Bacteria in Atherosclerotic plaques and adverse events

Study Protocol

ClinicalTrials.gov ID：NCT06935279

Department of Neurosurgery

Tangdu Hospital

Date: 01 Jan 2024

Bacteria in Atherosclerotic plaques and adverse events

1. Integrity Statement

All physicians and staff members involved in the study solemnly declare:

The application materials submitted herein are true and valid. All physicians and staff members involved in the study guarantee that all procedures were strictly conducted in accordance with the trial protocol, ensuring the authenticity of all data recorded. All physicians and staff members involved in the study have no conflicts of interest of any kind, whether personal, corporate, commercial, or related to scientific research.

2. Research Background

2.1 The Harmful Effects of Bacteria (Especially Intracellular Bacteria) in Atherosclerotic Plaques.

Atherosclerosis is not merely a disease of lipid deposition, and bacteria within plaques are not harmless bystanders. Instead, they actively participate in and drive disease progression through multiple mechanisms. Bacteria (especially intracellular bacteria) serve as significant destabilizing factors that promote inflammation and plaque formation. Their detrimental effects span the entire process of plaque formation, progression, and rupture. Their core hazards can be summarized as follows:

2.1.1 Trigger and continuously amplify the local inflammatory response in the plaque.

Intracellular bacteria (such as Chlamydia pneumoniae, Porphyromonas gingivalis, Helicobacter pylori, etc.) can invade and colonize core cells within plaques, including vascular endothelial cells, macrophages, and smooth muscle cells. They evade host immune clearance by continuously releasing lipopolysaccharides (LPS), lipoproteins, and virulence factors. This activates inflammatory pathways like NF-κB and MAPK, driving cells to secrete pro-inflammatory mediators such as TNF-α, IL-6, and IL-1β.

2.1.2 Disrupting plaque structural stability.

Degradation of the extracellular matrix: Intracellular bacteria induce macrophages and smooth muscle cells to secrete matrix metalloproteinases (MMPs, such as MMP-2 and MMP-9), which degrade structural components like collagen in the fibrous cap of atherosclerotic plaques. This leads to thinning of the fibrous cap and increased fragility.

Promoting foam cell formation: Intracellular bacteria disrupt macrophage lipid metabolism, inhibit cholesterol reverse transport, accelerate foam cell accumulation, and enlarge the plaque core lipid pool, leading to the formation of vulnerable plaques (thin fibrous caps over large lipid cores).

Induction of apoptosis/pyroptosis: Intracellular bacterial infection can trigger apoptosis or pyroptosis in host cells, leading to reduced extracellular matrix synthesis within plaques and massive accumulation of inflammatory cells, which further compromises the structural stability of the plaque.

2.1.3 Induce intraluminal thrombosis.

Intracellular bacteria can directly activate the coagulation system: On one hand, their surface pathogen-associated molecular patterns (PAMPs) activate platelets, promoting platelet adhesion and aggregation; On the other hand, they can infect cells and induce the release of inflammatory mediators (such as tissue factor), initiating the extrinsic coagulation pathway. This leads to microthrombus formation within plaques, exacerbating plaque stenosis while also laying the groundwork for subsequent acute thrombotic events caused by plaque

rupture.

2.1.4 The Interplay Between Systemic Inflammation and Metabolic Dysregulation.

Bacteria (including intracellular bacteria) can spread through the blood and lymphatic circulation, triggering low-grade systemic inflammation that disrupts insulin sensitivity and lipid metabolism, thereby indirectly accelerating the progression of atherosclerosis. Concurrently, the systemic inflammatory state further diminishes the vascular endothelium's resistance to injury, forming a chain reaction of "local infection - systemic inflammation - vascular damage".

