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## Choice of ANesthesia for EndoVAScular Treatment of Acute Ischemic Stroke at Posterior Circulation (CANVAS II): Protocol for an Exploratory Randomized Controlled Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-036358
Article Type:	Protocol
Date Submitted by the Author:	12-Dec-2019
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Keywords:	Anaesthesia in neurology < ANAESTHETICS, Neurology < INTERNAL MEDICINE, Stroke medicine < INTERNAL MEDICINE, Neuroradiology < NEUROLOGY

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4 **Choice of ANesthesia for EndoVAScular Treatment of Acute**  
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6 **Ischemic Stroke at Posterior Circulation (CANVAS II):**  
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8 **Protocol for an Exploratory Randomized Controlled Study**  
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For peer review only

## ABSTRACT

### Introduction

Observational studies indicate that the type of anesthesia may be associated with the post-procedural neurological function in patients with acute ischemic stroke patients undergoing endovascular treatment. Patients with acute posterior circulation ischemic stroke may experience different physiological changes and result in severe neurological outcome. However, the effect of the type of anesthesia on post-procedure neurological function has remained unclear.

### Methods and analysis

This is an exploratory randomized controlled trial which will be carried out at Beijing Tiantan Hospital, Capital Medical University. Patients with acute posterior circulation ischemic stroke and deemed suitable for emergency endovascular recanalization will be recruited in this trial. Eighty-four patients will be randomized to receive either general anesthesia or local anesthesia/conscious sedation with 1:1 allocation ratio. The primary endpoint is the 90-day modified Rankin Score postoperatively.

### Ethics and dissemination

The study is registered at the ClinicalTrials.gov (NCT03317535) and has been reviewed by and approved by Ethics Committee of Beijing Tiantan Hospital of Capital Medical University (KY2017-074-02). If the results are positive, the study will indicate that whether the type of anesthesia affects neurological outcome after endovascular treatment. The findings of the study will be published in peer-reviewed journals and will be presented at national or international conferences.

**Trial registration number:** NCT03317535

### Keywords

General anesthesia, Local anesthesia, Conscious sedation, Endovascular treatment, Posterior circulation, Acute ischemic stroke, Neurological outcome

## Article Summary

### Strengths and limitations of this study

- This is the first randomized control study to determine the effect of anesthesia modality on neurological outcome on patients with posterior circulation acute ischemia stroke.
- The findings of the study would contribute to being as a reference for a future multi-centric trial to verify the effects of anesthesia on patients with posterior circulation AIS undergoing EVT.
- One limitation of the study is it is a single-centered trial. Future multi-centric trial is need to verify the effects of anesthesia on patients with posterior circulation acute ischemia stroke undergoing endovascular treatment.

## INTRODUCTION

Acute ischemic stroke (AIS) at posterior circulation account for 17%-60% of acute ischemia stroke with difficulty in treatment, which result in poor outcomes and a high mortality of 80%-95%<sup>1-5</sup>. Early recanalization is one of the most important predictors of favorable outcome for posterior circulation AIS patients at 90 days <sup>6</sup>. Though endovascular therapy (EVT) has been demonstrated to be an effective and safe treatment for patients' neurological function with around 30% good clinical outcome improvement and 35% mortality decrease at 90 days after interventional procedure, there is a substantial proportion of patients suffered from poor clinical outcomes even undergoing timely successful reperfusion<sup>7-10</sup>. Many factors may contribute to the mismatched association of high reperfusion rate and poor clinical outcome, including patient-specific factors (age, collaterals status, initial stroke severity, infarct volume and site, and distal artery emboli, etc.), procedural-specific factors (time from onset to recanalization, degree of recanalization) and anesthesia management<sup>2 11 12</sup>.

The optimal anesthesia choice and management for AIS patients during EVT, general anesthesia (GA) or local anesthesia/conscious sedation (LA/CS), is still remain unclear. Benefits of GA with tracheal intubation or laryngeal mask include secured airway to avoid aspiration, body immobility to avoid intracranial vessel perforation and better digital subtraction angiography imaging. On the other hand, hypotension, nosocomial infection, delayed procedure initiation and neurological evaluation, and hyperventilation may contribute to poor outcomes, even yielding devastating complications. LA/CS management permits neurological function assessment, shortens mean time from door to groin puncture and minimizes hemodynamic changes associate with airway manipulation. However, the risk of aspiration and substantial movement during endovascular procedural are the main two disadvantages associated with LA/CS<sup>13-15</sup>.

Three randomized controlled trials have compared the neurological outcomes after EVT with GA or LA/CS in AIS patients. The Sedation vs. Intubation for Endovascular



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4 Stroke TreAtment (SIESTA) trial reported similar National Institute of Health stroke  
5 scale (NIHSS) scores at 24 hours between GA and LA/CS, but favorable outcomes,  
6 measured by modified Rankin scale (mRS) score was found in patients with GA 3  
7 months after treatment<sup>14</sup>. Similarly, the General Or Local anesthesia in Intra Arterial  
8 THerapy (GOLIATH) trial reported growing brain infarct volume decreased and  
9 favorable 90-day mRS score increased with GA <sup>16</sup>. However, The Anesthesia during  
10 Stroke (AnStroke) trial reported no difference between GA and LA/CS in 90-day  
11 mRS<sup>17</sup>. Recently, a meta-analysis using fixed-effects model by obtaining individual  
12 patient data from the above-3 trials with blinded endpoint evaluation, indicated that  
13 significantly different results in favor of the GA group (cOR=1.58, 95%CI: 1.09-2.29)<sup>18</sup>.  
14 Nevertheless, these findings should be interpreted with caution. Firstly, these trials only  
15 provided insight into choice of anesthesia modality in the anterior circulation AIS  
16 population, the result of above researches are not appropriate for patients with posterior  
17 circulation occlusions. Secondly, only AnStroke trial analyzed the neurological  
18 function at 90 days as the primary outcome, while in other 2 trials, it was analyzed as  
19 as the secondary outcome. Hence the conclusion on relationship between anesthesia  
20 and neurological function at 90 days should be drawn with caution <sup>17</sup>. Therefore, result  
21 of above trials is not suitable for posterior circulation AIS, concerning the relationship  
22 between neurological outcome and anesthesia modality.  
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42 A few studies observed the feasibility of monitoring anesthesia care for elective  
43 endovascular procedures either in anterior or posterior circulations, and demonstrated  
44 high technical success with low rates of peri-procedural complications and mortality<sup>19</sup>  
45 <sup>20</sup>. Although theses study included a relatively large proportion of posterior circulation  
46 interventions and showed promising results, it is unreasonable to employ previous  
47 results in emergent setting, with potential presence of severe brain stem ischemia.  
48 Moreover, only one study focused purely on the posterior circulation patients and  
49 investigated the influence of anesthesia modality and management on clinical and  
50 angiographic outcomes<sup>19</sup>. In this retrospective, matched, observatory study, LA/CS was  
51 found to be feasible and appeared to be as safe and effective as GA. However,  
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retrospective design and relatively limited sample size may introduce undetected biases. Furthermore, there is no randomized controlled trial to study whether GA and LA/CS own the different neurological outcome at 90 days undergoing EVT for posterior circulation AIS.

On the basis of the findings of previous studies, we propose to conduct a trial to compare neurological outcome in posterior circulation AIS patients receiving GA with those receiving LA/CS for EVT.

## **METHODS**

The protocol has been prepared according to Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)<sup>21</sup>. All trial procedures are summarized in Table 1. For completed checklists, see Supplementary file 1.

### **Study design**

This is a randomized, parallel-group, exploratory trial with blinded endpoint evaluation to determine whether GA or LA/CS produces different neurological outcomes in posterior circulation AIS patients undergoing EVT. Posterior circulation AIS patients will be enrolled from Beijing Tiantan Hospital, Capital Medical University from 2018 to 2020. This trial was approved by the Ethics Committee of Beijing Tiantan Hospital of Capital Medical University (KY2017-074-02) and registered in [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (NCT03317535). The participants flowchart is briefly illustrated in Figure 1

### **Participants**

Posterior circulation AIS Patients who deemed suitable for recanalization of the culprit's vessels will be considered for recruiting the study. The inclusion criteria are vertebral artery and/or basilar artery responsible for posterior circulation ischemia confirmed by CTA/MRA, age  $\geq 18$  years, stroke onset to treatment time  $\leq 24$  hours, modified Rankin Score  $\leq 2$  before onset.

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4 Patients with unclear radiological image to identify infarction and vessel occlusion,  
5 with intracranial hemorrhage, anterior circulation occlusion, Glasgow coma score  $\leq$   
6 8, NIHSS score  $< 6$  or  $> 30$ , severe agitation or seizures, loss of airway protective  
7 reflexes and/or vomiting on admission, intubated before EVT, and known allergy to  
8 anesthetics or analgesics will be excluded from the study. Both the neuro-radiologists  
9 and the attending anesthesiologists must agree that the patient is suitable with either  
10 GA or LA/CS management before recruiting. The reasons that eligible patients are not  
11 recruited to the trial will be documented.  
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### 20 **Randomization and blinding**

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22 Randomization occurs on the time of EVT when patients are sent to the interventional  
23 neuroradiology suite, the decision for EVT has been made, and written informed  
24 consent is obtained from patient or his/her legal representatives. Randomization will be  
25 conducted via a computer-generated table. Patients will be randomly allocated to  
26 receive either GA or LA/CS in a 1 to 1 ratio. A designated staff who will neither  
27 involved in anesthesia management nor follow-up will perform recruitment as well as  
28 allocation randomization sequence. This designated staff will implement the allocation  
29 sequence through opaque, sealed and stapled envelopes. The endpoint assessors will be  
30 blinded to the randomization group.  
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42 Standard operating procedures are applied to both groups to ensure no principal  
43 differences generated and uniform protocol implemented. The outcome assessors are  
44 blinded to the information of treatment for the enrolled patients and will evaluate the  
45 outcome variables for this study to ensure unbiased reporting. The anesthesiologist,  
46 neuro-radiologist as well as attending doctors in neurological intensive care unit (NICU)  
47 will not be blinded as they need to participate in the safe administration of GA or LA/CS  
48 and related medical care. The enrolled patients and his/her legal representatives will not  
49 be blinded, either.  
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### 58 **Interventions**

GA and LA/CS in this trial are defined according to the Practice Guidelines for Sedation and Analgesia by Non-Anesthesiologists due to the continuum ranging of level of sedation from minimal sedation to GA<sup>22</sup>. In LA/CS group, patients will receive sedative drugs if necessary but still following instruction to verbal stimulation. Patients with LA/CS will follow the sedation protocol as following: bolus propofol of 0.3-0.5mg/kg, following continuous propofol infusion of 1-2 mg/kg/h and remifentanyl infusion of 0.01-0.06 ug/kg/min while saturation of pulse oximetry (SpO<sub>2</sub>) will be kept above 94% with inhaled oxygen flow at 3L/min and end-tidal carbon dioxide (ETCO<sub>2</sub>) monitored via nasal cannula<sup>23 24 13</sup>. The bispectral index (BIS) value will be maintained above 70 via adjusting the infusion of sedative drugs.

In GA group, patients will receive rapid sequence induction with endotracheal intubation or laryngeal mask implementation with propofol, remifentanyl and muscle relaxant. Anesthesia will be induced with infusion of propofol of 1-2mg/kg and remifentanyl of 0.2-0.8 ug/kg for anesthesia induction<sup>25</sup>. Muscle relaxation will be achieved with rocuronium (0.6 mg/kg). After endotracheal intubation or laryngeal mask implementation, mechanically ventilation will initiate to achieve normocapnia with a 40%-60% fraction of inspired oxygen. Anesthesia will then be maintained with propofol (4-6mg/kg/h) and remifentanyl (0.05 to 0.1 ug/kg/min) infusion to maintain the BIS value between 40 and 60.

Converting from LA/CS to GA is an important issue in this trial. In cases of procedural emergency including vessel perforation, intracranial hemorrhage (ICH), subarachnoid hemorrhage(SAH), seizures, deep coma (GCS decrease to 8), respiratory failure (PaCO<sub>2</sub> ≥ 60 mmHg, or SpO<sub>2</sub><94% without relevant improvement by increasing inhaled oxygen fraction), cardiovascular fluctuation and severe disturbance of the treatment procedure (vomiting, substantial movement and uncoordinated dysphoria), LA/CS will be converted to GA. The decision to convert from LA/CS to GA will be made by the neuro-radiologist in charge and the attending anesthesiologist. The number of patients and reasons for the conversion will be recorded in detail. A guideline for

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4 airway management on conversion population is listed in Table 2.  
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### 7 **Standard anesthesia management protocols during EVT (Concomitant treatment)**

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9 All randomized patients will receive standard monitoring, including  
10 electrocardiography (ECG), non-invasive blood pressure (BP), heart rate (HR), pulse  
11 oxygen saturation ( $S_pO_2$ ), invasive arterial pressure monitoring,  $PaCO_2$ ,  $ETCO_2$ ,  
12 inspired oxygen fraction ( $FiO_2$ ) and blood glucose. All patients will receive BIS  
13 monitoring to assess the depth of sedation or anesthesia with BIS probe placed on the  
14 forehead. Physiologic parameters will be recorded using purposely designed data  
15 collection table. BP and blood glucose will be controlled according to current guidelines  
16 for stroke therapy<sup>24 26</sup>. Specifically, systolic blood pressure (SBP) is aimed to be kept  
17 between 140 and 180 mmHg and diastolic blood pressure (DBP) less than 105 mmHg,  
18 with phenylephrine or norepinephrine infusion. Plasma glucose will be maintained at  
19 level of 140-180 mg/dl and  $ETCO_2$  will be maintained between 35 and 45 mmHg, while  
20  $S_pO_2$  is aimed to be over 94%, with  $FiO_2$  at a range from 40% to 60%<sup>25</sup>. It is anticipated  
21 that patients in the LA group may deteriorate during EVT and may, therefore, require  
22 endotracheal intubation for airway protection.  
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### 37 **Measurements**

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39 All patients will be regularly visited while in hospital by outcome assessors who are  
40 blinded to the treatment allocation. The incidence of complications, including  
41 myocardial infarction, non-fatal cardiac arrest, new stroke, pulmonary embolism and  
42 deep venous thrombosis will be recorded. All patients will receive brain imaging,  
43 including computed tomography (CT), CT angiography (CTA), magnetic resonance  
44 (MR) or MR angiography (MRA) before, 24 hours, 7 days (or at discharge, whichever  
45 sooner), 30 days and 90 days after randomization. Brain image will be used to assess  
46 new brain hemorrhage (if present) and infarct volume. Efficacy of vessels  
47 recanalization will be assessed by the modified Thrombolysis in Cerebral Infarction  
48 (mTICI) scale. The severity of stroke will be assessed using the NIHSS scale during  
49 the same period. Disability will be rated at discharge and three months after EVT and  
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4 rated using mRS. To minimize loss of follow-up after discharge, study coordinators  
5 will contact the patients and his/her next-of-kin on a weekly basis. Besides, adverse  
6 effect will be also recorded.  
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### 10 **Study objectives**

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12 The study aims to detect the difference of the post-procedural neurological function in  
13 patients with posterior circulation AIS under GA and LA/CS, and hence to observe the  
14 effect of anesthesia type on outcomes after EVT.  
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### 18 **Primary endpoint**

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20 The primary endpoint is the neurological disability at 90-day after EVT measured by  
21 mRS and a favorable neurological outcome is identified as  $mRS \leq 2$ . The score will be  
22 evaluated by outcomes assessor who are blinded to allocation.  
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### 28 **Secondary endpoints**

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30 The secondary endpoints include the followings:  
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- 32 1. Change in NIHSS before, 24 h, 7 days (or at discharge), 30 days and 3 months after  
33 randomization.
- 34 2. The score of mTICI will be evaluated before and after endovascular treatment.
- 35 3. All-cause mortality up to 3 months after randomization.
- 36 4. The incidence of complications up to 3 months after randomization.
- 37 5. The length of stay in the hospital or intensive care unit after randomization.
- 38 6. The rate of converting from LA/CS to GA.
- 39 7. All adverse events associated with this study will be recorded.  
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### 49 **Data Monitoring Committee (DMC)**

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51 The project will be monitored by a Data Monitoring Committee (DMC) composed of  
52 specialists in anesthesiology, ethics, statistics and methodology. The DMC will audit  
53 through regular interviews or telephone calls.  
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### 58 **Statistical analysis plan**

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4 Descriptive statistics will be reported as means with standard deviation and medians  
5 with interquartile range for normally distributed data and skewed continuous data,  
6 respectively, and counts (percentage) for categorical data. The analysis will be based  
7 on intention-to-treat. Differences in the primary endpoint will be compared between  
8 groups using Cochran-Mantel-Haenszel test. Furthermore, primary outcome will be  
9 analyzed in following subgroups: age, gender, baseline NIHSS score; time from onset  
10 of stroke to EVT, site of arterial occlusion, and TICI score. Other categorical variables  
11 will be analyzed by  $\chi^2$  test and continuous variables using Student-t test or Mann-  
12 Whitney U test.  
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22 To allow for a varying number of follow-up measurements, the repeated measure  
23 ANOVA methods with a mixed model approach (treating time as a random effect and  
24 other covariates as fixed effects) will be utilized, and the specific comparison of change  
25 in each of those measurements between baseline and any specific post-baseline time  
26 point can be tested using linear contrast. In addition, missing data will be imputed using  
27 inverse probability weighting and worst case imputation scenarios. STATA 14.0  
28 (StataCorp LP, College Station, TX) for windows will be used for all statistical analyses.  
29 The statistical significance will be declared at type I error of 0.05.  
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### 39 **Sample size calculation**

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41 The PASS 15 software (NCSS, LLC, USA) is used to calculate the sample size based  
42 on the primary endpoint – favorable outcome (mRS 0-2) at three months after  
43 randomization. Several trials focused on the neurological outcome of patients with  
44 posterior circulation AIS, however, only two indicated the association between  
45 anesthesia type and neurological outcome. In the case-control study of Ashutosh et al,  
46 they reported the incidence of mRS  $\leq 2$  at 90-day was 38.3% in LA/CS and 31.1% in  
47 GA<sup>19</sup>. On the other hand, a retrospective observational study in our institution reported  
48 a higher incidence of favorable neurological outcome at 90-day in LA/CS compared to  
49 GA group (68.7% vs 35.6%)<sup>27</sup>. However, other factors including pre-operative NIHSS  
50 score, pre-operative intravenous thrombolysis treatment et al. confound the results  
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4 validity<sup>27</sup>. Meanwhile, in previous anterior circulation research, AIS patients receiving  
5 GA presented a favorable or similar neurological outcome at 90 days compared with  
6 LA/CS<sup>13 17 28</sup>. Taking this into account, we consider that the sample size to detect 30%  
7 difference in mRS 0-2 would require 44 in each group to achieve power of 80% at a  
8 two-tailed significant level of 0.05, with a drop-out rate of 5%<sup>29</sup>.  
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### 13 14 15 **Reporting of adverse events**

16 All adverse events associated with this trial will be recorded and closely monitored until  
17 resolution or stabilization or until it has been shown that potential conflicts of interest  
18 regarding the study treatment are not the cause of the event. The principal investigator  
19 is responsible for reporting all adverse events. Once adverse events occur, it should be  
20 immediately reported to the research department and informed to the principal  
21 investigator to determine the severity of the adverse events and their consequence of  
22 the injury. All adverse events associated with this study will be recorded and reported  
23 to the Ethics Committee within 24 hours.  
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### 33 34 **Protocol Amendment**

35 The chief investigator will be responsible for any decision to amend the protocol. If  
36 there is any modification (eg, changes to eligibility criteria, outcomes, analyses) the  
37 principle investigator will communicate and gain approval from the Ethical Committee  
38 of Beijing Tiantan Hospital, Capital Medical University prior to implementation, and  
39 communicate with relevant parties.  
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### 46 47 **Ethics and dissemination**

48 The approval for the study was certificated by the Ethical Committee of Beijing Tiantan  
49 Hospital, Capital Medical University on 19 December, 2017 (reference number:  
50 KY2017- 074-02). The study was registered on clinicaltrials.gov on 23 October, 2017  
51 (NCT03317535). The study recruited the first patient on 1 February, 2018, and the  
52 estimated study completion date will be 31 Dec, 2020. The findings of the study will be  
53 published in peer-reviewed journals and will be presented at national or international  
54 conferences.  
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## DISCUSSION

This is an exploratory controlled randomized study aiming to detect the effect of anesthesia choice on the neurological outcome in the patients with posterior circulation AIS undergoing EVT. The study aims to test the hypothesis that GA and LA/CS have different effects on the post-endovascular procedure neurological outcomes in patients with posterior circulation AIS.

