tasks** **1: Correctly performs 1 task** **2: Does not correctly perform either task**			
3. Horizontal Eye Movement	**0: Normal; Able to follow pen or finger to both sides** **1: Partial gaze palsy; gaze is abnormal in one or both eyes, but gaze is not totally paralyzed. Patient can gaze towards hemisphere of infarct, but cannot go past midline** **2: Total gaze paresis; gaze is fixed to one side**			
4. Visual field test	**0: No vision loss** **1: Partial hemianopia or complete quadrantanopia; patient recognizes no visual stimulus in one specific quadrant** **2: Complete hemianopia; patient recognizes no visual stimulus in one half of the visual field** **3: Bilateral Blindness, including blindness from any cause**			
5. Facial palsy	**0: Normal and symmetrical movement** **1: Minor paralysis; function is less than clearly normal, such as flattened nasolabial fold or minor asymmetry in smile** **2: Partial paralysis; particularly paralysis in lower face**			

	3: Complete facial Hemiparesis, total paralysis in upper and lower portions of one face side				
6. **Motor Arm**	**0: No arm drift; the arm remains in the initial position for the full 10 seconds** **1: Drift; the arm drifts to an intermediate position prior to the end of the full 10 seconds, but not at any point relies on a support** **2: Limited effort against gravity; the arm is able to obtain the starting position, but drifts down from the initial position to a physical support prior to the end of the 10 seconds** **3: No effort against gravity; the arm falls immediately after being helped to the initial position, however the patient is able to move the arm in some form (e.g. shoulder shrug)** **4: No movement; patient has no ability to enact voluntary movement in this arm**	**Left (5a)**			
		Right (5b)			
6. Motor Leg	**0: No leg drift; the leg remains in the initial**	**Left (6a)**			

	position for the full 5 seconds **1: Drift; the leg drifts to an intermediate position prior to the end of the full 5 seconds, but at no point touches the bed for support** **2: Limited effort against gravity; the leg is able to obtain the starting position, but drifts down from the initial position to physical support prior to the end of the 5 seconds** **3: No effort against gravity; the leg falls immediately after being helped to the initial position, however, the patient is able to move the leg in some form (e.g. hip flex)** **4: No movement; patient has no ability to enact voluntary movement in this leg**	**Right (6b)**			
7. Limb ataxia	**0: Normal coordination; smooth and accurate movement** **1: Ataxia present in 1 limb; rigid and inaccurate movement in one limb** **2: Ataxia present in 2 or more limbs: rigid and inaccurate movement in both limbs on one side**				

8. Sensory	**0: No evidence of sensory loss** **1: Mild-to-Moderate sensory loss; patient feels the pinprick, however he or she feels as if it is duller on one side** **2: Severe to total sensory loss on one side; patient is not aware he or she is being touched in all unilateral extremities**				
9. Language	**0: Normal; no obvious speech deficit** **1: Mild-to-moderate aphasia; detectable loss in fluency, however, the examiner should still be able to extract information from patient's speech** **2: Severe aphasia; all speech is fragmented, and examiner is unable to extract the figure's content from the patient's speech.** **3: Unable to speak or understand speech**				
10. Speech	**0: Normal; clear and smooth speech** **1: Mild-to-moderate dysarthria; some slurring of speech, however the patient can be understood** **2: Severe dysarthria; speech is so slurred that he or she cannot be understood, or patients that cannot produce any speech**				
11. Extinction and Inattention	**0: Normal; patient correctly answers all questions** **1: Inattention on one side in one modality; visual, tactile, auditory, or spatial** **2: Hemi-inattention; does not recognize stimuli in more than one modality on the same side**				
Scores (0-42)					

6. Confusion Assessment Method (CAM): assessed before procedure and day 1 and 7 after EVT, and the day at discharge, respectively**.**

Confusion Assessment Method (CAM)	Date of Assessment	Before EVT	D1 after EVT	D7 after EVT	Day at discharge

Diagnostic Algorithm	Time of Assessment				
		Yes or No	Yes or No	Yes or No	Yes or No
1. Acute onset and fluctuating course? (Acute change in mental status from baseline, fluctuating behavior through the day)					
2. Inattention? (Difficulty focusing attention, easily distracted, difficulty keeping track of what is being said)					
3. Disorganized thinking? (disorganized or incoherent thinking, rambling or irrelevant conversation, unclear or illogical flow of ideas)					
4. Altered level of consciousness? (This feature is shown by any answer other than "alert", including: hyper-alert, lethargic, stupor, or coma)					
The diagnosis of Delirium by CAM requires the presence of features 1 and 2 AND EITHER 3 or 4					
Delirium detected		Yes No (Circle)	Yes No (Circle)	Yes No (Circle)	Yes No (Circle)