2.2 Association Between Bacteria-Related Atherosclerotic Plaques and Stroke.

One of the core pathological mechanisms underlying stroke (particularly ischemic stroke, accounting for approximately 70% of cases) involves the formation of atherosclerotic plaques in locations such as the carotid arteries and intracranial arteries. These plaques lead to vascular stenosis, plaque rupture, or thrombus detachment. Bacteria, especially intracellular bacteria, directly or indirectly exacerbate the risk and severity of stroke through the following mechanisms:

2.2.1 Accelerated arterial stenosis leads to insufficient cerebral perfusion.

Chronic inflammation driven by bacteria, particularly intracellular bacteria, causes persistent damage to cerebral vascular endothelium, accelerating plaque formation and progression. This leads to luminal narrowing in critical vessels such as the carotid artery and middle cerebral artery: When stenosis reaches $\geqslant 70\%$, cerebral blood flow significantly decreases, placing brain tissue in a state of chronic ischemia and hypoxia, which can trigger ischemic stroke. If combined with factors such as hypotension or increased blood viscosity, the risk of ischemia further escalates.

2.2.2 Induce vulnerable plaque rupture, leading to acute thrombotic stroke.

Intracellular bacteria destabilize the fibrous cap of atherosclerotic plaques, making them more prone to rupture. The exposed lipid core and collagen, which are procoagulant substances, can rapidly activate the coagulation system, forming acute thrombi that completely occlude cerebral vessels and trigger acute ischemic stroke (such as cerebral infarction). Even if the plaque does not rupture completely, microemboli (containing bacteria, platelets, and fibrin) detaching from its surface can travel through the bloodstream and block small cerebral arteries, leading to lacunar infarction.

2.2.3 Exacerbate brain tissue damage following stroke.

Following a stroke, systemic and local inflammatory responses induced by bacteria (particularly intracellular bacteria) spread to brain tissue: On one hand, pro-inflammatory cytokines breach the blood-brain barrier, exacerbating ischemic-reperfusion injury and enlarging the infarct area; On the other hand, intracellular bacteria may directly invade ischemic brain tissue (due to blood-brain barrier disruption), triggering intracranial infections such as encephalitis or meningitis, which significantly increase the disability and mortality rates associated with stroke.

2.2.4 Targeted harm by specific intracellular bacteria

Chlamydia pneumoniae is the most common intracellular bacterium in cerebral atherosclerotic plaques. It can directly invade intracranial vascular endothelial cells, inducing local inflammation and plaque formation. Multiple cohort studies have confirmed that patients with positive serum Chlamydia pneumoniae show a 2- to

3-fold increased risk of ischemic stroke.

Porphyromonas gingivalis originates from periodontal infections and can colonize carotid plaques via the bloodstream. The gingiphin it secretes degrades vascular endothelial adhesion molecules, accelerating plaque instability and increasing the risk of recurrent stroke.

Helicobacter pylori can indirectly promote cerebral vascular plaque progression by inducing systemic inflammation and disrupting lipid metabolism (e.g., elevating LDL-C). It is significantly associated with the onset of ischemic stroke in middle-aged and young patients.

Bacteria, especially intracellular bacteria, act as key drivers of atherosclerotic plaque progression and instability through a cascade reaction involving "colonization - pro-inflammatory response - disruption of plaque structure - activation of coagulation".

Narrowing, rupture, or microembolism of atherosclerotic plaques in cerebral vessels (carotid arteries, intracranial arteries) are core triggers of ischemic stroke. Intracellular bacteria not only elevate stroke risk but also exacerbate disease severity and recurrence risk. This association also offers potential directions for stroke prevention, such as targeted antimicrobial therapy and management of chronic infections.

This prospective cohort study can be used to assess whether the research question truly exists in clinical practice and to analyze its risk factors. This project aims to collect patient demographics and research data through an Electronic Data Capture (EDC) system to establish a postoperative registry database. To identify suitable carotid plaques for carotid endarterectomy, healthcare providers will strictly adhere to clinical pathway protocols for diagnosis and treatment, implementing standardized management to effectively alleviate patient symptoms and reduce physical and psychological distress. Simultaneously, by analyzing bacterial populations within carotid plaques, identifying intracellular bacterial species, and integrating clinical data for risk factor analysis, we aim to distinguish bacterial types associated with adverse outcomes (cerebral infarction, carotid restenosis, mortality). This approach will enhance the clinical efficacy of carotid stenosis treatment, offering practical clinical value in ultimately preventing cerebral infarction and conserving healthcare resources.