Anesthetic selection and peri-procedural management appear to be closely associated with outcomes in patients with posterior circulation AIS undergoing EVT. The hemodynamics disturbance and the changes in ETCO<sub>2</sub> may be associated with the poor outcomes. However, no consistent agreement about the anesthesia modality has been reached, the anesthetic protocols varies among different stroke centers. In daily clinical work, the actual practice of anesthesia for EVT, especially for posterior circulation AIS patients, largely base on local protocols and individual preference of neuro-radiologists or anesthesiologists. LA/CS may be used for cooperative patients and GA for severely agitated, non-conscious and unprotected airway patients<sup>13</sup>. A small number of retrospective studies (concluding patients with posterior circulation AIS) show that LA/CS groups have better clinical outcomes, lower complication rate, shorter reperfusion time and less changes in hemodynamics and respiration<sup>19 20 27</sup>. In contrary, GA groups suffer from worse neurological function, lower blood pressure, aspiration pneumonia and/or high mortality<sup>30-37</sup>. A recent retrospective, matched, case-control study of patients with posterior circulation AIS is the only study to detect the effect of anesthesia management on outcome of patients with posterior AIS, however, great limitation and drawbacks in terms of study design, including selection bias and information bias impede the credibility of the results<sup>19</sup>. As to above, several confounding factors contribute inconclusive results, including specific information of peri-interventional management, such as blood pressure, partial pressure of carbon dioxide, and strict uniform anesthesia protocol, etc. Therefore, a prospective, randomized, controlled trial is required to account for the peri-procedural confounders and demonstrate the effects of anesthesia (type and management) on outcomes for

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4 patients with posterior AIS undergoing EVT.  
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7 This trial aims to find the effect of anesthesia choice on the post-endovascular  
8 procedure outcomes in patients with posterior circulation AIS using a randomized  
9 controlled trial design. The features of the current study involve strict randomized  
10 system, clear inclusion and exclusion criteria, a rigorous uniform protocol to manage  
11 hemodynamic, respiratory parameters and blood glucose in GA and LA/CS group, and  
12 full-time attending anesthesiologists in each procedure. The findings of the study would  
13 contribute to being as a reference for a future multi-centric trial to verify the effects of  
14 anesthesia on patients with posterior circulation AIS undergoing EVT.  
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### 23 **Patient and public involvement**

24 Patients and the public were not directly consulted in the development of the research  
25 question or outcome measures. Patients were not involved in the design, the recruitment  
26 and conduct of the study. At the completion of this trial, a manuscript will be prepared  
27 to present the trial results. Results of the final study will be disseminated to all study  
28 participants through their preferred method of communication indicated at the time of  
29 enrollment. The burden of intervention will not be taken by participants themselves.  
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### 38 **Competing interests**

39 None declared.  
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### 44 **Funding**

45 The trial is supported by the Beijing Municipal Administration of Hospitals of Ascent  
46 Plan (Grant No.:DFL20180502), Beijing Municipal Administration of Hospitals  
47 Clinical Medical Development of Special Funding Support (Grant No.:ZYLX201708)  
48 and Beijing Municipal Science & Technology Commission (Grant No.:  
49 Z191100006619068).  
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### 56 **Author contributions**

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4 FL and YZ conceived the study. FL, YZ, SL, ZM, YP and RH initiated the study design  
5 and helped with protocol development and implementation. FL, YX, YW, YZ and MJ  
6 helped in data collection and manuscript revision. YP and RH are the grant holders. FL  
7 and YZ are the co-first authors. YP is the responsible author. All authors contributed to  
8 refinement of the study protocol. All authors have read and approved the final  
9 manuscript.  
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### 15 16 17 **Ethics approval**

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20 This study is approved by the Ethical Committee of Beijing Tiantan Hospital, Capital  
21 Medical University (reference number: KY2017- 074-02).  
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### 25 26 **Data sharing statement**

27 This manuscript is a protocol for a randomized controlled trial, which does not include  
28 data.  
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### 32 33 **List of tables and figures:**

34 Table 1. Schedule of enrollment, intervention and assessment.

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36 Table 2. Guidelines for airway management in local anesthesia/conscious sedation  
37 group  
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40 Figure 1. CONSORT flow diagram for CANVAS II clinical trial.

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42 Supplementary file 1 SPIRIT checklist.  
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### 45 46 **References**

- 47  
48  
49 1. Raymond S, Rost NS, Schaefer PW, et al. Patient selection for mechanical  
50 thrombectomy in posterior circulation emergent large-vessel occlusion. *Interv*  
51 *Neuroradiol* 2018;24(3):309-16.  
52  
53 2. Luo G, Mo D, Tong X, et al. Factors Associated with 90-Day Outcomes of Patients  
54 with Acute Posterior Circulation Stroke Treated By Mechanical Thrombectomy. *World*  
55 *neurosurgery* 2018;109:e318-e28.  
56  
57 3. Lee YY, Yoon W, Kim SK, et al. Acute Basilar Artery Occlusion: Differences in  
58  
59  
60

1  
2  
3  
4 Characteristics and Outcomes after Endovascular Therapy between Patients with and  
5 without Underlying Severe Atherosclerotic Stenosis. *AJNR Am J Neuroradiol*  
6 2017;38(8):1600-04.  
7

8  
9 4. Kim YW, Hong JM, Park DG, et al. Effect of Intracranial Atherosclerotic Disease  
10 on Endovascular Treatment for Patients with Acute Vertebrobasilar Occlusion. *AJNR*  
11 *Am J Neuroradiol* 2016;37(11):2072-78.  
12  
13

14  
15 5. Gao F, Lo WT, Sun X, et al. Combined Use of Mechanical Thrombectomy with  
16 Angioplasty and Stenting for Acute Basilar Occlusions with Underlying Severe  
17 Intracranial Vertebrobasilar Stenosis: Preliminary Experience from a Single Chinese  
18 Center. *AJNR Am J Neuroradiol* 2015;36(10):1947-52.  
19  
20  
21

22  
23 6. Mokin M, Sonig A, Sivakanthan S, et al. Clinical and Procedural Predictors of  
24 Outcomes From the Endovascular Treatment of Posterior Circulation Strokes. *Stroke*  
25 2016;47(3):782-8.  
26  
27

28  
29 7. Gory B, Eldesouky I, Sivan-Hoffmann R, et al. Outcomes of stent retriever  
30 thrombectomy in basilar artery occlusion: an observational study and systematic review.  
31 *J Neurol Neurosurg Psychiatry* 2016;87(5):520-5.  
32  
33

34  
35 8. van Houwelingen RC, Luijckx GJ, Mazuri A, et al. Safety and Outcome of Intra-  
36 Arterial Treatment for Basilar Artery Occlusion. *JAMA Neurol* 2016;73(10):1225-30.  
37  
38

39  
40 9. Huo X, Gao F, Sun X, et al. Endovascular Mechanical Thrombectomy with the  
41 Solitaire Device for the Treatment of Acute Basilar Artery Occlusion. *World*  
42 *neurosurgery* 2016;89:301-8.  
43  
44

45  
46 10. Singer OC, Berkefeld J, Nolte CH, et al. Mechanical recanalization in basilar artery  
47 occlusion: the ENDOSTROKE study. *Ann Neurol* 2015;77(3):415-24.  
48

49  
50 11. Brinjikji W, Murad MH, Rabinstein AA, et al. Conscious sedation versus general  
51 anesthesia during endovascular acute ischemic stroke treatment: a systematic review  
52 and meta-analysis. *AJNR Am J Neuroradiol* 2015;36(3):525-9.  
53

54  
55 12. Yeo LLL, Holmberg A, Mpotsaris A, et al. Posterior Circulation Occlusions May  
56 Be Associated with Distal Emboli During Thrombectomy : Factors for Distal  
57 Embolization and a Review of the Literature. *Clin Neuroradiol* 2018  
58

59  
60 13. Simonsen CZ, Sorensen LH, Juul N, et al. Anesthetic strategy during endovascular

1  
2  
3  
4 therapy: General anesthesia or conscious sedation? (GOLIATH - General or Local  
5 Anesthesia in Intra Arterial Therapy) A single-center randomized trial. *Int J Stroke*  
6 2016;11(9):1045-52.  
7

8  
9 14. Schonenberger S, Mohlenbruch M, Pfaff J, et al. Sedation vs. Intubation for  
10 Endovascular Stroke Treatment (SIESTA) - a randomized monocentric trial. *Int J*  
11 *Stroke* 2015;10(6):969-78.  
12  
13

14  
15 15. Brinjikji W, Pasternak J, Murad MH, et al. Anesthesia-Related Outcomes for  
16 Endovascular Stroke Revascularization: A Systematic Review and Meta-Analysis.  
17 *Stroke* 2017;48(10):2784-91.  
18  
19

20  
21 16. Simonsen CZ, Yoo AJ, Sorensen LH, et al. Effect of General Anesthesia and  
22 Conscious Sedation During Endovascular Therapy on Infarct Growth and Clinical  
23 Outcomes in Acute Ischemic Stroke: A Randomized Clinical Trial. *JAMA Neurol*  
24 2018;75(4):470-77.  
25  
26

27  
28 17. Lowhagen Henden P, Rentzos A, Karlsson JE, et al. General Anesthesia Versus  
29 Conscious Sedation for Endovascular Treatment of Acute Ischemic Stroke: The  
30 AnStroke Trial (Anesthesia During Stroke). *Stroke* 2017;48(6):1601-07.  
31  
32

33  
34 18. Schonenberger S, Henden PL, Simonsen CZ, et al. Association of General  
35 Anesthesia vs Procedural Sedation With Functional Outcome Among Patients With  
36 Acute Ischemic Stroke Undergoing Thrombectomy: A Systematic Review and Meta-  
37 analysis. *Jama* 2019;322(13):1283-93.  
38  
39

40  
41 19. Jadhav AP, Bouzlama M, Aghaebrahim A, et al. Monitored Anesthesia Care vs  
42 Intubation for Vertebrobasilar Stroke Endovascular Therapy. *JAMA Neurol*  
43 2017;74(6):704-09.  
44  
45

46  
47 20. Taqi MA, Suriya SS, Sodhi A, et al. Ideal sedation for stroke thrombectomy: a  
48 prospective pilot single-center observational study. *Neurosurgical focus*  
49 2019;46(2):E16.  
50  
51

52  
53 21. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining  
54 standard protocol items for clinical trials. *Annals of internal medicine* 2013;158(3):200-  
55 7.  
56  
57

58  
59 22. van den Berg LA, Koelman DL, Berkhemer OA, et al. Type of anesthesia and  
60

1  
2  
3  
4 differences in clinical outcome after intra-arterial treatment for ischemic stroke. *Stroke*  
5 2015;46(5):1257-62.

6  
7 23. Janssen H, Buchholz G, Killer M, et al. General Anesthesia Versus Conscious  
8 Sedation in Acute Stroke Treatment: The Importance of Head Immobilization.  
9 *Cardiovascular and interventional radiology* 2016;39(9):1239-44.

10  
11 24. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 Guidelines for the Early  
12 Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare  
13 Professionals From the American Heart Association/American Stroke Association.  
14 *Stroke* 2018;49(3):e46-e110.

15  
16 25. Peng Y, Li Y, Jian M, et al. Choice of ANesthesia for EndoVAscular Treatment of  
17 Acute Ischemic Stroke: Protocol for a randomized controlled (CANVAS) trial. *Int J*  
18 *Stroke* 2017;12(9):991-97.

19  
20 26. Talke PO, Sharma D, Heyer EJ, et al. Republished: Society for Neuroscience in  
21 Anesthesiology and Critical Care expert consensus statement: Anesthetic management  
22 of endovascular treatment for acute ischemic stroke. *Stroke* 2014;45(8):e138-50.

23  
24 27. Zhang X, Luo G, Mo D, et al. Predictors of Good Outcome After Endovascular  
25 Treatment for Patients with Vertebrobasilar Artery Occlusion due to Intracranial  
26 Atherosclerotic Stenosis. *Clin Neuroradiol* 2018

27  
28 28. Schonenberger S, Uhlmann L, Hacke W, et al. Effect of Conscious Sedation vs  
29 General Anesthesia on Early Neurological Improvement Among Patients With  
30 Ischemic Stroke Undergoing Endovascular Thrombectomy: A Randomized Clinical  
31 Trial. *JAMA* 2016;316(19):1986-96.

32  
33 29. Hulley SB CS, Browner WS, Grady D, Newman TB. Designing clinical research :  
34 an epidemiologic approach. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins  
35 2013:75.

36  
37 30. Sugg RM, Jackson AS, Holloway W, et al. Is mechanical embolectomy performed  
38 in nonanesthetized patients effective? *AJNR Am J Neuroradiol* 2010;31(8):1533-5.

39  
40 31. Davis MJ, Menon BK, Baghirzada LB, et al. Anesthetic management and outcome  
41 in patients during endovascular therapy for acute stroke. *Anesthesiology*  
42 2012;116(2):396-405.

- 1  
2  
3  
4 32. Langner S, Khaw AV, Fretwurst T, et al. Endovascular treatment of acute ischemic  
5 stroke under conscious sedation compared to general anesthesia - safety, feasibility and  
6 clinical and radiological outcome. *Rofa* 2013;185(4):320-7.  
7  
8  
9 33. Hassan AE, Akbar U, Chaudhry SA, et al. Rate and prognosis of patients under  
10 conscious sedation requiring emergent intubation during neuroendovascular procedures.  
11 *AJNR Am J Neuroradiol* 2013;34(7):1375-9.  
12  
13 34. Abou-Chebl A, Zaidat OO, Castonguay AC, et al. North American SOLITAIRE  
14 Stent-Retriever Acute Stroke Registry: choice of anesthesia and outcomes. *Stroke*  
15 2014;45(5):1396-401.  
16  
17 35. Athiraman U, Sultan-Qurraie A, Nair B, et al. Endovascular Treatment of Acute  
18 Ischemic Stroke Under General Anesthesia: Predictors of Good Outcome. *J Neurosurg*  
19 *Anesthesiol* 2017;30(3):223-30.  
20  
21 36. Mundiyanapurath S, Schonenberger S, Rosales ML, et al. Circulatory and  
22 Respiratory Parameters during Acute Endovascular Stroke Therapy in Conscious  
23 Sedation or General Anesthesia. *J Stroke Cerebrovasc Dis* 2015;24(6):1244-9.  
24  
25 37. Hassan AE, Chaudhry SA, Zacharatos H, et al. Increased rate of aspiration  
26 pneumonia and poor discharge outcome among acute ischemic stroke patients  
27 following intubation for endovascular treatment. *Neurocrit Care* 2012;16(2):246-50.  
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Table 1. Schedule of enrollment, intervention and assessment.

	STUDY PERIOD							
	Enrolment	Allocation	Post-allocation					
TIMEPOINT	<i>At arrival</i>	After evaluation	<i>During treatment</i>	<i>24h after treatment</i>	<i>7 days after treatment</i>	<i>Discharge</i>	<i>30 days after treatment</i>	<i>90 days after treatment</i>
<b>ENROLMENT:</b>								
Eligibility screen	X							
Informed consent	X							
Allocation		X						
<b>INTERVENTIONS:</b>								
GA			X					
LA/CS			X					
<b>ASSESSMENTS:</b>								
<i>Baseline variables</i>	X	X						
<i>Brain image</i>	X			X				
<i>mRS</i>							X	X
<i>NIHSS</i>	X			X	X		X	X
<i>mTICI</i>			X					
<i>All-cause mortality</i>								X
<i>length of stay</i>								X
<i>ICU stay and length</i>								X
<i>Converting rate</i>			X					
<i>Adverse event</i>			X					X

GA: general anesthesia; LA/CS: local anesthesia/conscious sedation; NIHSS: National Institute of Health Stroke Scale; mRS: modified Rankin Score; mTICI: modified Thrombolysis in Cerebral Infarction Scale



Table 2 Guidelines for airway management in local anesthesia/conscious sedation group.