3. Research Objectives

3.1 Primary research objectives

This project aims to establish a registry center for patients and specimen banks following carotid endarterectomy. Conduct plaque detection and analysis in patients undergoing carotid endarterectomy over a defined period, perform follow-up monitoring, track blood laboratory indicators, execute data cleansing, analyze bacterial species within plaques, identify bacteria associated with postoperative adverse events, and derive corresponding expected conclusions.

3.2 Secondary research objectives

a. Assess bacterial species within carotid plaques; identify bacterial differences and perform functional analysis in atherosclerotic plaques across distinct disease types.

b. Detect bacterial species within plaques associated with adverse postoperative events (cerebral infarction, carotid restenosis, death), identify risk bacteria linked to poor outcomes, and perform functional analysis.

c. Cleanse clinical data, analyze the correlation between postoperative adverse events and bacteria within

high-risk plaques, and adjust for confounding factors including age, gender, body mass index, total cholesterol, high-density lipoprotein, low-density lipoprotein cholesterol, triglycerides, creatinine, diabetes, and hypertension to enhance the reliability of research findings.

4. Overall Design

This study is a prospective, multicenter cohort study in western China.

This registration study was primarily conducted in the Department of Neurosurgery at Tangdu Hospital, with participation from the Departments of Neurosurgery at the Second Affiliated Hospital of Xi'an Medical University, Hanzhong Central Hospital, Hanzhong 3201 Hospital, Baoji People's Hospital, and Pucheng County People's Hospital. The study population consisted of patients aged 18 to 90 years who underwent CEA surgery. Patients who meet all inclusion criteria and none of the exclusion criteria may be considered for enrollment after demonstrating informed consent to participate in this registry study and agreeing to sign the informed consent form.

All patients participating in this study underwent a comprehensive standardized evaluation conducted by a multidisciplinary team comprising neurologists, neurosurgeons, hematologists, endocrinologists, and other practitioners. The assessment included examinations of neurological, neuropsychological, and psychiatric conditions, endocrine disorders, and hematological parameters. Bacterial species identification was performed using 16SrDNA sequencing, with further validation through transmission electron microscopy.

Selected patients will undergo routine surgical treatment and attend follow-up appointments as recommended by their physicians, while accurately recording relevant data generated during clinical practice. Data information from patients' clinical visits will be documented, including preoperative assessment, preoperative care, operating room care, anesthesia management, intraoperative procedures, postoperative medical management, postoperative nursing care, and follow-up information.

4.1 Inclusion Criteria

- Patients clinically diagnosed with moderate to severe carotid artery stenosis
- Age 18 ⩽ age ⩽ 90
- Patients undergoing carotid endarterectomy (CEA)
- Preoperative MRS score for stroke patients: 0-2
- Preoperative NIHSS score for stroke patients: 0–20
- Patient's Glasgow Coma Scale (GCS) score upon admission: 8-15 points
- No fever or evidence of infection at admission
- Informed consent signed by the subject or their legal representative
- Good compliance with follow-up visits

4.2 Exclusion Criteria

- Brain tumor (presence of mass effect)
- Patient's Glasgow Coma Scale (GCS) score < 8
- Refractory hypertension unresponsive to medication (defined as sustained systolic blood pressure >185 mmHg or diastolic blood pressure >110 mmHg)

- History of severe infection within the past three months
- Severe or acute heart failure
- Acute myocardial infarction or severe arrhythmia
- Undergone major organ surgery or biopsy within the past month
- Any active bleeding or recent bleeding (gastrointestinal, urinary tract, etc.) within the past month
- Currently undergoing hemodialysis or peritoneal dialysis; known severe renal impairment (glomerular filtration rate < 220 mmol/L (2.5 mg/dL))
- Concurrent malignant tumors, severe cardiopulmonary disease, or other conditions rendering the patient unable to tolerate surgery
- Has participated in other interventional clinical studies that may influence the outcome assessment
- Severe liver function abnormalities
- Other circumstances deemed by the investigator to make participation in this study inappropriate or pose significant risk to the patient (e.g., inability to understand and/or comply with study procedures and/or follow-up due to psychiatric, cognitive, or emotional disorders)
- Currently receiving immunosuppressive agents or undergoing immunotherapy
- Severe chest or abdominal trauma requiring surgery、Severe Traumatic Brain Injury
- Infectious Diseases such as Syphilis, AIDS, Hepatitis, and Tuberculosis
- Patients with both hypertension and diabetes

5. Research Design Plan

5.1 Research Methodology: This study is a prospective, multicenter cohort study.

This registry study is primarily conducted in the Department of Neurosurgery at Tangdu Hospital. The target population consists of adults aged 18 to 90 years who present to the neurosurgery department and require carotid endarterectomy. Patients meeting all inclusion criteria and none of the exclusion criteria may be considered for enrollment after demonstrating informed consent to participate in this registry study and agreeing to sign the informed consent form.