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A. Criteria for tracheal intubation

- a. Unconscious with GCS score <8 points;
- b. Increase of  $\text{ETCO}_2 >60$  mmHg and/or a decrease in  $\text{SpO}_2 <94\%$  despite oxygen supplementation;
- c. Agitation that cannot be controlled with sedation and/or restraint;
- d. Seizure attack;
- e. Vomiting;
- f. Recognized complications from endovascular therapy, such as vessel puncture leading to intracerebral hemorrhage or subarachnoid hemorrhage.

B. Tracheal intubation, with or without anesthetic agents, may be performed.

C. Anesthetic agents, including propofol or barbiturate infusion, with or without muscle relaxants could be used so that patients will tolerate tracheal intubation and allow effective lung ventilation.

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GCS: Glasgow coma scale;  $\text{SpO}_2$ : pulse oxygen saturation;  $\text{ETCO}_2$ : end-tidal carbon dioxide.

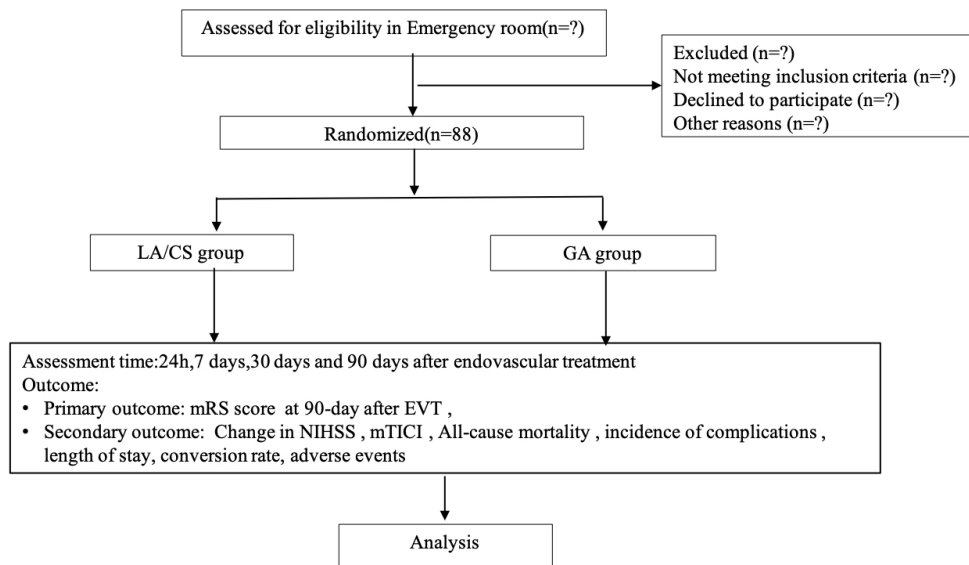


Figure 1. CONSORT flow diagram for CANVAS II clinical trial.

Figure 1. CONSORT flow diagram for CANVAS II clinical trial.

216x142mm (150 x 150 DPI)

Additional file 1: SPIRIT checklist.

Section/item	ItemNo	Description	page
<b>Administrative information</b>			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
Trial registration	2b	All items from the World Health Organization Trial Registration Data Set	1,7
	3	Date and version identifier	NA
Funding	4	Sources and types of financial, material, and other support	15
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,15
	5b	Name and contact information for the trial sponsor	1,15

1				
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3				
4			Role of study sponsor and funders, if any, in study design; collection, management,	
5		5c	analysis, and interpretation of data; writing of the report; and the decision to submit the	15
6			report for publication, including whether they will have ultimate authority over any of	
7			these activities	
8			Composition, roles, and responsibilities of the coordinating centre, steering committee,	
9		5d	endpoint adjudication committee, data management team, and other individuals or groups	11
10			overseeing the trial, if applicable (see Item 21a for data monitoring committee)	
11				
12				
13	<b>Introduction</b>			
14				
15				
16	Background and		Description of research question and justification for undertaking the trial, including	
17	rationale	6a	summary of relevant studies (published and unpublished) examining benefits and harms	5
18			for each intervention	
19				
20		6b	Explanation for choice of comparators	5-6
21				
22				
23	Objectives	7	Specific objectives or hypotheses	7
24				
25				
26	Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial,	
27			single group), allocation ratio, and framework (eg, superiority, equivalence,	7
28			noninferiority, exploratory)	
29				
30				
31	<b>Methods: Participants, interventions, and outcomes</b>			
32				
33				
34	Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of	
35			countries where data will be collected. Reference to where list of study sites can be	7
36			obtained	
37				
38	Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study	
39			centres and individuals who will perform the interventions (eg, surgeons,	7-8
40			psychotherapists)	
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4		11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-9
5				
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8		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	8-9
9				
10	Interventions			
11				
12		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8,11
13				
14				
15		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	10
16				
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20	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11
21				
22				
23				
24	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Table 1
25				
26				
27				
28	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12
29				
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31	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	11
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### Methods: Assignment of interventions (for controlled trials)

## Allocation:

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7			Method of generating the allocation sequence (eg, computer-generated random numbers),	
8	Sequence		and list of any factors for stratification. To reduce predictability of a random sequence,	8
9	generation	16a	details of any planned restriction (eg, blocking) should be provided in a separate	
10			document that is unavailable to those who enrol participants or assign interventions	
11	Allocation		Mechanism of implementing the allocation sequence (eg, central telephone; sequentially	
12	concealment		numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until	8
13	mechanism	16b	interventions are assigned	
14				
15				
16	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will	8
17			assign participants to interventions	
18				
19	Blinding		Who will be blinded after assignment to interventions (eg, trial participants, care	8
20	(masking)	17a	providers, outcome assessors, data analysts), and how	
21				
22				
23		17b	If blinded, circumstances under which unblinding is permissible, and procedure for	8
24			revealing a participant's allocated intervention during the trial	
25				
26				

**Methods: Data collection, management, and analysis**

27				
28				
29			Plans for assessment and collection of outcome, baseline, and other trial data, including	
30	Data collection		any related processes to promote data quality (eg, duplicate measurements, training of	
31	methods	18a	assessors) and a description of study instruments (eg, questionnaires, laboratory tests)	10, Table 1
32			along with their reliability and validity, if known. Reference to where data collection	
33			forms can be found, if not in the protocol	
34				
35			Plans to promote participant retention and complete follow-up, including list of any	
36		18b	outcome data to be collected for participants who discontinue or deviate from	11
37			intervention protocols	
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Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	11
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11-12
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	12
<b>Methods: Monitoring</b>			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	13
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA

**Ethics and dissemination**

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4	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	13
5				
6				
7	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	13
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11	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
12				
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15		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
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17				
18	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	NA
19				
20				
21				
22	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	15
23				
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25				
26	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	16
27				
28				
29	Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
30				
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33	Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	13
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38		31b	Authorship eligibility guidelines and any intended use of professional writers	NA
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31c Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code 15

**Appendices**

Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	NA
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

# BMJ Open

## Choice of ANesthesia for EndoVAScular Treatment of Acute Ischemic Stroke at Posterior Circulation (CANVAS II): Protocol for an Exploratory Randomized Controlled Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-036358.R1
Article Type:	Protocol
Date Submitted by the Author:	18-Mar-2020
Complete List of Authors:	Liang, Fa; Beijing Tiantan Hospital, Anesthesiology Zhao, Yan; Beijing Tiantan Hospital, Anesthesiology Yan, Xiang; Beijing Tiantan Hospital, Anesthesiology Wu, Youxuan; Beijing Tiantan Hospital, Anesthesiology Li, Xiuheng; Beijing Tiantan Hospital, Anesthesiology Zhou, Yang; Beijing Tiantan Hospital, Anesthesiology Jian, Minyu; Beijing Tiantan Hospital, Anesthesiology Li, Shu; Beijing Tiantan Hospital, Anesthesiology; Beijing Tian Tan Hospital, Capital Medical University Miao, Zhongrong; Beijing Tiantan Hospital, Neurology Han, Ruquan; Beijing Tiantan Hospital, Anesthesiology Peng, Yuming; Beijing Tiantan Hospital, Anesthesiology
<b>Primary Subject Heading</b>:	Anaesthesia
Secondary Subject Heading:	Neurology
Keywords:	Anaesthesia in neurology < ANAESTHETICS, Neurology < INTERNAL MEDICINE, Stroke medicine < INTERNAL MEDICINE, Neuroradiology < NEUROLOGY

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4 **Choice of ANesthesia for EndoVAScular Treatment of Acute**  
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6 **Ischemic Stroke at Posterior Circulation (CANVAS II):**  
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8 **Protocol for an Exploratory Randomized Controlled Study**  
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For peer review only

## ABSTRACT

### Introduction

Observational and interventional studies indicate that the type of anesthesia may be associated with the post-procedural neurological function in patients with anterior circulation acute ischemic stroke undergoing endovascular treatment. Patients with acute posterior circulation ischemic stroke may experience different physiological changes and result in severe neurological outcome. However, the effect of the type of anesthesia on post-procedure neurological function remained unclear in this population.

### Methods and analysis

This is an exploratory randomized controlled trial that will be carried out at Beijing Tiantan Hospital, Capital Medical University. Patients with acute posterior circulation ischemic stroke and deemed suitable for emergency endovascular recanalization will be recruited in this trial. Eighty-four patients will be randomized to receive either general anesthesia or conscious sedation with 1:1 allocation ratio. The primary endpoint is the 90-day modified Rankin Scale.

### Ethics and dissemination

The study is registered at the ClinicalTrials.gov (NCT03317535) and has been reviewed by and approved by Ethics Committee of Beijing Tiantan Hospital of Capital Medical University (KY2017-074-02). If the results are positive, the study will indicate whether the type of anesthesia affects neurological outcome after endovascular treatment of posterior stroke. The findings of the study will be published in peer-reviewed journals and presented at national or international conferences.

**Trial registration number:** NCT03317535

### Keywords

General anesthesia, Conscious sedation, Endovascular treatment, Posterior circulation, Acute ischemic stroke, Neurological outcome

## Article Summary

### Strengths and limitations of this study

- This is the first randomized control study to observe the effect of anesthesia modality on neurological outcome of patients with posterior circulation acute ischemic stroke.
- The findings of the study would contribute to serve as a reference for a future trial to verify the effects of anesthesia on patients with posterior circulation acute ischemic stroke undergoing endovascular therapy.
- One limitation of the study is it is a single-centered trial. Future multicenter trial is needed to verify the effects of anesthesia on patients with posterior circulation acute ischemic stroke undergoing endovascular treatment.
- The sample size is relatively small and the result will need to be confirmed by larger-size trials.
- Patients are selected mainly based on time window, salvageable ischemic brain tissue and initial infarct size might be considered in the inclusion criteria.

## INTRODUCTION

Acute ischemic stroke (AIS) at posterior circulation account for 17%-60% of acute ischemic stroke with difficulty in treatment, which result in a poor outcome and mortality rate of 80%-95%<sup>1-5</sup>. Early recanalization is one of the most important predictors of favorable outcome for posterior circulation AIS patients at 90 days <sup>6</sup>. Though endovascular therapy (EVT) has been demonstrated to be an effective and safe treatment with around 30% good clinical outcome improvement and 35% mortality decrease at 90 days, there is a substantial proportion of patients with poor clinical outcomes even after timely successful reperfusion<sup>7-10</sup>. Many factors may contribute to the mismatched association of high reperfusion rate and poor clinical outcome, including patient-specific factors (age, collaterals status, initial stroke severity, infarct volume and site, and distal artery emboli, etc.), procedural-specific factors (time from onset to recanalization, degree of recanalization) and anesthesia management<sup>2 11 12</sup>.

The optimal anesthesia choice and management for AIS patients during EVT, general anesthesia (GA) or conscious sedation (CS), is still unclear. Benefits of GA with tracheal intubation or laryngeal mask include secured airway to avoid aspiration, body immobility to avoid vessel perforation and better digital subtraction angiography imaging. On the other hand, hypotension, nosocomial infection, delayed procedure initiation, loss of neurological evaluation, and hyperventilation may contribute to poor outcomes. CS management permits neurological function assessment, shortens mean time from door to groin puncture and minimizes hemodynamic changes associate with GA. However, the risk of aspiration and substantial movement during endovascular procedural are the main two disadvantages associated with CS <sup>13-17</sup>.

Three randomized controlled trials have compared the neurological outcomes after EVT with GA or CS in anterior circulation. The Sedation vs. Intubation for Endovascular Stroke TreAtment (SIESTA) trial reported similar National Institute of Health stroke scale (NIHSS) scores at 24 hours between GA and CS, but favorable outcomes, measured by modified Rankin scale (mRS) was found in patients with GA <sup>3</sup>



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4 months after treatment as a secondary outcome measure<sup>14</sup>. Similarly, the General Or  
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6 Local anesthesia in Intra Arterial THERapy (GOLIATH) trial reported similar brain  
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8 infarct volume and favorable 90-day mRS score increased with GA<sup>18</sup>. However, The  
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10 Anesthesia during Stroke (AnStroke) trial reported no difference between GA and CS  
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12 in 90-day mRS<sup>19</sup>. Recently, a meta-analysis using fixed-effects model by obtaining  
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14 individual patient data from the above-3 trials with blinded endpoint evaluation,  
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16 indicated significantly different results in favor of the GA group (cOR=1.58, 95% CI  
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18 1.09-2.29)<sup>20</sup>. Nevertheless, these findings should be interpreted with caution. Firstly,  
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20 these trials only provided insight into choice of anesthesia modality in the anterior  
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22 circulation AIS population, the result of above researches are not appropriate for  
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24 patients with posterior circulation occlusions. Secondly, only AnStroke trial analyzed  
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26 the neurological function at 90 days as the primary outcome, while in other 2 trials, it  
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28 was analyzed as a secondary outcome. Hence the conclusion on relationship between  
29  
30 anesthesia and neurological function at 90 days should be drawn with caution<sup>19</sup>.

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32 A few studies observed the feasibility of monitored anesthesia care for elective  
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34 endovascular procedures either in anterior or posterior circulations, and demonstrated  
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36 high technical success with low rates of peri-procedural complications and mortality<sup>21</sup>  
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38 <sup>22</sup>. Although these studies included a relatively large proportion of posterior circulation  
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40 interventions and showed promising results about feasibility of monitored anesthesia  
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42 care, it is unreasonable to employ previous results in emergent setting, with potential  
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44 presence of severe midbrain ischemia. Moreover, only one study focused purely on the  
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46 posterior circulation patients and investigated the influence of anesthesia modality and  
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48 management on clinical and angiographic outcomes<sup>21</sup>. In this retrospective, matched,  
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50 case-control study, CS was found to be feasible and appeared to be as safe and effective  
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52 as GA. However, retrospective design and relatively limited sample size may introduce  
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54 undetected biases. Furthermore, there is no published randomized controlled trial that  
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56 explored whether GA or CS are associated with different neurological outcome at 90  
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58 days in patients undergoing EVT for posterior circulation AIS.

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4 On the basis of previous studies, we propose to conduct a trial to compare neurological  
5 outcome in posterior circulation AIS patients receiving GA with those receiving CS for  
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7 EVT.  
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## 10 **METHODS**

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12 The protocol has been prepared according to Standard Protocol Items:  
13 Recommendations for Interventional Trials (SPIRIT)<sup>23</sup>. All trial procedures are  
14 summarized in Table 1. For completed checklists, see Supplementary file 1.  
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### 20 **Study design**

21  
22 This is a randomized, parallel-group, exploratory trial with blinded endpoint evaluation  
23 to determine whether GA or CS produces different neurological outcomes in posterior  
24 circulation AIS patients undergoing EVT. Posterior circulation AIS patients will be  
25 enrolled from Beijing Tiantan Hospital, Capital Medical University from 2018 to 2020.  
26 This trial was approved by the Ethics Committee of Beijing Tiantan Hospital of Capital  
27 Medical University (KY2017-074-02) and registered in [www.clinicaltrials.gov](http://www.clinicaltrials.gov)  
28 (NCT03317535). The participants flowchart is briefly illustrated in Figure 1  
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### 36 **Participants**

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38 Posterior circulation AIS Patients who deemed suitable for recanalization of the  
39 culprit's vessels will be considered for recruitment in the study. The inclusion criteria  
40 are vertebral artery and/or basilar artery responsible for posterior circulation ischemia  
41 confirmed by computed tomography angiography (CTA)/ magnetic resonance  
42 angiography (MRA), the modified Thrombolysis in Myocardial Infarction (mTIMI)  
43 score  $\leq 1$ , age  $\geq 18$  years, stroke onset to treatment time  $\leq 24$  hours, and modified  
44 Rankin Score  $\leq 2$  before onset.  
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53 Patients with unclear radiological image to identify infarction and vessel occlusion,  
54 with intracranial hemorrhage, anterior circulation occlusion, Glasgow coma score  
55 (GCS)  $\leq 8$ , NIHSS score  $< 6$  or  $> 30$ , post-circulation Alberta Stroke Program  
56 Early CT Score (pc-ASPECTS)  $< 6$ , pons-midbrain index  $\geq 3$ , severe agitation or  
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4 seizures, loss of airway protective reflexes and/or vomiting on admission, intubated  
5 before EVT, unconsciousness, and known allergy to anesthetics or analgesics will be  
6 excluded from the study. Patient whose legal relative refuses to participate will be  
7 excluded. Both the neuro-radiologists and the attending anesthesiologist must agree that  
8 the patient is suitable with either GA or CS management before recruiting. Reasons  
9 why eligible patients are not recruited to the trial will be documented.  
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### 15 16 **Randomization and blinding**

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18 Randomization occurs on the time of EVT when patients are admitted to the  
19 interventional neuroradiology suite, the decision for EVT has been made, and written  
20 informed consent is obtained from patient's legal representatives. Randomization will  
21 be conducted via a computer-generated table. Patients will be randomly allocated to  
22 receive either GA or CS in a 1 to 1 ratio. A designated staff who will neither be involved  
23 in anesthesia management nor follow-up will perform recruitment as well as allocation  
24 randomization sequence. This designated staff will implement the allocation sequence  
25 through opaque, sealed and stapled envelopes. The endpoint assessors will be blinded  
26 to the randomization group.  
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38 Standard operating procedures are applied to both groups to ensure no principal  
39 differences generated and uniform protocol implemented. Patients in both groups will  
40 receive local anesthesia at puncture site, with 3-5 ml of 1% lidocaine hydrochloride  
41 prior to arterial puncture. The outcome assessors are blinded to the information of  
42 treatment for the enrolled patients and will evaluate the outcome variables for this study  
43 to ensure unbiased reporting. The anesthesiologist, neuro-radiologist as well as  
44 attending doctors in neurological intensive care unit (NICU) will not be blinded as they  
45 need to participate in the safe administration of GA or CS and related medical care. The  
46 enrolled patients and his/her legal representatives will not be blinded, either.  
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57 Standard anesthesia management protocols during EVT (Concomitant treatment) All  
58 randomized patients will receive standard monitoring, including electrocardiography  
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(ECG), non-invasive blood pressure (BP), heart rate (HR), pulse oxygen saturation (SpO<sub>2</sub>), invasive arterial pressure monitoring on radiologist arterial access line, arterial partial pressure of carbon dioxide (PaCO<sub>2</sub>), end-tidal carbon dioxide (ETCO<sub>2</sub>), inspired oxygen fraction (FiO<sub>2</sub>) and blood glucose. All patients will receive bispectral index (BIS) monitoring to assess the depth of sedation or anesthesia with BIS probe placed on the forehead. Physiologic parameters will be recorded using purposely designed data collection table. BP and blood glucose will be controlled according to current guidelines for stroke therapy<sup>24-26</sup>. Specifically, systolic blood pressure (SBP) is aimed to be kept between 140 and 180 mmHg and diastolic blood pressure (DBP) less than 105 mmHg, with vasopressor support if necessary. Plasma glucose will be maintained at level of 140-180 mg/dl while SPO<sub>2</sub> is aimed to be over 94%, with FiO<sub>2</sub> at a range from 40% to 60%<sup>27</sup>. It is anticipated that patients in the CS group may deteriorate during EVT and may, therefore, require endotracheal intubation or laryngeal mask insertion for airway protection<sup>17</sup>. All anesthesia related treatment will be performed by anesthesiologists of ischemia stroke team.