5.2 All patients participating in this study underwent a comprehensive standardized evaluation conducted by a multidisciplinary team comprising neurologists, neurosurgeons, hematologists, endocrinologists, and other practitioners. The evaluation included examinations of neurological status, neuropsychological and psychiatric conditions, endocrine disorders, and hematological parameters.

5.3 Patients enrolled in the study will undergo routine surgical treatment and attend follow-up visits as recommended by their physicians, while accurately recording all relevant data generated during clinical practice. Data information from patients' clinical visits will be documented, including preoperative assessment, preoperative care, operating room care, anesthesia management, intraoperative procedures, postoperative medical management, postoperative nursing care, and follow-up information.

5.4 Major Research Projects and Content

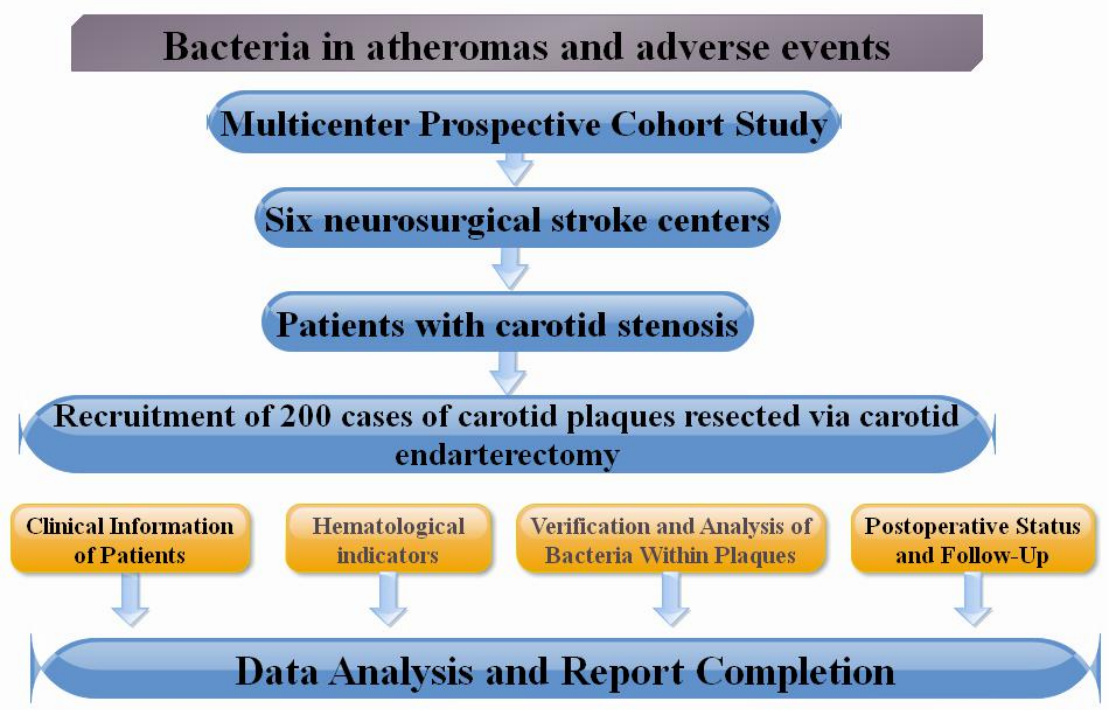
5.4.1 Assess the types of bacteria present in carotid plaques to preliminarily identify the relationship between bacteria and plaque associated with different disease types;

5.4.2 Detect bacteria within plaques associated with adverse postoperative outcomes (cerebral infarction,

carotid restenosis, death), identify risk bacteria linked to poor outcomes, and conduct preliminary functional analysis of these bacteria.

5.4.3 Analyze clinical data to investigate the correlation between postoperative adverse events and bacteria within high-risk plaques, while adjusting for confounding factors such as age, gender, body mass index, total cholesterol, high-density lipoprotein, low-density lipoprotein, cholesterol, triglycerides, creatinine, diabetes, and hypertension to enhance the reliability of the study findings.

5.5 Research Flowchart



6. Key Statistical Indicators

This study will collect all data during the inpatient period (baseline phase) for patients requiring surgical intervention, as well as follow-up data after discharge. Data points to be collected for patients with carotid stenosis include:

6.1 Baseline Information Collection

Admission Assessment and Enrollment: Demographic Data: Date of Birth, Gender, Educational Attainment, Ethnicity, Occupation Type, Health Insurance Type, Nature of Employment;

Carotid Artery Stenosis Assessment: Document the degree of carotid artery stenosis in the patient;

Preoperative Preparation: Past medical history and current medical history, including hypertension, diabetes, hyperlipidemia, cerebral infarction, renal disease, history of cardiovascular and cerebrovascular diseases, and other chronic conditions. Whether antibiotics were administered during surgery, types and reasons for previous surgeries, surgical sites, and use of analgesics postoperatively. Additionally, collect history of previous drug therapy, including medications used to treat and control related comorbidities.

Physical Examination: Nutritional Assessment Status: Including height, weight, body fat percentage, muscle mass, grip strength; heart rate, respiratory rate, body temperature, systolic/diastolic blood pressure; Assessment of Positive Findings in Neurological Examination: Optic nerve damage, oculomotor nerve damage, limb paralysis,

neck resistance;

Comprehensive Patient Assessment and Optimization: Whether relevant assessments and optimization measures have been conducted, including water and electrolyte balance, complete blood count, biochemical tests, coagulation function tests, and status of vital organ function (lungs, heart, kidneys, liver).

Scale Assessment: Evaluate patients' functional status preoperatively, intraoperatively, and postoperatively using the American Society of Anesthesiologists (ASA) risk classification, long-term quality of life assessment, and the General Hospital Anxiety/Depression Scale (GHAS), Depression Scale, NRS2002 score, VTE Caprini Risk Assessment Scale, Autar DVT Risk Scale, Operating Room Pressure Ulcer Risk Assessment (Braden), PONV Risk Score for preventing postoperative nausea and vomiting, and Visual Analogue Scale (VAS) for nausea and vomiting.

Preoperative Communication: Patients receive counseling and guidance regarding the surgical and anesthetic procedures prior to surgery. Whether the patient received counseling and guidance from the surgeon, anesthesiologist, and nurse/head nurse regarding the surgical and anesthetic procedures. Record the duration of the communication visit (in minutes).

Antihypertensive drug therapy: Initiate with low doses, prioritize long-acting formulations, employ combination therapy, and tailor treatment to individual needs. Common antihypertensive agents include five classes: beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and diuretics, as well as fixed-dose combination formulations comprising these drugs. In the absence of concomitant vascular stenosis, post-CEA surgery blood pressure control below 140/90 mmHg is recommended.

Diabetes Medication Management: Patients with carotid artery stenosis and concomitant diabetes must intensify dietary control. Target blood glucose levels: non-fasting glucose below 11.1 mmol/L, with HbA1c <7% during treatment.

Lipid-lowering medication: Statin therapy is recommended for patients with carotid stenosis. For those at high risk of stroke, low-density lipoprotein (LDL) levels should be controlled below 100 mg/dL. Niacin or fibrate-based lipid-lowering agents may be considered for patients with hypertriglyceridemia.

Smoking Cessation: Quitting smoking is a critical preventive and therapeutic measure for carotid stenosis. Smokers should be strictly required and encouraged to quit, and exposure to secondhand smoke should be avoided.

Antiplatelet and Anticoagulant Therapy: Recommended antiplatelet agents include aspirin and clopidogrel. Low-dose aspirin (75–150 mg/day) achieves equivalent efficacy to high-dose regimens. Heparin therapy should be administered prior to carotid artery occlusion during surgery.