### **Interventions**

GA and CS in this trial are defined according to the Practice guidelines for sedation and analgesia by non-anesthesiologists due to the continuum ranging of level of sedation from minimal sedation to GA<sup>28</sup>. Both GA and CS will be monitored and applied by anesthesiologist. In CS group, patients will receive sedative drugs and follow the sedation protocol as following: bolus propofol of 0.3-0.5 mg/kg, following continuous propofol infusion of 1-2 mg/kg/h and remifentanil infusion of 0.01-0.06 ug/kg/min. SpO<sub>2</sub> will be kept above 94% with 40%-60% inhaled oxygen at 3L/min flow and ETCO<sub>2</sub> is monitored via anesthetic gas sample line at nasal vestibule and kept normocapnia. The BIS value will be maintained above 70 via adjusting the infusion of sedative drugs.

In GA group, patients will receive rapid sequence induction with endotracheal

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4 intubation or laryngeal mask insertion with propofol, remifentanyl and muscle relaxant.  
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6 Anesthesia will be induced with infusion of propofol of 1-2 mg/kg and remifentanyl of  
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8 0.2-0.8 ug/kg for anesthesia induction<sup>27</sup>. Muscle relaxation will be achieved with  
9  
10 rocuronium (0.6 mg/kg). After endotracheal intubation or laryngeal mask insertion,  
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12 suction will be performed to mitigate risk of aspiration. Mechanical ventilation will be  
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14 initiated to achieve normocapnia (ETCO<sub>2</sub> between 35 and 45 mmHg) with a 40%-60%  
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16 fraction of inspired oxygen. Anesthesia will then be maintained with propofol (4-6  
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18 mg/kg/h) and remifentanyl (0.05 to 0.1 ug/kg/min) infusion to maintain the BIS value  
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20 between 40 and 60.

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23 Converting from CS to GA is an important issue in this trial. In cases of procedural  
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25 emergency including vessel perforation, intracranial hemorrhage (ICH), subarachnoid  
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27 hemorrhage (SAH), seizures, deep coma, GCS decrease to or less than 8, respiratory  
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29 failure (ETCO<sub>2</sub> ≥ 60 mmHg, or SpO<sub>2</sub> < 94% without relevant improvement by  
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31 increasing inhaled oxygen fraction) and severe disturbance of the treatment procedure  
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33 (vomiting, substantial movement and uncoordinated dysphoria), CS will be converted  
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35 to GA. The decision to convert from CS to GA will be made by the neuro-radiologist  
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37 in charge and the attending anesthesiologist. The number of patients and reasons for the  
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39 conversion will be recorded in detail. Criteria for converting from CS to GA is listed in  
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41 Table 2.

### 42 43 **Measurements**

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45 All patients will be regularly visited while in hospital by outcome assessors who are  
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47 blinded to the treatment allocation. The incidence of complications, including  
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49 myocardial infarction, non-fatal cardiac arrest, new stroke, pulmonary embolism and  
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51 deep venous thrombosis will be recorded. All patients will receive brain imaging,  
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53 including CTA, MRA before, 24 hours, 7 days (or at discharge, whichever sooner), 30  
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55 days and 90 days after randomization. Brain image will be used to assess new brain  
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57 hemorrhage (if present) and infarct volume. Efficacy of vessels recanalization will be  
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59 assessed by mTICI scale. The severity of stroke will be assessed using the NIHSS scale  
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4 during the same period. Disability will be rated at discharge and three months after EVT  
5 and rated using mRS. A glossary of measurements is shown in Supplementary file 2.  
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7 To minimize loss of follow-up after discharge, study coordinators will contact the  
8 patients and his/her next-of-kin on a weekly basis. Besides, adverse effect will be also  
9 recorded.  
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### 13 14 15 **Study objectives**

16 The study aims to detect the difference of the post-procedural neurological function in  
17 patients with posterior circulation AIS under GA and CS, and hence to observe the  
18 effect of anesthesia type on outcomes after EVT.  
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### 22 23 24 **Primary endpoint**

25 The primary endpoint is the neurological disability at 90-day after EVT measured by  
26 mRS, which ranges from 0 (no symptoms) to 5 (severe disability), and a favorable  
27 neurological outcome is defined as no symptom or no significant disability with mRS  
28  $\leq 2$ <sup>3 15 29 30</sup>. The score will be evaluated by outcomes assessor who are blinded to  
29 allocation.  
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### 36 37 **Secondary endpoints**

38 The secondary endpoints include the followings:  
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- 40 1. Change in NIHSS, from baseline to 24 h, 7 days (or at discharge), 30 days and 3  
41 months after randomization.
- 42 2. The score of mTICI will be evaluated before and after endovascular treatment.
- 43 3. All-cause mortality up to 3 months after randomization.
- 44 4. The incidence of complications up to 3 months after randomization.
- 45 5. The length of stay in the hospital and in intensive care unit after randomization.
- 46 6. The rate of conversion from CS to GA.
- 47 7. Work-flow time, including door to door, door to groin puncture, puncture complete,  
48 groin puncture to recanalization and treatment time.
- 49 8. All adverse events associated with this study will be recorded.  
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### **Data Monitoring Committee (DMC)**

The project will be monitored by a Data Monitoring Committee (DMC) composed of specialists in anesthesiology, ethics, statistics and methodology. The DMC will audit through regular interviews or telephone calls. The DMC are responsible for terminating the research in case of severe adverse events.

### **Statistical analysis plan**

Descriptive statistics will be reported as means with standard deviation and medians with interquartile range for normally distributed data and skewed continuous data, respectively, and counts (percentage) for categorical data. The data will be analyzed on intention to treat and per protocol, however, the conclusion will be drawn according to the intention-to-treat analysis. The intention-to-treat analysis will depend on the allocated population while the per-protocol analysis will depend on the actual anesthesia method the population receive. Differences in the primary endpoint will be compared between groups using Cochran-Mantel-Haenszel test. Furthermore, primary outcome will be analyzed in following subgroups: age, gender, baseline NIHSS score; time from onset of stroke to EVT, site of arterial occlusion, and mTICI score. Other categorical variables will be analyzed by  $\chi^2$  test and continuous variables using Student-t test or Mann-Whitney U test.

To allow for a varying number of follow-up measurements, the repeated measure ANOVA methods with a mixed model approach (treating time as a random effect and other covariates as fixed effects) will be utilized, and the specific comparison of change in each of those measurements between baseline and any specific post-baseline time point can be tested using linear contrast. In addition, missing data will be imputed using inverse probability weighting and the worst-case imputation scenarios. STATA 14.0 (StataCorp LP, College Station, TX) for windows will be used for all statistical analyses. The statistical significance will be declared at type I error of 0.05.

### **Sample size calculation**

The PASS 15 software (NCSS, LLC, USA) is used to calculate the sample size based



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4 on the primary endpoint – favorable outcome (mRS 0-2) at three months after  
5 randomization. Several trials focused on the neurological outcome of patients with  
6 posterior circulation AIS, however, only two indicated the association between  
7 anesthesia type and neurological outcome. In the case-control study of Ashutosh et al,  
8 they reported the incidence of mRS $\leq$ 2 at 90-day was 38.3% in CS and 31.1% in GA<sup>21</sup>.  
9  
10 On the other hand, a retrospective observational study in our institution reported a  
11 higher incidence of favorable neurological outcome at 90-day in CS compared to GA  
12 group (68.7% vs 35.6%)<sup>31</sup>. However, other factors including pre-operative NIHSS  
13 score, pre-operative intravenous thrombolysis treatment confound the results validity<sup>31</sup>.  
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15 Meanwhile, in previous anterior circulation research, AIS patients receiving GA  
16 presented a favorable or similar neurological outcome at 90 days compared with CS<sup>13</sup>  
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19<sup>32</sup>. Taking this into account, we consider that the sample size to detect 30% difference in mRS 0-2 would require 44 in each group to achieve power of 80% at a two-tailed significant level of 0.05, with a drop-out rate of 5%<sup>33</sup>.

### **Reporting of adverse events**

All adverse events associated with this trial will be recorded and closely monitored until resolution or stabilization or until it has been shown that study treatment is not the cause of the event. The principal investigator is responsible for reporting all adverse events. Once adverse events occur, it should be immediately reported to the research department and informed to the principal investigator to determine the severity of the adverse events. All adverse events associated with this study will be recorded and reported to the Ethics Committee within 24 hours.

### **Protocol Amendment**

The chief investigator will be responsible for any decision to amend the protocol. If there is any modification (eg, changes to eligibility criteria, outcomes, analyses) the principle investigator will communicate and gain approval from the Ethical Committee of Beijing Tiantan Hospital, Capital Medical University prior to implementation, and communicate with relevant parties.



### **Ethics and dissemination**

The approval for the study was certificated by the Ethical Committee of Beijing Tiantan Hospital, Capital Medical University on 19 December, 2017 (reference number: KY2017- 074-02). The study was registered on clinicaltrials.gov on 23 October, 2017 (NCT03317535). The study recruited the first patient on 1 February, 2018, and the estimated study completion date will be 31 Dec, 2020. The findings of the study will be published in peer-reviewed journals and will be presented at national or international conferences.

### **DISCUSSION**

This is an exploratory controlled randomized study aiming to detect the effect of anesthesia choice on the neurological outcome in the patients with posterior circulation AIS undergoing EVT. The study aims to test the hypothesis that GA and CS have different effects on the post-endovascular procedure neurological outcomes in patients with posterior circulation AIS.

Anesthetic selection and peri-procedural management could be associated with outcomes in patients with posterior circulation AIS undergoing EVT. The hemodynamics disturbance and the changes in carbon dioxide tension may be associated with the outcomes. However, no consistent agreement about the anesthesia modality has been reached, the anesthetic protocols vary among different stroke centers. In daily clinical work, the actual practice of anesthesia for EVT, especially for posterior circulation AIS patients, largely rely on local protocols and individual preference of neuro-radiologists or anesthesiologists. CS may be used for cooperative patients and GA for severely agitated, non-conscious and unprotected airway patients<sup>13</sup>. A small number of retrospective studies (including patients with posterior circulation AIS) show that CS groups have better clinical outcomes, lower complication rate, shorter reperfusion time and less changes in hemodynamics and respiration<sup>21 22 31</sup>. In contrary, GA groups could suffer from worse neurological function, lower blood pressure, aspiration pneumonia and/or high mortality<sup>34-41</sup>. A recent retrospective, matched, case-

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4 control study of patients with posterior circulation AIS is the only study to explore the  
5 effect of anesthesia management on outcome of patients with posterior AIS, however,  
6 great limitation and drawbacks in terms of study design, including selection bias and  
7 information bias impede the credibility of the results<sup>21</sup>. Several confounding factors  
8 contribute to inconclusive results, including specific information of peri-interventional  
9 management, such as blood pressure, partial pressure of carbon dioxide, and strict  
10 uniform anesthesia protocol. Therefore, a prospective, randomized, controlled trial is  
11 required to account for the peri-procedural confounders and demonstrate the effects of  
12 anesthesia (type and management) on outcomes for patients with posterior AIS  
13 undergoing EVT.  
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24 This trial aims to explore the effect of anesthesia choice on the post-endovascular  
25 procedure outcomes in patients with posterior circulation AIS using a randomized  
26 controlled trial design. The features of the current study involve strict randomized  
27 system, clear inclusion and exclusion criteria, a rigorous uniform protocol to manage  
28 hemodynamic, respiratory parameters and blood glucose in GA and CS group, and full-  
29 time attending anesthesiologists in each procedure. The findings of the study would  
30 contribute to serve as a reference for a future multi-center trial to verify the effects of  
31 anesthesia on patients with posterior circulation AIS undergoing EVT.  
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#### 41 **Patient and public involvement**

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43 Patients and the public were not directly consulted in the development of the research  
44 question or outcome measures. Patients were not involved in the design, the recruitment  
45 and conduct of the study. At the completion of this trial, a manuscript will be prepared  
46 to present the trial results. Results of the final study will be disseminated to all study  
47 participants through their preferred method of communication indicated at the time of  
48 enrollment.  
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#### 55 **Competing interests**

56  
57 None declared.  
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## **Funding**

The trial is supported by the Beijing Municipal Administration of Hospitals of Ascent Plan (Grant No.: DFL20180502), Beijing Municipal Administration of Hospitals Clinical Medical Development of Special Funding Support (Grant No.:ZYLX201708) and Beijing Municipal Science & Technology Commission (Grant No.: Z191100006619068).

## **Author contributions**

FL and YZ conceived the study. FL, YZ, SL, ZM, YP and RH initiated the study design and helped with protocol development and implementation. FL, YX, YW, YZ and MJ helped in data collection and manuscript revision. YP and RH are the grant holders. FL and YZ are the co-first authors. YP is the responsible author. All authors contributed to refinement of the study protocol. All authors have read and approved the final manuscript.

## **Ethics approval**

This study is approved by the Ethical Committee of Beijing Tiantan Hospital, Capital Medical University (reference number: KY2017- 074-02).

## **Data sharing statement**

This manuscript is a protocol for a randomized controlled trial, which does not include data.

## **List of tables and figures:**

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Supplementary file 2 Measurement glossary.

## References

1. Raymond S, Rost NS, Schaefer PW, et al. Patient selection for mechanical thrombectomy in posterior circulation emergent large-vessel occlusion. *Interv Neuroradiol* 2018;24(3):309-16.
2. Luo G, Mo D, Tong X, et al. Factors Associated with 90-Day Outcomes of Patients with Acute Posterior Circulation Stroke Treated By Mechanical Thrombectomy. *World neurosurgery* 2018;109:e318-e28.
3. Lee YY, Yoon W, Kim SK, et al. Acute Basilar Artery Occlusion: Differences in Characteristics and Outcomes after Endovascular Therapy between Patients with and without Underlying Severe Atherosclerotic Stenosis. *AJNR Am J Neuroradiol* 2017;38(8):1600-04.
4. Kim YW, Hong JM, Park DG, et al. Effect of Intracranial Atherosclerotic Disease on Endovascular Treatment for Patients with Acute Vertebrobasilar Occlusion. *AJNR Am J Neuroradiol* 2016;37(11):2072-78.
5. Gao F, Lo WT, Sun X, et al. Combined Use of Mechanical Thrombectomy with Angioplasty and Stenting for Acute Basilar Occlusions with Underlying Severe Intracranial Vertebrobasilar Stenosis: Preliminary Experience from a Single Chinese Center. *AJNR Am J Neuroradiol* 2015;36(10):1947-52.
6. Mokin M, Sonig A, Sivakanthan S, et al. Clinical and Procedural Predictors of Outcomes From the Endovascular Treatment of Posterior Circulation Strokes. *Stroke* 2016;47(3):782-8.
7. Gory B, Eldesouky I, Sivan-Hoffmann R, et al. Outcomes of stent retriever thrombectomy in basilar artery occlusion: an observational study and systematic review. *J Neurol Neurosurg Psychiatry* 2016;87(5):520-5.
8. van Houwelingen RC, Luijckx GJ, Mazuri A, et al. Safety and Outcome of Intra-Arterial Treatment for Basilar Artery Occlusion. *JAMA Neurol* 2016;73(10):1225-30.
9. Huo X, Gao F, Sun X, et al. Endovascular Mechanical Thrombectomy with the

1  
2  
3  
4 Solitaire Device for the Treatment of Acute Basilar Artery Occlusion. *World*  
5 *neurosurgery* 2016;89:301-8.

6  
7 10. Singer OC, Berkefeld J, Nolte CH, et al. Mechanical recanalization in basilar artery  
8 occlusion: the ENDOSTROKE study. *Ann Neurol* 2015;77(3):415-24.

9  
10 11. Brinjikji W, Murad MH, Rabinstein AA, et al. Conscious sedation versus general  
11 anesthesia during endovascular acute ischemic stroke treatment: a systematic review  
12 and meta-analysis. *AJNR Am J Neuroradiol* 2015;36(3):525-9.

13  
14 12. Yeo LLL, Holmberg A, Mpotsaris A, et al. Posterior Circulation Occlusions May  
15 Be Associated with Distal Emboli During Thrombectomy : Factors for Distal  
16 Embolization and a Review of the Literature. *Clin Neuroradiol* 2018

17  
18 13. Simonsen CZ, Sorensen LH, Juul N, et al. Anesthetic strategy during endovascular  
19 therapy: General anesthesia or conscious sedation? (GOLIATH - General or Local  
20 Anesthesia in Intra Arterial Therapy) A single-center randomized trial. *Int J Stroke*  
21 2016;11(9):1045-52.

22  
23 14. Schonenberger S, Mohlenbruch M, Pfaff J, et al. Sedation vs. Intubation for  
24 Endovascular Stroke Treatment (SIESTA) - a randomized monocentric trial. *Int J*  
25 *Stroke* 2015;10(6):969-78.

26  
27 15. Brinjikji W, Pasternak J, Murad MH, et al. Anesthesia-Related Outcomes for  
28 Endovascular Stroke Revascularization: A Systematic Review and Meta-Analysis.  
29 *Stroke* 2017;48(10):2784-91.

30  
31 16. Kılıç Y, Baş SŞ, Aykaç Ö, et al. Nonoperating Room Anesthesia for Interventional  
32 Neuroangiographic Procedures: Outcomes of 105 Patients. *J Stroke Cerebrovasc*  
33 *Dis*;29(2)

34  
35 17. Ozhan MO, Eskin MB, Atik B, et al. Laryngeal Mask Airway for General  
36 Anesthesia in Interventional Neuroradiology Procedures. *Saudi Med J* 2019;40(5):463-  
37 68.

38  
39 18. Simonsen CZ, Yoo AJ, Sorensen LH, et al. Effect of General Anesthesia and  
40 Conscious Sedation During Endovascular Therapy on Infarct Growth and Clinical  
41 Outcomes in Acute Ischemic Stroke: A Randomized Clinical Trial. *JAMA Neurol*  
42 2018;75(4):470-77.

- 1  
2  
3  
4 19. Lowhagen Henden P, Rentzos A, Karlsson JE, et al. General Anesthesia Versus  
5 Conscious Sedation for Endovascular Treatment of Acute Ischemic Stroke: The  
6 AnStroke Trial (Anesthesia During Stroke). *Stroke* 2017;48(6):1601-07.  
7  
8  
9 20. Schonenberger S, Henden PL, Simonsen CZ, et al. Association of General  
10 Anesthesia vs Procedural Sedation With Functional Outcome Among Patients With  
11 Acute Ischemic Stroke Undergoing Thrombectomy: A Systematic Review and Meta-  
12 analysis. *Jama* 2019;322(13):1283-93.  
13  
14 21. Jadhav AP, Bouzlama M, Aghaebrahim A, et al. Monitored Anesthesia Care vs  
15 Intubation for Vertebrobasilar Stroke Endovascular Therapy. *JAMA Neurol*  
16 2017;74(6):704-09.  
17  
18 22. Taqi MA, Suriya SS, Sodhi A, et al. Ideal sedation for stroke thrombectomy: a  
19 prospective pilot single-center observational study. *Neurosurgical focus*  
20 2019;46(2):E16.  
21  
22 23. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining  
23 standard protocol items for clinical trials. *Annals of internal medicine* 2013;158(3):200-  
24 7.  
25  
26 24. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 Guidelines for the Early  
27 Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare  
28 Professionals From the American Heart Association/American Stroke Association.  
29 *Stroke* 2018;49(3):e46-e110.  
30  
31 25. Talke PO, Sharma D, Heyer EJ, et al. Republished: Society for Neuroscience in  
32 Anesthesiology and Critical Care expert consensus statement: Anesthetic management  
33 of endovascular treatment for acute ischemic stroke. *Stroke* 2014;45(8):e138-50.  
34  
35 26. Warner JJ, Harrington RA, Sacco RL, et al. Guidelines for the Early Management  
36 of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the  
37 Early Management of Acute Ischemic Stroke. *Stroke*;50(12):3331-32.  
38  
39 27. Peng Y, Li Y, Jian M, et al. Choice of ANesthesia for EndoVAScular Treatment of  
40 Acute Ischemic Stroke: Protocol for a randomized controlled (CANVAS) trial. *Int J*  
41 *Stroke* 2017;12(9):991-97.  
42  
43 28. American Society of Anesthesiologists Task Force on S, Analgesia by N-A. Practice  
44  
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4 Guidelines for Sedation and Analgesia by Non-Anesthesiologists by the American  
5 Society of Anesthesiology. *Anesthesiology* 2002;96(4):1004-17.  
6  
7  
8 29. Lindsberg PJ, Mattle HP. Therapy of basilar artery occlusion: a systematic analysis  
9 comparing intra-arterial and intravenous thrombolysis. *Stroke* 2006;37(3):922-8.  
10  
11 30. Wang A, Stellfox M, Moy F, et al. General Anesthesia During Endovascular Stroke  
12 Therapy Does Not Negatively Impact Outcome. *World neurosurgery* 2017;99:638-43.  
13  
14 31. Zhang X, Luo G, Mo D, et al. Predictors of Good Outcome After Endovascular  
15 Treatment for Patients with Vertebrobasilar Artery Occlusion due to Intracranial  
16 Atherosclerotic Stenosis. *Clin Neuroradiol* 2018  
17  
18 32. Schonenberger S, Uhlmann L, Hacke W, et al. Effect of Conscious Sedation vs  
19 General Anesthesia on Early Neurological Improvement Among Patients With  
20 Ischemic Stroke Undergoing Endovascular Thrombectomy: A Randomized Clinical  
21 Trial. *JAMA* 2016;316(19):1986-96.  
22  
23 33. Hulley SB CS, Browner WS, Grady D, Newman TB. Designing clinical research :  
24 an epidemiologic approach. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins  
25 2013:75.  
26  
27 34. Sugg RM, Jackson AS, Holloway W, et al. Is mechanical embolectomy performed  
28 in nonanesthetized patients effective? *AJNR Am J Neuroradiol* 2010;31(8):1533-5.  
29  
30 35. Davis MJ, Menon BK, Baghirzada LB, et al. Anesthetic management and outcome  
31 in patients during endovascular therapy for acute stroke. *Anesthesiology*  
32 2012;116(2):396-405.  
33  
34 36. Langner S, Khaw AV, Fretwurst T, et al. Endovascular treatment of acute ischemic  
35 stroke under conscious sedation compared to general anesthesia - safety, feasibility and  
36 clinical and radiological outcome. *Rofo* 2013;185(4):320-7.  
37  
38 37. Hassan AE, Akbar U, Chaudhry SA, et al. Rate and prognosis of patients under  
39 conscious sedation requiring emergent intubation during neuroendovascular procedures.  
40 *AJNR Am J Neuroradiol* 2013;34(7):1375-9.  
41  
42 38. Abou-Chebl A, Zaidat OO, Castonguay AC, et al. North American SOLITAIRE  
43 Stent-Retriever Acute Stroke Registry: choice of anesthesia and outcomes. *Stroke*  
44 2014;45(5):1396-401.  
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4 39. Athiraman U, Sultan-Qurraie A, Nair B, et al. Endovascular Treatment of Acute  
5 Ischemic Stroke Under General Anesthesia: Predictors of Good Outcome. *J Neurosurg*  
6 *Anesthesiol* 2017;30(3):223-30.  
7

8  
9 40. Mundiyanapurath S, Schonenberger S, Rosales ML, et al. Circulatory and  
10 Respiratory Parameters during Acute Endovascular Stroke Therapy in Conscious  
11 Sedation or General Anesthesia. *J Stroke Cerebrovasc Dis* 2015;24(6):1244-9.  
12  
13

14 41. Hassan AE, Chaudhry SA, Zacharatos H, et al. Increased rate of aspiration  
15 pneumonia and poor discharge outcome among acute ischemic stroke patients  
16 following intubation for endovascular treatment. *Neurocrit Care* 2012;16(2):246-50.  
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Table 1. Schedule of enrollment, intervention and assessment.

	STUDY PERIOD							
	Enrolment	Allocation	Post-allocation					
TIMEPOINT	<i>At arrival</i>	After evaluation	<i>During treatment</i>	<i>24h after treatment</i>	<i>7 days after treatment</i>	<i>Discharge</i>	<i>30 days after treatment</i>	<i>90 days after treatment</i>
<b>ENROLMENT:</b>								
Eligibility screen	X							
Informed consent	X							
Allocation		X						
<b>INTERVENTIONS:</b>								
GA			X					
CS			X					
<b>ASSESSMENTS:</b>								
<i>Baseline variables</i>	X	X						
<i>Brain image</i>	X			X				
<i>mRS</i>							X	X
<i>NIHSS</i>	X			X	X		X	X
<i>mTICI</i>			X					
<i>All-cause mortality</i>								X
<i>length of stay</i>								X
<i>ICU stay and length</i>								X
<i>Converting rate</i>			X					
<i>Adverse event</i>			X					X

GA: general anesthesia; CS: conscious sedation; NIHSS: National Institute of Health Stroke Scale;

mRS: modified Rankin Score; mTICI: modified Thrombolysis in Cerebral Infarction Scale

Table 2 Criteria for converting from conscious sedation to general anesthesia.

- 
1. Unconscious;
  2. GCS decrease to or less than 8;
  3. Increase of ETCO<sub>2</sub>  $\geq$ 60 mmHg and/or a decrease in S<sub>p</sub>O<sub>2</sub><94% despite oxygen supplementation;
  4. Agitation that cannot be controlled with sedation and/or restraint;
  - 5 Seizure attack;
  6. Vomiting;
  7. Recognized complications from endovascular therapy, such as vessel perforation leading to intracerebral hemorrhage or subarachnoid hemorrhage.
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GCS: Glasgow coma scale; S<sub>p</sub>O<sub>2</sub>: pulse oxygen saturation; ETCO<sub>2</sub>: end-tidal carbon dioxide.

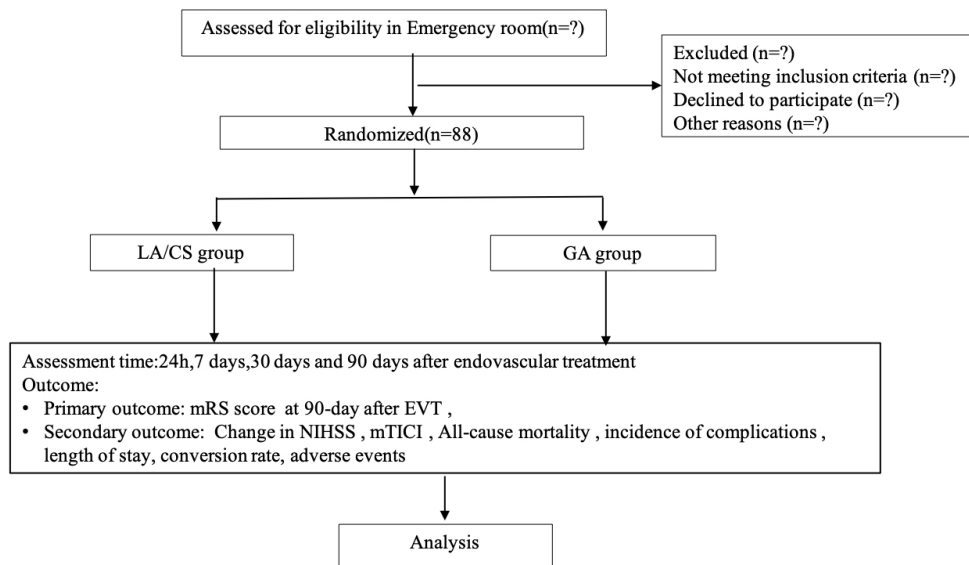


Figure 1. CONSORT flow diagram for CANVAS II clinical trial.

Figure 1. CONSORT flow diagram for CANVAS II clinical trial.

216x142mm (150 x 150 DPI)

Supplementary file 1: SPIRIT checklist.

Section/item	ItemNo	Description	page
<b>Administrative information</b>			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
	2b	All items from the World Health Organization Trial Registration Data Set	1,7
Protocol version	3	Date and version identifier	NA
Funding	4	Sources and types of financial, material, and other support	15
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,15
	5b	Name and contact information for the trial sponsor	1,15

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	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	15
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	11
<b>Introduction</b>			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5
	6b	Explanation for choice of comparators	5-6
Objectives	7	Specific objectives or hypotheses	7
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	7
<b>Methods: Participants, interventions, and outcomes</b>			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8

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4		11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-9
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8		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	8-9
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10	Interventions			
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12		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8,11
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15		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	10
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20	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11
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24	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Table 1
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28	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12
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32	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	11
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### Methods: Assignment of interventions (for controlled trials)

## Allocation:

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7			Method of generating the allocation sequence (eg, computer-generated random numbers),	
8	Sequence		and list of any factors for stratification. To reduce predictability of a random sequence,	8
9	generation	16a	details of any planned restriction (eg, blocking) should be provided in a separate	
10			document that is unavailable to those who enrol participants or assign interventions	
11	Allocation		Mechanism of implementing the allocation sequence (eg, central telephone; sequentially	
12	concealment		numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until	8
13	mechanism	16b	interventions are assigned	
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16	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will	8
17			assign participants to interventions	
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19	Blinding		Who will be blinded after assignment to interventions (eg, trial participants, care	8
20	(masking)	17a	providers, outcome assessors, data analysts), and how	
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23		17b	If blinded, circumstances under which unblinding is permissible, and procedure for	8
24			revealing a participant's allocated intervention during the trial	
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**Methods: Data collection, management, and analysis**

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29			Plans for assessment and collection of outcome, baseline, and other trial data, including	
30	Data collection		any related processes to promote data quality (eg, duplicate measurements, training of	
31	methods	18a	assessors) and a description of study instruments (eg, questionnaires, laboratory tests)	10, Table 1
32			along with their reliability and validity, if known. Reference to where data collection	
33			forms can be found, if not in the protocol	
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35			Plans to promote participant retention and complete follow-up, including list of any	
36		18b	outcome data to be collected for participants who discontinue or deviate from	11
37			intervention protocols	
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4	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	11
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7	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11-12
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11		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12
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15		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	12
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19	<b>Methods: Monitoring</b>			
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21	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11
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23		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
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27	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	13
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30	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
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38	<b>Ethics and dissemination</b>			
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Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	13
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	13
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	NA
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	15
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	16
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	13
	31b	Authorship eligibility guidelines and any intended use of professional writers	NA

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4 31c Plans, if any, for granting public access to the full protocol, participant-level dataset, and 15  
5 statistical code  
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7

## 8 Appendices

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11 Informed consent 32 Model consent form and other related documentation given to participants and authorised 15  
12 materials surrogates Yes  
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14 Biological 33 Plans for collection, laboratory evaluation, and storage of biological specimens for 15  
15 specimens genetic or molecular analysis in the current trial and for future use in ancillary studies, if NA  
16 applicable  
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## Supplementary file 2 Measurement glossary

Physiological parameters		
Acronyms	Full Names	Definition and Measurement description
SBP	systolic blood pressure	Recorded 10 min before treatment and every 10min during procedure in case report form (CRF) table, every 5min in electronic medical record system. Target value:>140mmHg, <180mmHg.
DBP	diastolic blood pressure	Recorded 10 min before treatment and every 10min during procedure in CRF table, every 5min in electronic medical record system. Target value:>105mmHg
FiO <sub>2</sub>	inspired oxygen fraction	Recorded 10 min before treatment and every 10min during procedure in CRF table, every 5min in electronic medical record system.
PaCO <sub>2</sub>	arterial partial pressure of carbon dioxide	Tested through arterial line access. Tested every 1 hour during endovascular therapy (EVT).
ETCO <sub>2</sub>	end-tidal carbon dioxide	Recorded 10 min before treatment and every 10min during procedure in CRF table, every 5min in electronic medical record system.
BIS	bispectral index	Recorded 10 min before treatment and every 10min during procedure in CRF table, every 5min in electronic medical record system.
ECG	electrocardiography	Recorded 5min in electronic medical record system.
HR	heart rate	Recorded 10 min before treatment and every 10min during procedure in CRF table, every 5min in electronic medical record system.

1	SpO <sub>2</sub>	pulse oxygen saturation	Recorded 10 min before treatment and every 10min during procedure in CRF table, every 5min in electronic medical record system.
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8	BP	blood pressure	Non-invasive blood pressure on either arm, measured every 5min during procedure. Recorded 10 min before treatment and every 10min during procedure in CRF table, every 5min in electronic medical record system.
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13	Glu	serum glucose	Tested before EVT treatment. During EVT, tested every 1 hour. Target value: 70-140mg/L
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17	MAP	mean artery pressure	Recorded 10 min before treatment and every 10min during procedure in CRF table, every 5min in electronic medical record system.
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21	ABG	arterial blood gas	Monitored before treatment and every one hour during treatment, including Na <sup>+</sup> , K <sup>+</sup> , Cl <sup>-</sup> , PaCO <sub>2</sub> , PaO <sub>2</sub> , PH, glucose.
22			
23	<b>Evaluation</b>		
24			
25	<b>Acronyms</b>	<b>Full Names</b>	<b>Definition and Measurement description</b>
26	mRS	modified Rankin scale	Measured before treatment, 24h and 90 days after treatment
27			
28	NIHSS	National Institute of Health stroke scale	Measured before treatment, 24h and 90 days after treatment
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31	mTIMI	modified Thrombolysis in Myocardial Infarction	Measured before EVT and immediately after recanalization.
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34	GCS	Glasgow coma score	Measured before treatment, 24h and 90 days after treatment
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36	pc-ASPECTS	post-circulation Alberta Stroke Program Early CT Score	Measured before treatment
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39	<b>Work flow</b>		
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Name	Definition and description
Onset to door	The duration between patient last know to be well and arriving to radiological suite.
Door to groin puncture	The duration between patient arriving at radiological suite and groin puncture initiating.
Puncture complete	The duration between groin puncture initiating and puncture completing.
Groin puncture to recanalization	The time duration between puncture complete and recanalization.
Recanalization time	The time duration between onset to recanalization success.
Recover time	The time duration between pressing against the puncture site and transferring to NICU.