Hyperhomocysteinemia management: Elevated homocysteine levels increase stroke risk. Patients with carotid stenosis and concomitant hyperhomocysteinemia should receive B-complex vitamin therapy preoperatively.

6.2 Preoperative Evaluation

Indications for Surgery: Absolute Indications: Symptomatic carotid stenosis with noninvasive testing showing ⩾ 70% stenosis or angiography revealing ⩾ 50% stenosis. Relative Indications: (1) Asymptomatic carotid stenosis with noninvasive testing showing ⩾70% stenosis or angiography revealing ⩾60% stenosis; (2) Asymptomatic carotid stenosis with noninvasive testing showing <70% stenosis, but angiography or other studies

indicating unstable stenotic lesions; (3) Symptomatic carotid stenosis with noninvasive testing showing 50%–69% stenosis.

Perioperative Pharmacotherapy: All enrolled patients are recommended to receive single antiplatelet therapy with aspirin (100 mg/day) or clopidogrel (75 mg/day) preoperatively to reduce thrombosis risk. High-dose antiplatelet agents are not recommended. Intraoperatively, administer heparin anticoagulation 5 minutes prior to arterial occlusion to prolong activated clotting time (ACT) or activated partial thromboplastin time (aPTT) by at least 1.5-fold. Postoperatively, continue single antiplatelet therapy for at least 4 weeks.

Timing of Surgery: (1) For acute ischemic stroke, surgery is relatively safe after 6 weeks post-onset. However, for patients with recent symptom onset and imaging evidence of unstable plaques, early intervention should be pursued whenever possible, ideally within 2 weeks. (2) For patients with TIA or minor stroke, intervention may be performed within 2 weeks of the event if there are no contraindications to early revascularization. (3) In cases of bilateral lesions, the interval between bilateral surgeries may range from 2 to 4 weeks based on clinical circumstances, with priority given to the symptomatic side and/or the side with more severe stenosis.

Choice of surgical approach: Includes two types: the eversion endometrial resection and the traditional longitudinal incision endometrial resection.

Complications and Prevention: (1) Stroke and Mortality. Stroke is associated with ischemia caused by plaque detachment and occlusion. Strict individualized perioperative blood pressure management is generally required. Intraoperative close monitoring is essential to reduce strokes due to hemodynamic disturbances. Intraoperative cerebral oxygen saturation monitoring, TCD monitoring, and intraoperative electrophysiological monitoring should be performed. Intraoperative stump pressure should be monitored. Perform gentle intraoperative maneuvers and selectively use bypass tubes. Anticoagulant therapy may be administered based on specific circumstances. Perioperative measures such as antiplatelet agents should be employed to reduce embolic risk. (2) Cranial Nerve Injury. The most commonly affected nerves include the hypoglossal, vagus, and accessory nerves, with injuries typically being transient. These may be related to surgical traction and edema. Intraoperative maneuvers should be gentle, with precise identification of delicate cervical anatomical structures to avoid nerve injury from surgical traction. Cutaneous nerve injury is generally difficult to prevent. Postoperative numbness around the jaw or behind the ear may occur. For all enrolled surgical patients, the length of the cervical surgical incision should be controlled at approximately 3-5 cm to minimize cutaneous nerve injury caused by excessive incision length. (3) Hyperperfusion Syndrome. Primary clinical manifestations include severe localized headache, localized and/or generalized convulsions, and cerebral hemorrhage in the ipsilateral hemisphere. Prophylactic administration of antihypertensive and dehydrating agents (e.g., mannitol) during carotid artery reperfusion and postoperatively may mitigate cerebral edema. (4) Neck hematoma and laryngeal edema. The former is often associated with incomplete local hemostasis or inadequate arterial suturing, while the latter may relate to anesthesia intubation. Closely monitor oxygen saturation, enhance suturing techniques, and meticulously control bleeding—particularly preventing damage to extensive veins and lymph nodes during dissection. Once hematoma or laryngeal edema occurs, prevent asphyxia. (5) Thrombosis and restenosis. Contributing factors include intraoperative mishandling, inadequate postoperative medication, and excessive smooth muscle or intimal hyperplasia. Monitor for heparin resistance. Administer perioperative oral antiplatelet agents and intimal

hyperplasia inhibitors; consider traditional Chinese medicine when indicated.