# BMJ Open

## Choice of ANesthesia for EndoVAScular Treatment of Acute Ischemic Stroke at Posterior Circulation (CANVAS II): Protocol for an Exploratory Randomized Controlled Study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-036358.R2
Article Type:	Protocol
Date Submitted by the Author:	16-Jun-2020
Complete List of Authors:	Liang, Fa; Beijing Tiantan Hospital, Anesthesiology Zhao, Yan; Beijing Tiantan Hospital, Anesthesiology Yan, Xiang; Beijing Tiantan Hospital, Anesthesiology Wu, Youxuan; Beijing Tiantan Hospital, Anesthesiology Li, Xiuheng; Beijing Tiantan Hospital, Anesthesiology Zhou, Yang; Beijing Tiantan Hospital, Anesthesiology Jian, Minyu; Beijing Tiantan Hospital, Anesthesiology Li, Shu; Beijing Tiantan Hospital, Anesthesiology; Beijing Tian Tan Hospital, Capital Medical University Miao, Zhongrong; Beijing Tiantan Hospital, Neurology Han, Ruquan; Beijing Tiantan Hospital, Anesthesiology Peng, Yuming; Beijing Tiantan Hospital, Anesthesiology
<b>Primary Subject Heading</b>:	Anaesthesia
Secondary Subject Heading:	Neurology
Keywords:	Anaesthesia in neurology < ANAESTHETICS, Neurology < INTERNAL MEDICINE, Stroke medicine < INTERNAL MEDICINE, Neuroradiology < NEUROLOGY

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4 **Choice of ANesthesia for EndoVAScular Treatment of Acute**  
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6 **Ischemic Stroke at Posterior Circulation (CANVAS II):**  
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8 **Protocol for an Exploratory Randomized Controlled Study**  
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For peer review only

## ABSTRACT

### Introduction

Observational and interventional studies indicate that the type of anesthesia may be associated with the post-procedural neurological function in patients with anterior circulation acute ischemic stroke undergoing endovascular treatment. Patients with acute posterior circulation ischemic stroke may experience different physiological changes and result in severe neurological outcome. However, the effect of the type of anesthesia on post-procedure neurological function remained unclear in this population.

### Methods and analysis

This is an exploratory randomized controlled trial that will be carried out at Beijing Tiantan Hospital, Capital Medical University. Patients with acute posterior circulation ischemic stroke and deemed suitable for emergency endovascular recanalization will be recruited in this trial. Eighty-four patients will be randomized to receive either general anesthesia or conscious sedation with 1:1 allocation ratio. The primary endpoint is the 90-day modified Rankin Scale.

### Ethics and dissemination

The study is registered at the ClinicalTrials.gov (NCT03317535) and has been reviewed by and approved by Ethics Committee of Beijing Tiantan Hospital of Capital Medical University (KY2017-074-02). If the results are positive, the study will indicate whether the type of anesthesia affects neurological outcome after endovascular treatment of posterior stroke. The findings of the study will be published in peer-reviewed journals and presented at national or international conferences.

**Trial registration number:** NCT03317535

### Keywords

General anesthesia, Conscious sedation, Endovascular treatment, Posterior circulation, Acute ischemic stroke, Neurological outcome

## Article Summary

### Strengths and limitations of this study

- This is the first randomized control study to observe the effect of anesthesia modality on neurological outcome of patients with posterior circulation acute ischemic stroke.
- This study involves strict randomized system, clear inclusion and exclusion criteria, a rigorous uniform protocol to balance intraoperative variables between groups.
- One limitation of the study is it is a single-centered trial, future multicenter trial is needed to verify the effects of anesthesia on patients with posterior circulation acute ischemic stroke undergoing endovascular treatment.
- The sample size is relatively small and the result will need to be confirmed by larger-size trials.
- Patients are selected mainly based on time window, salvageable ischemic brain tissue and initial infarct size might be considered in the inclusion criteria.

## INTRODUCTION

Acute ischemic stroke (AIS) at posterior circulation account for 17%-60% of acute ischemic stroke with difficulty in treatment, which result in a poor outcome and mortality rate of 80%-95%<sup>1-5</sup>. Early recanalization is one of the most important predictors of favorable outcome for posterior circulation AIS patients at 90 days <sup>6</sup>. Though endovascular therapy (EVT) has been demonstrated to be an effective and safe treatment with around 30% good clinical outcome improvement and 35% mortality decrease at 90 days, there is a substantial proportion of patients with poor clinical outcomes even after timely successful reperfusion<sup>7-10</sup>. Many factors may contribute to the mismatched association of high reperfusion rate and poor clinical outcome, including patient-specific factors (age, collaterals status, initial stroke severity, infarct volume and site, and distal artery emboli, etc.), procedural-specific factors (time from onset to recanalization, degree of recanalization) and anesthesia management<sup>2 11 12</sup>.

The optimal anesthesia choice and management for AIS patients during EVT, general anesthesia (GA) or conscious sedation (CS), is still unclear. Benefits of GA with tracheal intubation or laryngeal mask include secured airway to avoid aspiration, body immobility to avoid vessel perforation and better digital subtraction angiography imaging. On the other hand, hypotension, nosocomial infection, delayed procedure initiation, loss of neurological evaluation, and hyperventilation may contribute to poor outcomes. CS management permits neurological function assessment, shortens mean time from door to groin puncture and minimizes hemodynamic changes associate with GA. However, the risk of aspiration and substantial movement during endovascular procedural are the main two disadvantages associated with CS <sup>13-17</sup>.

Three randomized controlled trials have compared the neurological outcomes after EVT with GA or CS in anterior circulation. The Sedation vs. Intubation for Endovascular Stroke TreAtment (SIESTA) trial reported similar National Institute of Health stroke scale (NIHSS) scores at 24 hours between GA and CS, but favorable outcomes, measured by modified Rankin scale (mRS) was found in patients with GA <sup>3</sup>

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4 months after treatment as a secondary outcome measure<sup>14</sup>. Similarly, the General Or  
5 Local anesthesia in Intra Arterial THERapy (GOLIATH) trial reported similar brain  
6 infarct volume and favorable 90-day mRS score increased with GA<sup>18</sup>. However, The  
7 Anesthesia during Stroke (AnStroke) trial reported no difference between GA and CS  
8 in 90-day mRS<sup>19</sup>. Recently, a meta-analysis using fixed-effects model by obtaining  
9 individual patient data from the above-3 trials with blinded endpoint evaluation,  
10 indicated significantly different results in favor of the GA group (cOR=1.58, 95% CI  
11 1.09-2.29)<sup>20</sup>. Nevertheless, these findings should be interpreted with caution. Firstly,  
12 these trials only provided insight into choice of anesthesia modality in the anterior  
13 circulation AIS population, the result of above researches are not appropriate for  
14 patients with posterior circulation occlusions. Secondly, only AnStroke trial analyzed  
15 the neurological function at 90 days as the primary outcome, while in other 2 trials, it  
16 was analyzed as a secondary outcome. Hence the conclusion on relationship between  
17 anesthesia and neurological function at 90 days should be drawn with caution<sup>19</sup>.

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32 A few studies observed the feasibility of monitored anesthesia care for elective  
33 endovascular procedures either in anterior or posterior circulations, and demonstrated  
34 high technical success with low rates of peri-procedural complications and mortality<sup>21</sup>  
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Although these studies included a relatively large proportion of posterior circulation  
interventions and showed promising results about feasibility of monitored anesthesia  
care, it is unreasonable to employ previous results in emergent setting, with potential  
presence of severe midbrain ischemia. Moreover, only one study focused purely on the  
posterior circulation patients and investigated the influence of anesthesia modality and  
management on clinical and angiographic outcomes<sup>21</sup>. In this retrospective, matched,  
case-control study, CS was found to be feasible and appeared to be as safe and effective  
as GA. However, retrospective design and relatively limited sample size may introduce  
undetected biases. Furthermore, there is no published randomized controlled trial that  
explored whether GA or CS are associated with different neurological outcome at 90  
days in patients undergoing EVT for posterior circulation AIS.

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4 On the basis of previous studies, we propose to conduct a trial to compare neurological  
5 outcome in posterior circulation AIS patients receiving GA with those receiving CS for  
6 EVT.  
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## 10 **METHODS**

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12 The protocol has been prepared according to Standard Protocol Items:  
13 Recommendations for Interventional Trials (SPIRIT)<sup>23</sup>. All trial procedures are  
14 summarized in Table 1. For completed checklists, see Supplementary file 1.  
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### 20 **Study design**

21  
22 This is a randomized, parallel-group, exploratory trial with blinded endpoint evaluation  
23 to determine whether GA or CS produces different neurological outcomes in posterior  
24 circulation AIS patients undergoing EVT. Posterior circulation AIS patients will be  
25 enrolled from Beijing Tiantan Hospital, Capital Medical University from 2018 to 2020.  
26 This trial was approved by the Ethics Committee of Beijing Tiantan Hospital of Capital  
27 Medical University (KY2017-074-02) and registered in [www.clinicaltrials.gov](http://www.clinicaltrials.gov)  
28 (NCT03317535). The participants flowchart is briefly illustrated in Figure 1  
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### 36 **Participants**

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38 Posterior circulation AIS Patients who deemed suitable for recanalization of the  
39 culprit's vessels will be considered for recruitment in the study. The inclusion criteria  
40 are vertebral artery and/or basilar artery responsible for posterior circulation ischemia  
41 confirmed by computed tomography angiography (CTA)/ magnetic resonance  
42 angiography (MRA), the modified Thrombolysis in Cerebral Infarction (mTICI) score  
43  $\leq 1$ , age  $\geq 18$  years, stroke onset to treatment time  $\leq 24$  hours, and modified Rankin  
44 Score  $\leq 2$  before onset.  
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53 Patients with unclear radiological image to identify infarction and vessel occlusion,  
54 with intracranial hemorrhage, anterior circulation occlusion, Glasgow coma score  
55 (GCS)  $\leq 8$ , NIHSS score  $< 6$  or  $> 30$ , post-circulation Alberta Stroke Program Early  
56 CT Score (pc-ASPECTS)  $< 6$ , pons-midbrain index  $\geq 3$ , severe agitation or seizures,  
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4 loss of airway protective reflexes and/or vomiting on admission, intubated before EVT,  
5 unconsciousness, and known allergy to anesthetics or analgesics will be excluded from  
6 the study. Patient whose legal relative refuses to participate will be excluded. Both the  
7 neuro-radiologists and the attending anesthesiologist must agree that the patient is  
8 suitable with either GA or CS management before recruiting. Reasons why eligible  
9 patients are not recruited to the trial will be documented.

### 16 **Randomization and blinding**

18 Randomization occurs on the time of EVT when patients are admitted to the  
19 interventional neuroradiology suite, the decision for EVT has been made, and written  
20 informed consent (Supplementary file 2) is obtained from patient's legal representatives.  
21 Randomization will be conducted via a computer-generated table. Patients will be  
22 randomly allocated to receive either GA or CS in a 1 to 1 ratio. A designated staff who  
23 will neither be involved in anesthesia management nor follow-up will perform  
24 recruitment as well as allocation randomization sequence. This designated staff will  
25 implement the allocation sequence through opaque, sealed and stapled envelopes. The  
26 endpoint assessors will be blinded to the randomization group.

38 Standard operating procedures are applied to both groups to ensure no principal  
39 differences generated and uniform protocol implemented. Patients in both groups will  
40 receive local anesthesia at puncture site, with 3-5 ml of 1% lidocaine hydrochloride  
41 prior to arterial puncture. The outcome assessors are blinded to the information of  
42 treatment for the enrolled patients and will evaluate the outcome variables for this study  
43 to ensure unbiased reporting. The anesthesiologist, neuro-radiologist as well as  
44 attending doctors in neurological intensive care unit (NICU) will not be blinded as they  
45 need to participate in the safe administration of GA or CS and related medical care. The  
46 enrolled patients and his/her legal representatives will not be blinded, either.

### 57 **Standard anesthesia management protocols during EVT (Concomitant treatment)**

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4 All randomized patients will receive standard monitoring, including  
5 electrocardiography (ECG), non-invasive blood pressure (BP), heart rate (HR), pulse  
6 oxygen saturation (SpO<sub>2</sub>), invasive arterial pressure monitoring on radiologist arterial  
7 access line, arterial partial pressure of carbon dioxide (PaCO<sub>2</sub>), end-tidal carbon  
8 dioxide (ETCO<sub>2</sub>), inspired oxygen fraction (FiO<sub>2</sub>) and blood glucose. All patients will  
9 receive bispectral index (BIS) monitoring to assess the depth of sedation or anesthesia  
10 with BIS probe placed on the forehead. Physiologic parameters will be recorded using  
11 purposely designed data collection table. BP and blood glucose will be controlled  
12 according to current guidelines for stroke therapy<sup>24-26</sup>. Specifically, systolic blood  
13 pressure (SBP) is aimed to be kept between 140 and 180 mmHg and diastolic blood  
14 pressure (DBP) less than 105 mmHg, with vasopressor support if necessary. Plasma  
15 glucose will be maintained at level of 140-180 mg/dl while SPO<sub>2</sub> is aimed to be over  
16 94%, with FiO<sub>2</sub> at a range from 40% to 60%<sup>27</sup>. It is anticipated that patients in the CS  
17 group may deteriorate during EVT and may, therefore, require endotracheal intubation  
18 or laryngeal mask insertion for airway protection<sup>17</sup>. All anesthesia related treatment will  
19 be performed by anesthesiologists of ischemia stroke team.  
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### 38 **Interventions**

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40 GA and CS in this trial are defined according to the Practice guidelines for sedation and  
41 analgesia by non-anesthesiologists due to the continuum ranging of level of sedation  
42 from minimal sedation to GA<sup>28</sup>. Both GA and CS will be monitored and applied by  
43 anesthesiologist. In CS group, patients will receive sedative drugs and follow the  
44 sedation protocol as following: bolus propofol of 0.3-0.5 mg/kg, following continuous  
45 propofol infusion of 1-2 mg/kg/h and remifentanil infusion of 0.01-0.06 ug/kg/min.  
46 SpO<sub>2</sub> will be kept above 94% with 40%-60% inhaled oxygen at 3L/min flow and  
47 ETCO<sub>2</sub> is monitored via anesthetic gas sample line at nasal vestibule and kept  
48 normocapnia. The BIS value will be maintained above 70 via adjusting the infusion of  
49 sedative drugs.  
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4 In GA group, patients will receive rapid sequence induction with endotracheal  
5 intubation or laryngeal mask insertion with propofol, remifentanyl and muscle relaxant.  
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7 Anesthesia will be induced with infusion of propofol of 1-2 mg/kg and remifentanyl of  
8 0.2-0.8 ug/kg for anesthesia induction<sup>27</sup>. Muscle relaxation will be achieved with  
9 rocuronium (0.6 mg/kg). After endotracheal intubation or laryngeal mask insertion,  
10 suction will be performed to mitigate risk of aspiration. Mechanical ventilation will be  
11 initiated to achieve normocapnia (ETCO<sub>2</sub> between 35 and 45 mmHg) with a 40%-60%  
12 fraction of inspired oxygen. Anesthesia will then be maintained with propofol (4-6  
13 mg/kg/h) and remifentanyl (0.05 to 0.1 ug/kg/min) infusion to maintain the BIS value  
14 between 40 and 60.  
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24 Converting from CS to GA is an important issue in this trial. In cases of procedural  
25 emergency including vessel perforation, intracranial hemorrhage (ICH), subarachnoid  
26 hemorrhage (SAH), seizures, deep coma, GCS decrease to or less than 8, respiratory  
27 failure (ETCO<sub>2</sub>≥60 mmHg, or SpO<sub>2</sub><94% without relevant improvement by increasing  
28 inhaled oxygen fraction) and severe disturbance of the treatment procedure (vomiting,  
29 substantial movement and uncoordinated dysphoria), CS will be converted to GA. The  
30 decision to convert from CS to GA will be made by the neuro-radiologist in charge and  
31 the attending anesthesiologist. The number of patients and reasons for the conversion  
32 will be recorded in detail. Criteria for converting from CS to GA is listed in Table 2.  
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### 43 **Measurements**

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45 All patients will be regularly visited while in hospital by outcome assessors who are  
46 blinded to the treatment allocation. The incidence of complications, including  
47 myocardial infarction, non-fatal cardiac arrest, new stroke, pulmonary embolism and  
48 deep venous thrombosis will be recorded. All patients will receive brain imaging,  
49 including CTA, MRA before, 24 hours, 7 days (or at discharge, whichever sooner), 30  
50 days and 90 days after randomization. Brain image will be used to assess new brain  
51 hemorrhage (if present) and infarct volume. Efficacy of vessels recanalization will be  
52 assessed by mTICI scale. The severity of stroke will be assessed using the NIHSS scale  
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4 during the same period. Disability will be rated at discharge and three months after EVT  
5 and rated using mRS. A glossary of measurements is shown in Supplementary file 3.  
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7 To minimize loss of follow-up after discharge, study coordinators will contact the  
8 patients and his/her next-of-kin on a weekly basis. Besides, adverse effect will be also  
9 recorded.  
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### 14 **Study objectives**

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16 The study aims to detect the difference of the post-procedural neurological function in  
17 patients with posterior circulation AIS under GA and CS, and hence to observe the  
18 effect of anesthesia type on outcomes after EVT.  
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### 23 **Primary endpoint**

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25 The primary endpoint is the neurological disability at 90-day after EVT measured by  
26 mRS, which ranges from 0 (no symptoms) to 5 (severe disability), and a favorable  
27 neurological outcome is defined as no symptom or no significant disability with  $mRS \leq$   
28  $2^3$  <sup>15 29 30</sup>. The score will be evaluated by outcomes assessor who are blinded to  
29 allocation.  
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### 36 **Secondary endpoints**

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38 The secondary endpoints include the followings:  
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- 40 1. Change in NIHSS, from baseline to 24 h, 7 days (or at discharge), 30 days and 3  
41 months after randomization.
- 42 2. The score of mTICI will be evaluated before and after endovascular treatment.
- 43 3. All-cause mortality up to 3 months after randomization.
- 44 4. The incidence of complications up to 3 months after randomization.
- 45 5. The length of stay in the hospital and in intensive care unit after randomization.
- 46 6. The rate of conversion from CS to GA.
- 47 7. Work-flow time, including door to door, door to groin puncture, puncture complete,  
48 groin puncture to recanalization and treatment time.
- 49 8. All adverse events associated with this study will be recorded.  
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### **Data Monitoring Committee (DMC)**

The project will be monitored by a Data Monitoring Committee (DMC) composed of specialists in anesthesiology, ethics, statistics and methodology. The DMC will audit through regular interviews or telephone calls. The DMC are responsible for terminating the research in case of severe adverse events.