Data Collection and Definition: Patient demographic and clinical data, including age, gender, smoking and drinking history, past medical history, echocardiography results, angiography assessment findings, and medications used at discharge, were collected from electronic medical record systems by physicians unaware of the study's purpose. All participants provided fasting (>8 h) peripheral venous blood for measurement of white blood cell count (WCC), platelet count (PLT), hemoglobin (HGB), fasting blood glucose (FBG), total bilirubin (TB), direct bilirubin (DBIL), indirect bilirubin (IBIL), creatine kinase (CK), creatine kinase isoenzyme (CK-MB), creatinine, uric acid (UA), high-sensitivity C-reactive protein (Hs-CRP), and lipid profile (total cholesterol (CHO), TG, LDL, high-density lipoprotein (HDL), lipoprotein a (Lpa)).

6.3 Intraoperative Management

Operating Room Nursing: Operating room parameters (temperature, humidity), entry/exit times, duration of surgery, level of consciousness upon entry, psychological status, catheterization method, antibiotic prophylaxis and allergic reactions, infusion reactions, hypothermia prevention status confirmation (including body temperature, use of warming blankets, infusion of fluids, use of irrigation solutions), VTE (Venous Thromboembolism) prevention and pressure ulcer prevention (including intraoperative positioning, care of pressure points, and care frequency); Pre-anesthesia management: Including anesthesia time, anesthesia method, monitoring parameters (anesthesia depth, cardiac output, neuromuscular blockade, temperature, arterial blood gas, etc.), presence of preoperative local anesthesia at incision site, presence of postoperative local anesthesia at incision site, intraoperative circulatory status, fluid output, fluid replacement volume, blood transfusion volume, transfusion reactions, level of consciousness grading, Steward recovery score, and extubation status prior to leaving the operating room. Also includes pre-anesthesia medication administration, recording brand name, generic name, dosage, frequency, and duration; Anesthetic induction: Record patient cardiopulmonary and renal function data. Routinely monitor electrocardiogram (ECG), invasive mean arterial pressure (IMAP), oxyhemoglobin saturation (SpO_2), partial pressure of carbon dioxide in end-tidal gas ($PetCO_2$), Bispectral Index (BIS). Document anesthetic induction medications, including brand name, generic name, dosage, frequency, and duration.

Anesthesia Maintenance Protocol: Record anesthesia maintenance protocol data, including drug brand names, generic names, dosages, frequency, and duration;

Blood Pressure Management: Document whether the patient experienced blood pressure fluctuations during surgery, including deviations exceeding ± 20% from baseline levels and SBP ⩾ 180 mmHg. Record corresponding blood pressure management medications, including brand names, generic names, dosages, frequency, and duration;

Fluid Therapy: Document fluid administration methods during surgery, including vasoactive agents, normal saline, sodium acetate Ringer's solution, and Ringer's lactate solution. Record events where plasma osmolarity or stroke volume variation (SVV) monitoring exceeded ⩾13%.

Ventilation Strategy: Document data points related to the ventilation strategy employed, including associated events.

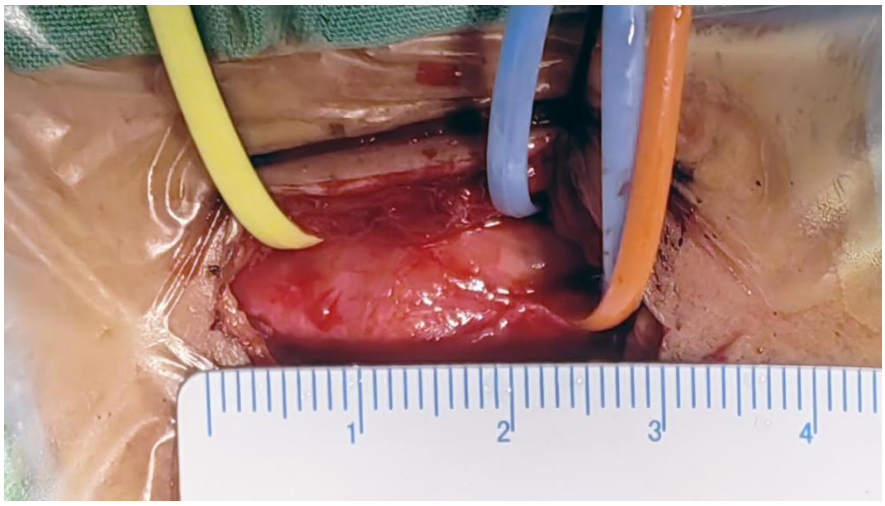
Temperature Monitoring and Warming: Prevent hypothermia during surgery. Document episodes of core temperature ⩽36°C.