### **Statistical analysis plan**

Descriptive statistics will be reported as means with standard deviation and medians with interquartile range for normally distributed data and skewed continuous data, respectively, and counts (percentage) for categorical data. The data will be analyzed on intention to treat and per protocol, however, the conclusion will be drawn according to the intention-to-treat analysis. The intention-to-treat analysis will depend on the allocated population while the per-protocol analysis will depend on the actual anesthesia method the population receive. Differences in the primary endpoint will be compared between groups using Cochran-Mantel-Haenszel test. Furthermore, primary outcome will be analyzed in following subgroups: age, gender, baseline NIHSS score; time from onset of stroke to EVT, site of arterial occlusion, and mTICI score. Other categorical variables will be analyzed by  $\chi^2$  test and continuous variables using Student-t test or Mann-Whitney U test.

To allow for a varying number of follow-up measurements, the repeated measure ANOVA methods with a mixed model approach (treating time as a random effect and other covariates as fixed effects) will be utilized, and the specific comparison of change in each of those measurements between baseline and any specific post-baseline time point can be tested using linear contrast. In addition, missing data will be imputed using inverse probability weighting and the worst-case imputation scenarios. STATA 14.0 (StataCorp LP, College Station, TX) for windows will be used for all statistical analyses. The statistical significance will be declared at type I error of 0.05.

### **Sample size calculation**

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4 The PASS 15 software (NCSS, LLC, USA) is used to calculate the sample size based  
5 on the primary endpoint – favorable outcome (mRS 0-2) at three months after  
6 randomization. Several trials focused on the neurological outcome of patients with  
7 posterior circulation AIS, however, only two indicated the association between  
8 anesthesia type and neurological outcome. In the case-control study of Ashutosh et al,  
9 they reported the incidence of  $mRS \leq 2$  at 90-day was 38.3% in CS and 31.1% in GA<sup>21</sup>.  
10 On the other hand, a retrospective observational study in our institution reported a  
11 higher incidence of favorable neurological outcome at 90-day in CS compared to GA  
12 group (68.7% vs 35.6%)<sup>31</sup>. However, other factors including pre-operative NIHSS  
13 score, pre-operative intravenous thrombolysis treatment confound the results validity<sup>31</sup>.  
14 Meanwhile, in previous anterior circulation research, AIS patients receiving GA  
15 presented a favorable or similar neurological outcome at 90 days compared with CS<sup>13</sup>  
16 <sup>19 32</sup>. Taking this into account, we consider that the sample size to detect 30% difference  
17 in mRS 0-2 would require 44 in each group to achieve power of 80% at a two-tailed  
18 significant level of 0.05, with a drop-out rate of 5%<sup>33</sup>.  
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### 34 **Reporting of adverse events**

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36 All adverse events associated with this trial will be recorded and closely monitored until  
37 resolution or stabilization or until it has been shown that study treatment is not the cause  
38 of the event. The principal investigator is responsible for reporting all adverse events.  
39 Once adverse events occur, it should be immediately reported to the research  
40 department and informed to the principal investigator to determine the severity of the  
41 adverse events. All adverse events associated with this study will be recorded and  
42 reported to the Ethics Committee within 24 hours.  
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### 51 **Protocol Amendment**

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53 The chief investigator will be responsible for any decision to amend the protocol. If  
54 there is any modification (eg, changes to eligibility criteria, outcomes, analyses) the  
55 principle investigator will communicate and gain approval from the Ethical Committee  
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4 of Beijing Tiantan Hospital, Capital Medical University prior to implementation, and  
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6 communicate with relevant parties.  
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### 8 9 **Ethics and dissemination**

10 The approval for the study was certificated by the Ethical Committee of Beijing Tiantan  
11 Hospital, Capital Medical University on 19 December, 2017 (reference number:  
12 KY2017- 074-02). The study was registered on clinicaltrials.gov on 23 October, 2017  
13 (NCT03317535). The study recruited the first patient on 1 February, 2018, and the  
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estimated study completion date will be 31 Dec, 2020. The findings of the study will be  
published in peer-reviewed journals and will be presented at national or international  
conferences.

### 26 **DISCUSSION**

27 This is an exploratory controlled randomized study aiming to detect the effect of  
28 anesthesia choice on the neurological outcome in the patients with posterior circulation  
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AIS undergoing EVT. The study aims to test the hypothesis that GA and CS have  
different effects on the post-endovascular procedure neurological outcomes in patients  
with posterior circulation AIS.

Anesthetic selection and peri-procedural management could be associated with  
outcomes in patients with posterior circulation AIS undergoing EVT. The  
hemodynamics disturbance and the changes in carbon dioxide tension may be  
associated with the outcomes. However, no consistent agreement about the anesthesia  
modality has been reached, the anesthetic protocols vary among different stroke centers.  
In daily clinical work, the actual practice of anesthesia for EVT, especially for posterior  
circulation AIS patients, largely rely on local protocols and individual preference of  
neuro-radiologists or anesthesiologists. CS may be used for cooperative patients and  
GA for severely agitated, non-conscious and unprotected airway patients<sup>13</sup>. A small  
number of retrospective studies (including patients with posterior circulation AIS) show  
that CS groups have better clinical outcomes, lower complication rate, shorter  
reperfusion time and less changes in hemodynamics and respiration<sup>21 22 31</sup>. In contrary,

GA groups could suffer from worse neurological function, lower blood pressure, aspiration pneumonia and/or high mortality<sup>34-41</sup>. A recent retrospective, matched, case-control study of patients with posterior circulation AIS is the only study to explore the effect of anesthesia management on outcome of patients with posterior AIS, however, great limitation and drawbacks in terms of study design, including selection bias and information bias impede the credibility of the results<sup>21</sup>. Several confounding factors contribute to inconclusive results, including specific information of peri-interventional management, such as blood pressure, partial pressure of carbon dioxide, and strict uniform anesthesia protocol. Therefore, a prospective, randomized, controlled trial is required to account for the peri-procedural confounders and demonstrate the effects of anesthesia (type and management) on outcomes for patients with posterior AIS undergoing EVT.

This trial aims to explore the effect of anesthesia choice on the post-endovascular procedure outcomes in patients with posterior circulation AIS using a randomized controlled trial design. The features of the current study involve strict randomized system, clear inclusion and exclusion criteria, a rigorous uniform protocol to manage hemodynamic, respiratory parameters and blood glucose in GA and CS group, and full-time attending anesthesiologists in each procedure. The findings of the study would contribute to serve as a reference for a future multi-center trial to verify the effects of anesthesia on patients with posterior circulation AIS undergoing EVT.

### **Patient and public involvement**

Patients and the public were not directly consulted in the development of the research question or outcome measures. Patients were not involved in the design, the recruitment and conduct of the study. At the completion of this trial, a manuscript will be prepared to present the trial results. Results of the final study will be disseminated to all study participants through their preferred method of communication indicated at the time of enrollment.

### **Competing interests**

None declared.

### **Funding**

The trial is supported by the Beijing Municipal Administration of Hospitals of Ascent Plan (Grant No.: DFL20180502), Beijing Municipal Administration of Hospitals Clinical Medical Development of Special Funding Support (Grant No.:ZYLX201708) and Beijing Municipal Science & Technology Commission (Grant No.: Z191100006619068).

### **Author contributions**

FL and Yan Zhao conceived the study. FL, YZ, SL, ZM, YP and RH initiated the study design and helped with protocol development and implementation. FL, XY, XL YW, Yang Zhou and MJ helped in data collection and manuscript revision. YP and RH are the grant holders. FL and Yan Zhao are the co-first authors. YP is the responsible author. All authors contributed to refinement of the study protocol. All authors have read and approved the final manuscript.

### **Ethics approval**

This study is approved by the Ethical Committee of Beijing Tiantan Hospital, Capital Medical University (reference number: KY2017- 074-02).

### **Data sharing statement**

This manuscript is a protocol for a randomized controlled trial, which does not include data.

### **List of tables and figures:**

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Table 2. Criteria for converting from conscious sedation to general anesthesia

Figure 1. CONSORT flow diagram for CANVAS II clinical trial.

Supplementary file 1 SPIRIT checklist.

Supplementary file 2 Informed consent



Supplementary file 3 Measurement glossary.

## References

1. Raymond S, Rost NS, Schaefer PW, et al. Patient selection for mechanical thrombectomy in posterior circulation emergent large-vessel occlusion. *Interv Neuroradiol* 2018;24(3):309-16.
2. Luo G, Mo D, Tong X, et al. Factors Associated with 90-Day Outcomes of Patients with Acute Posterior Circulation Stroke Treated By Mechanical Thrombectomy. *World neurosurgery* 2018;109:e318-e28.
3. Lee YY, Yoon W, Kim SK, et al. Acute Basilar Artery Occlusion: Differences in Characteristics and Outcomes after Endovascular Therapy between Patients with and without Underlying Severe Atherosclerotic Stenosis. *AJNR Am J Neuroradiol* 2017;38(8):1600-04.
4. Kim YW, Hong JM, Park DG, et al. Effect of Intracranial Atherosclerotic Disease on Endovascular Treatment for Patients with Acute Vertebrobasilar Occlusion. *AJNR Am J Neuroradiol* 2016;37(11):2072-78.
5. Gao F, Lo WT, Sun X, et al. Combined Use of Mechanical Thrombectomy with Angioplasty and Stenting for Acute Basilar Occlusions with Underlying Severe Intracranial Vertebrobasilar Stenosis: Preliminary Experience from a Single Chinese Center. *AJNR Am J Neuroradiol* 2015;36(10):1947-52.
6. Mokin M, Sonig A, Sivakanthan S, et al. Clinical and Procedural Predictors of Outcomes From the Endovascular Treatment of Posterior Circulation Strokes. *Stroke* 2016;47(3):782-8.
7. Gory B, Eldesouky I, Sivan-Hoffmann R, et al. Outcomes of stent retriever thrombectomy in basilar artery occlusion: an observational study and systematic review. *J Neurol Neurosurg Psychiatry* 2016;87(5):520-5.
8. van Houwelingen RC, Luijckx GJ, Mazuri A, et al. Safety and Outcome of Intra-Arterial Treatment for Basilar Artery Occlusion. *JAMA Neurol* 2016;73(10):1225-30.



- 1  
2  
3  
4 9. Huo X, Gao F, Sun X, et al. Endovascular Mechanical Thrombectomy with the  
5 Solitaire Device for the Treatment of Acute Basilar Artery Occlusion. *World*  
6 *neurosurgery* 2016;89:301-8.
- 7  
8  
9 10. Singer OC, Berkefeld J, Nolte CH, et al. Mechanical recanalization in basilar artery  
10 occlusion: the ENDOSTROKE study. *Ann Neurol* 2015;77(3):415-24.
- 11  
12  
13 11. Brinjikji W, Murad MH, Rabinstein AA, et al. Conscious sedation versus general  
14 anesthesia during endovascular acute ischemic stroke treatment: a systematic review  
15 and meta-analysis. *AJNR Am J Neuroradiol* 2015;36(3):525-9.
- 16  
17  
18 12. Yeo LLL, Holmberg A, Mpotsaris A, et al. Posterior Circulation Occlusions May  
19 Be Associated with Distal Emboli During Thrombectomy : Factors for Distal  
20 Embolization and a Review of the Literature. *Clin Neuroradiol* 2018
- 21  
22  
23 13. Simonsen CZ, Sorensen LH, Juul N, et al. Anesthetic strategy during endovascular  
24 therapy: General anesthesia or conscious sedation? (GOLIATH - General or Local  
25 Anesthesia in Intra Arterial Therapy) A single-center randomized trial. *Int J Stroke*  
26 2016;11(9):1045-52.
- 27  
28  
29 14. Schonenberger S, Mohlenbruch M, Pfaff J, et al. Sedation vs. Intubation for  
30 Endovascular Stroke Treatment (SIESTA) - a randomized monocentric trial. *Int J*  
31 *Stroke* 2015;10(6):969-78.
- 32  
33  
34 15. Brinjikji W, Pasternak J, Murad MH, et al. Anesthesia-Related Outcomes for  
35 Endovascular Stroke Revascularization: A Systematic Review and Meta-Analysis.  
36 *Stroke* 2017;48(10):2784-91.
- 37  
38  
39 16. Kılıç Y, Baş SŞ, Aykaç Ö, et al. Nonoperating Room Anesthesia for Interventional  
40 Neuroangiographic Procedures: Outcomes of 105 Patients. *J Stroke Cerebrovasc*  
41 *Dis*;29(2)
- 42  
43  
44 17. Ozhan MO, Eskin MB, Atik B, et al. Laryngeal Mask Airway for General  
45 Anesthesia in Interventional Neuroradiology Procedures. *Saudi Med J* 2019;40(5):463-  
46 68.
- 47  
48  
49 18. Simonsen CZ, Yoo AJ, Sorensen LH, et al. Effect of General Anesthesia and  
50 Conscious Sedation During Endovascular Therapy on Infarct Growth and Clinical  
51  
52  
53  
54  
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56  
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59  
60

1  
2  
3  
4 Outcomes in Acute Ischemic Stroke: A Randomized Clinical Trial. *JAMA Neurol*  
5 2018;75(4):470-77.  
6

7 19. Lowhagen Henden P, Rentzos A, Karlsson JE, et al. General Anesthesia Versus  
8 Conscious Sedation for Endovascular Treatment of Acute Ischemic Stroke: The  
9 AnStroke Trial (Anesthesia During Stroke). *Stroke* 2017;48(6):1601-07.  
10  
11

12 20. Schonenberger S, Henden PL, Simonsen CZ, et al. Association of General  
13 Anesthesia vs Procedural Sedation With Functional Outcome Among Patients With  
14 Acute Ischemic Stroke Undergoing Thrombectomy: A Systematic Review and Meta-  
15 analysis. *Jama* 2019;322(13):1283-93.  
16  
17

18 21. Jadhav AP, Bousslama M, Aghaebrahim A, et al. Monitored Anesthesia Care vs  
19 Intubation for Vertebrobasilar Stroke Endovascular Therapy. *JAMA Neurol*  
20 2017;74(6):704-09.  
21  
22

23 22. Taqi MA, Suriya SS, Sodhi A, et al. Ideal sedation for stroke thrombectomy: a  
24 prospective pilot single-center observational study. *Neurosurgical focus*  
25 2019;46(2):E16.  
26  
27

28 23. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining  
29 standard protocol items for clinical trials. *Annals of internal medicine* 2013;158(3):200-  
30 7.  
31  
32

33 24. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 Guidelines for the Early  
34 Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare  
35 Professionals From the American Heart Association/American Stroke Association.  
36 *Stroke* 2018;49(3):e46-e110.  
37  
38

39 25. Talke PO, Sharma D, Heyer EJ, et al. Republished: Society for Neuroscience in  
40 Anesthesiology and Critical Care expert consensus statement: Anesthetic management  
41 of endovascular treatment for acute ischemic stroke. *Stroke* 2014;45(8):e138-50.  
42  
43

44 26. Warner JJ, Harrington RA, Sacco RL, et al. Guidelines for the Early Management  
45 of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the  
46 Early Management of Acute Ischemic Stroke. *Stroke*;50(12):3331-32.  
47  
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4 27. Peng Y, Li Y, Jian M, et al. Choice of ANesthesia for EndoVAscular Treatment of  
5 Acute Ischemic Stroke: Protocol for a randomized controlled (CANVAS) trial. *Int J*  
6 *Stroke* 2017;12(9):991-97.  
7  
8  
9 28. American Society of Anesthesiologists Task Force on S, Analgesia by N-A. Practice  
10 Guidelines for Sedation and Analgesia by Non-Anesthesiologists by the American  
11 Society of Anesthesiology. *Anesthesiology* 2002;96(4):1004-17.  
12  
13 29. Lindsberg PJ, Mattle HP. Therapy of basilar artery occlusion: a systematic analysis  
14 comparing intra-arterial and intravenous thrombolysis. *Stroke* 2006;37(3):922-8.  
15  
16 30. Wang A, Stellfox M, Moy F, et al. General Anesthesia During Endovascular Stroke  
17 Therapy Does Not Negatively Impact Outcome. *World neurosurgery* 2017;99:638-43.  
18  
19 31. Zhang X, Luo G, Mo D, et al. Predictors of Good Outcome After Endovascular  
20 Treatment for Patients with Vertebrobasilar Artery Occlusion due to Intracranial  
21 Atherosclerotic Stenosis. *Clin Neuroradiol* 2018  
22  
23 32. Schonenberger S, Uhlmann L, Hacke W, et al. Effect of Conscious Sedation vs  
24 General Anesthesia on Early Neurological Improvement Among Patients With  
25 Ischemic Stroke Undergoing Endovascular Thrombectomy: A Randomized Clinical  
26 Trial. *JAMA* 2016;316(19):1986-96.  
27  
28 33. Hulley SB CS, Browner WS, Grady D, Newman TB. Designing clinical research :  
29 an epidemiologic approach. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins  
30 2013:75.  
31  
32 34. Sugg RM, Jackson AS, Holloway W, et al. Is mechanical embolectomy performed  
33 in nonanesthetized patients effective? *AJNR Am J Neuroradiol* 2010;31(8):1533-5.  
34  
35 35. Davis MJ, Menon BK, Baghirzada LB, et al. Anesthetic management and outcome  
36 in patients during endovascular therapy for acute stroke. *Anesthesiology*  
37 2012;116(2):396-405.  
38  
39 36. Langner S, Khaw AV, Fretwurst T, et al. Endovascular treatment of acute ischemic  
40 stroke under conscious sedation compared to general anesthesia - safety, feasibility and  
41 clinical and radiological outcome. *Rofo* 2013;185(4):320-7.  
42  
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4 37. Hassan AE, Akbar U, Chaudhry SA, et al. Rate and prognosis of patients under  
5 conscious sedation requiring emergent intubation during neuroendovascular procedures.  
6 *AJNR Am J Neuroradiol* 2013;34(7):1375-9.  
7  
8  
9 38. Abou-Chebl A, Zaidat OO, Castonguay AC, et al. North American SOLITAIRE  
10 Stent-Retriever Acute Stroke Registry: choice of anesthesia and outcomes. *Stroke*  
11 2014;45(5):1396-401.  
12  
13  
14 39. Athiraman U, Sultan-Qurraie A, Nair B, et al. Endovascular Treatment of Acute  
15 Ischemic Stroke Under General Anesthesia: Predictors of Good Outcome. *J Neurosurg*  
16 *Anesthesiol* 2017;30(3):223-30.  
17  
18  
19 40. Mundiyanapurath S, Schonenberger S, Rosales ML, et al. Circulatory and  
20 Respiratory Parameters during Acute Endovascular Stroke Therapy in Conscious  
21 Sedation or General Anesthesia. *J Stroke Cerebrovasc Dis* 2015;24(6):1244-9.  
22  
23  
24 41. Hassan AE, Chaudhry SA, Zacharatos H, et al. Increased rate of aspiration  
25 pneumonia and poor discharge outcome among acute ischemic stroke patients  
26 following intubation for endovascular treatment. *Neurocrit Care* 2012;16(2):246-50.  
27  
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Table 1. Schedule of enrollment, intervention and assessment.

	STUDY PERIOD							
	Enrolment	Allocation	Post-allocation					
TIMEPOINT	<i>At arrival</i>	After evaluation	<i>During treatment</i>	<i>24h after treatment</i>	<i>7 days after treatment</i>	<i>Discharge</i>	<i>30 days after treatment</i>	<i>90 days after treatment</i>
<b>ENROLMENT:</b>								
Eligibility screen	X							
Informed consent	X							
Allocation		X						
<b>INTERVENTIONS:</b>								
GA			X					
CS			X					
<b>ASSESSMENTS:</b>								
<i>Baseline variables</i>	X	X						
<i>Brain image</i>	X			X				
<i>mRS</i>							X	X
<i>NIHSS</i>	X			X	X		X	X
<i>mTICI</i>			X					
<i>All-cause mortality</i>								X
<i>length of stay</i>								X
<i>ICU stay and length</i>								X
<i>Converting rate</i>			X					
<i>Adverse event</i>			X					X

GA: general anesthesia; CS: conscious sedation; NIHSS: National Institute of Health Stroke Scale; mRS: modified Rankin Score; mTICI: modified Thrombolysis in Cerebral Infarction Scale

Table 2 Criteria for converting from conscious sedation to general anesthesia.

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1. Unconscious;
  2. GCS decrease to or less than 8;
  3. Increase of ET $\text{CO}_2$   $\geq 60$  mmHg and/or a decrease in  $\text{S}_\text{p}\text{O}_2 < 94\%$  despite oxygen supplementation;
  4. Agitation that cannot be controlled with sedation and/or restraint;
  5. Seizure attack;
  6. Vomiting;
  7. Recognized complications from endovascular therapy, such as vessel perforation leading to intracerebral hemorrhage or subarachnoid hemorrhage.
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GCS: Glasgow coma scale;  $\text{S}_\text{p}\text{O}_2$ : pulse oxygen saturation; ET $\text{CO}_2$ : end-tidal carbon dioxide.

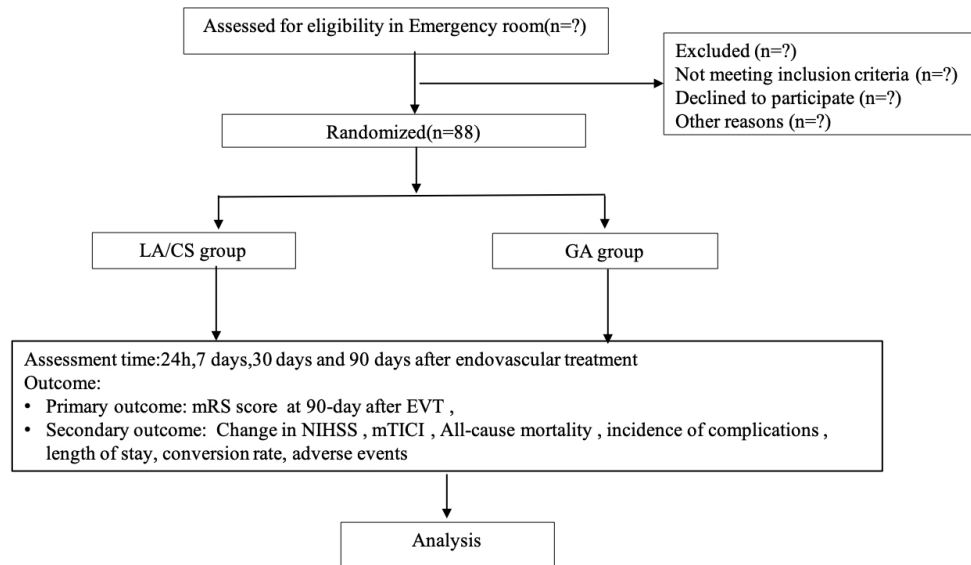


Figure 1. CONSORT flow diagram for CANVAS II clinical trial.

Figure 1. CONSORT flow diagram for CANVAS II clinical trial.

216x142mm (150 x 150 DPI)

Supplementary file 1: SPIRIT checklist.

Section/item	ItemNo	Description	page
<b>Administrative information</b>			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
	2b	All items from the World Health Organization Trial Registration Data Set	1,7
Protocol version	3	Date and version identifier	NA
Funding	4	Sources and types of financial, material, and other support	15
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1,15
	5b	Name and contact information for the trial sponsor	1,15



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	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	15
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	11
<b>Introduction</b>			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5
	6b	Explanation for choice of comparators	5-6
Objectives	7	Specific objectives or hypotheses	7
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	7
<b>Methods: Participants, interventions, and outcomes</b>			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8

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4		11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-9
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8		11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	8-9
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10	Interventions			
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12		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	8,11
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15		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	10
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20	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11
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24	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	Table 1
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28	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	12
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32	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	11
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35	<b>Methods: Assignment of interventions (for controlled trials)</b>			
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Allocation:

Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant’s allocated intervention during the trial	8

**Methods: Data collection, management, and analysis**

Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10, Table 1
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	11

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4	Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	11
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7	Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11-12
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11		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12
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15		20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	12
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19	<b>Methods: Monitoring</b>			
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22	Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11
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26		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
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30	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	13
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34	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
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38	<b>Ethics and dissemination</b>			
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Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	13
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	13
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	NA
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	15
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	16
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	13
	31b	Authorship eligibility guidelines and any intended use of professional writers	NA

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4 31c Plans, if any, for granting public access to the full protocol, participant-level dataset, and 15  
5 statistical code  
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## 8 Appendices

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11 Informed consent 32 Model consent form and other related documentation given to participants and authorised 15  
12 materials surrogates Yes  
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14 Biological 33 Plans for collection, laboratory evaluation, and storage of biological specimens for 15  
15 specimens genetic or molecular analysis in the current trial and for future use in ancillary studies, if NA  
16 applicable  
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# INFORMED CONSENT

## Choice of ANesthesia for EndoVAscular Treatment of Acute Ischemic Stroke at Posterior Circulation (CANVAS II)

Project entrust organization: Beijing Tian Tan Hospital, CMU

Contract Research Organization: N/A

Version: 1.3

28th, Dec, 2017

## INFORMATION SHEET

You have been diagnosed with ***acute ischemic stroke in posterior circulation*** and you will receive emergency endovascular treatment.

We would like to invite you to participate our study, which is "***Choice of ANesthesia for EndoVAscular Treatment of Acute Ischemic Stroke at Posterior Circulation***", to observe the effect of general anesthesia and conscious sedation on clinical outcome. This study is approved by Ethics Committee of Beijing Tiantan Hospital of Capital Medical University. During our study, we will follow the Declaration of Helsinki.

Before you decide whether participate this clinical trial, please take time to review this information carefully. This form describes the purpose, procedure, study duration, risks and possible benefits of participating the study. You may also wish to talk to others, including your friends, family, or discuss with your anesthesiologist, about your participation in this study.

### 1. PURPOSE of THIS STUDY

In China, cerebrovascular disease is the first cause of death. For acute ischemic stroke patients, endovascular therapy is a very important supplementary treatment to improve neurological outcome, in case of thrombolytic therapy failed. Factors associated with clinical outcome of acute ischemic patients including baseline, comorbidity, onset to treatment time and so on. Observational studies indicated that, compared to general anesthesia, conscious sedative ischemic stroke patients may have lower death, better neurological improvement. This indicated that management of anesthesia may effect neurological outcome. However, the research about relationship between acute ischemic stroke and anesthesia management is merely focus on anterior circulation population, while posterior circulation ischemia account for a large amount of stroke and prospective research is need to demonstrate the association between anesthesia management and neurological outcome.

### 2. NUMBER of PARTICIPANTS

In total, 88 patients will be included in the study.

### 3. DURATION OF THIS STUDY

This study will last 3 years and we will collect your postoperative information until 90 days postoperatively.

### 4. PROCESS OF THIS STUDY

If you are willing to participate in the study, please sign this informed consent, and you will be examined including:

- Physical examination and medical history inquiry
- Vital signs: respiratory, body temperature, heart rate, blood pressure.
- Neurological scales: cognitive function, delirium, living quality as well as physical status



- Blood test
- Electrocardiography

If you met the inclusion and exclusion criteria, neuro-radiologist as well as anesthesiologist will evaluate your safety and with the agreement of both of them, you could be allocated into two groups randomly. With the computer-generated table, you will be randomly allocated to receive one of anesthesia management in an equal chance. We will implement your anesthesia according to your group. During the whole study, we will collect your response to different anesthesia methods and your health status through closely intraoperative monitoring. This study will compare your post-treatment neurological outcome, complication, to find out which anesthesia treatment is better for acute posterior circulation ischemic patient, and finally to optimize treatment of patients as you.

## 5. THE DIFFERENCE OF TWO ANESTHESIA MANAGEMENT

There are most common clinical used anesthesia treatment for your condition, general anesthesia and conscious sedation. However, considering there is no clinical trial to answer this question, it is still unclear which treatment is better. According to experience, general anesthesia may supply a safer airway management. Compared to conscious sedation, you may have a lower chance of respiratory dysfunction for secured airway. Nevertheless, general anesthesia has a higher chance of circulation fluctuation and higher chances of intraoperative hypotension. Moreover, conscious sedative patients are awake during the procedure and be able to do neurological evaluation at any time, to assess the neurological status. Conscious sedative patients may under light agitated status and unable to complete surgery. Therefore, we still unable to answer the question which treatment is better. In conclusion, the purpose of this study is to find out which anesthesia treatment is better for acute posterior circulation ischemic stroke patients and finally to improve the treatment you future patients.

## 6. OTHER TREATMENT CHOICE

In clinical practice, the anesthesia management for acute stroke patients includes general anesthesia and conscious sedation. If you do not participate in this study, you can choose your anesthesia treatment according to your anesthesiologist's suggestion.

## 7. WHO SHOULD NOT PARTICIPATE in the STUDY

If you have following condition, you should not participate in the study:

- 1) Anterior circulation occlusion
- 2)  $GCS \leq 8$ ,
- 3) Intracranial hemorrhage
- 4) Seizure or severe agitation
- 5) Intubated before treatment
- 6) Unconsciousness
- 7) Known allergy to anesthetics or analgesics
- 8) loss of airway protective reflexes and/or vomiting on admission

## 8. POSSIBLE BENEFITS of PARTICIPATING in the STUDY

Your prognosis may or may not improve as a result of participating in this study, and the information from this study will help determine which anesthesia management are safer and more effective in treating other patients with similar conditions of yours.

## 9. POSSIBLE ADVERSE REACTIONS, RISKS and DISCOMFORT, INCONVENIENCES of PARTICIPATING in the STUDY

The monitoring methods, anesthesia methods, anesthetic drugs and anesthesia maintenance used in this study are all routine clinical practice. It is possible that related discomfort or adverse event will happened during your anesthesia and operation, including respiratory depression, circulation depression, arrest, cardiac arhythm, myocadial infarction, pulmonary embolism, drug adverse react as well as cerebrovascular complication (hemorrhage and infarction) If you experience adverse reactions or discomfort due to surgical procedures, anesthesia, or changes in your condition during the course of the study, the researchers will make corrections promptly.

During the study, you need to undergo doctors inquiry, laboratory tests and questionnaire, which may cause inconvenience to you.

## 10. CONFIDENTIALITY of PERSONAL INFORMATION

Your medical records (study records /CRF, lab sheets, etc.) will be kept intact at the hospital. Your doctor will record the results of tests and other tests on your medical record. Researchers, ethics committees, and drug regulators will be allowed access to your medical records. Any public reports on the results of this study will not disclose your personal identity. We will make every effort to protect the privacy of your personal medical data within the law.

## 11. HOW TO GET MORE INFORMATION?

You can ask any questions about this study at any time and get answers. Your anesthesiologist will be ready to answer any of your questions before, during and after the study.

## 12. RELATED EXPENSES

Anesthetic drugs and surgical procedures are not free of charge. If you combine the treatment and examination required for other diseases, and if the treatment fails, the cost of changing to other treatment is not free of charge. If any medical expense happened due to adverse event, you will be exempted from the charge.

## 13. YOU MAY VOLUNTARILY CHOOSE TO PARTICIPATE in the STUDY and WITHDRAW from the STUDY

Whether to participate in the study is entirely up to you. You may refuse to participate in the study or withdraw from the study at any time during the study, which will not affect your relationship with your doctor or affect your medical service or other benefits.

Before making decision, you can discuss with your family or friend, or you can talk with your doctor for any question, until you fully understand this study.

**14. HOW THE STUDY MAY EFFECT YOUR LIFE?**

You may feel the visit and examination uncomfortable and special arrangement is needed. You can consult your doctor in any steps of the study.

**15. CONSULTING**

If you have any related questions, please contact Dr.Liang Fa (phone: 010-67096658 or cell phone:18810084538).

If you have any concernes about your personal benefit, or you want to complain or express your concers about the study, please contact the Ethics Committee of Beijing Tiantan Hospital of Capital Medical University (phone: 010-67098555).

For peer review only

## SIGNATURE PAGE of AGREEMENT

**Study title: Choice of ANesthesia for EndoVAScular Treatment of Acute Ischemic Stroke at Posterior Circulation**

**Principal investigator: Ruquan Han, Beijing Tiantan Hospital, CMU**

### DECLARATION of CONSENT

I have read the introduction about the study above and have the opportunity to discuss with doctors and ask the questions about the study. All my questions have been answered satisfactorily.

I am aware of the possible risk and benefits of participating in this study. I know that participating in the study is voluntary. I have taken it into full consideration, and known that:

- I can ask my doctor for more information at any time.
- I can withdraw from this study at any time without discrimination or retaliation, and my medical treatment and rights will not be affected.

I am also aware that if I withdraw from the study, especially if I withdraw due to medication, it will be of great benefit to the whole study if I tell my doctor about my condition and complete the corresponding physical examination and physical and chemical inspection.

If I need to take any other medication due to a change in my condition, I will consult my doctor beforehand or tell him afterwards truthfully.

I agree that the ethics committee of the drug regulatory authority or the representative of the sponsor may have access to my research information.

I will be provided with a signed and dated copy of the informed consent.

In the end, I agreed to participate in the study and promised to follow my doctors advice as much as possible.

**Signature of patient/legal relative:** \_\_\_\_\_

**Relation: :** \_\_\_\_\_

**Date:** \_\_\_\_\_ (yyyy/mm/dd)

I confirm that I have explained the details of the trial to the patients, including its rights and possible benefits and risks, and have given them a signed copy of the informed consent.

**Aignature of doctor:** \_\_\_\_\_

**Date:** \_\_\_\_\_ (yyyy/mm/dd)

## Supplementary file 3 Measurement glossary

Physiological parameters		
Acronyms	Full Names	Definition and Measurement description
SBP	systolic blood pressure	Recorded 10 min before treatment and every 10 min during procedure in case report form (CRF) table, every 5 min in electronic medical record system. Target value:>140 mmHg, <180 mmHg.
DBP	diastolic blood pressure	Recorded 10 min before treatment and every 10 min during procedure in CRF table, every 5 min in electronic medical record system. Target value:>105 mmHg
FiO <sub>2</sub>	inspired oxygen fraction	Recorded 10 min before treatment and every 10 min during procedure in CRF table, every 5 min in electronic medical record system.
PaCO <sub>2</sub>	arterial partial pressure of carbon dioxide	Tested through arterial line access. Tested every 1 hour during endovascular therapy (EVT).
ETCO <sub>2</sub>	end-tidal carbon dioxide	Recorded 10 min before treatment and every 10 min during procedure in CRF table, every 5 min in electronic medical record system.
BIS	bispectral index	Recorded 10 min before treatment and every 10 min during procedure in CRF table, every 5 min in electronic medical record system.
ECG	electrocardiography	Recorded 5 min in electronic medical record system.
HR	heart rate	Recorded 10 min before treatment and every 10 min during procedure in CRF table, every 5 min in electronic medical record system.

1	SpO <sub>2</sub>	pulse oxygen saturation	Recorded 10 min before treatment and every 10 min during procedure in CRF table, every 5 min in electronic medical record system.
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8	BP	blood pressure	Non-invasive blood pressure on either arm, measured every 5 min during procedure. Recorded 10 min before treatment and every 10 min during procedure in CRF table, every 5 min in electronic medical record system.
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13	Glu	serum glucose	Tested before EVT treatment. During EVT, tested every 1 hour. Target value: 70-140 mg/L
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17	MAP	mean artery pressure	Recorded 10 min before treatment and every 10 min during procedure in CRF table, every 5 min in electronic medical record system.
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21	ABG	arterial blood gas	Monitored before treatment and every one hour during treatment, including Na <sup>+</sup> , K <sup>+</sup> , Cl <sup>-</sup> , PaCO <sub>2</sub> , PaO <sub>2</sub> , PH, glucose.
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23	<b>Evaluation</b>		
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25	<b>Acronyms</b>	<b>Full Names</b>	<b>Definition and Measurement description</b>
26	mRS	modified Rankin scale	Measured before treatment, 24h and 90 days after treatment
27			
28	NIHSS	National Institute of Health stroke scale	Measured before treatment, 24h and 90 days after treatment
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31	mTICI	modified Thrombolysis in Cerebral Infarction	Measured before EVT and immediately after recanalization.
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34	GCS	Glasgow coma score	Measured before treatment, 24h and 90 days after treatment
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36	pc-ASPECTS	post-circulation Alberta Stroke Program Early CT Score	Measured before treatment
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39	<b>Work flow</b>		
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Name	Definition and description
Onset to door	The duration between patient last know to be well and arriving to radiological suite.
Door to groin puncture	The duration between patient arriving at radiological suite and groin puncture initiating.
Puncture complete	The duration between groin puncture initiating and puncture completing.
Groin puncture to recanalization	The time duration between puncture complete and recanalization.
Recanalization time	The time duration between onset to recanalization success.
Recover time	The time duration between pressing against the puncture site and transferring to NICU.