Thromboprophylaxis: Include thromboprophylactic measures, medications, or adjunctive products.

Document occurrence of postoperative venous thromboembolic events.

CEA Surgical Procedure Flowchart: All surgeries in this study were performed by Associate Professor Liu Bei as the primary surgeon. Intraoperative cerebral oxygenation monitoring, electrophysiological monitoring, and transcranial Doppler ultrasound monitoring were performed. The patient was positioned supine with the head hyperextended, tilted backward, and deviated toward the contralateral side. Marked an anterior sternocleidomastoid muscle incision approximately 3-5 cm in length. Following routine disinfection and draping, sequentially incised the skin, subcutaneous tissue, and platysma muscle. Make a sharp dissection along the anterior border of the sternocleidomastoid muscle to deeper structures, dissecting and exposing the carotid sheath. Following exposure of the carotid sheath, administer heparin at a dose of 83 IU/kg. Utilized specialized CEA instruments to dissect the carotid sheath, progressively exposing the common carotid artery (CCA), internal carotid artery (ICA), and external carotid artery (ECA). Administer lidocaine block at the carotid sinus location at the bifurcation site. Sequentially occlude the superior thyroid artery, internal carotid artery, external carotid artery, and common carotid artery, controlling arterial occlusion time between 10-20 minutes. Under microscopic visualization, make a longitudinal incision in the artery. Carefully dissect and remove the plaque. Irrigate repeatedly with heparinized saline. Microscopically remove any residual plaque. After confirming a smooth intima, perform continuous suturing from the distal ICA toward the CCA at approximately 1 mm intervals. Following the procedure, perform intraoperative fluorescein angiography to assess vascular patency.

Schematic Diagram of Intraoperative Incision:



Sample Processing and Storage: After plaque sampling, immediately rinse with saline solution on the operating table to remove blood stains. Rapidly freeze in liquid nitrogen, then transfer to pre-chilled cryopreservation tubes. Seal with a sealing film and immediately store at -80°C.

6.4 Postoperative Management

Secondary prevention strategies for postoperative patients should be implemented according to current guidelines. Maintain activated clotting time (>24 hours) with unfractionated heparin (83 IU/kg, titrated as needed) postoperatively.

Postoperative Diet: Document time to clear liquid intake, time to clear liquid diet, and time to regular diet following surgery.

Pain Management: Record location, nature, intensity score, duration, analgesic usage, and use of analgesic pumps. Conduct daily pain assessments throughout hospitalization until discharge, documenting the highest pain

score recorded that day.

Respiratory Management: Document tracheal intubation status and extubation time; record postoperative use of intravenous (pre-ambulation) and nebulized medications;

Gastrointestinal Management: Includes mucosal protection measures and mucosal lesions;

Imaging Follow-up: Document results of follow-up imaging studies, including head/chest CT, head MRI, head and neck CTA;

Other Postoperative Management Principles: Including parenteral nutrition, time of postoperative fluid cessation, fluid reactions, nutritional assessment at discharge, mental status at discharge, KPS score at discharge, and other scale assessments; inpatient parameters (including hospitalization costs, total hospitalization days, postoperative hospitalization days). If secondary surgery occurs during hospitalization, corresponding records must be made;

Satisfaction: Assess patient satisfaction with clinical services at discharge;

Patch collection and preservation: Atherosclerotic plaque samples excised from the carotid bifurcation during endarterectomy are collected in Eppendorf tubes, rapidly frozen in liquid nitrogen, stored at -80°C, or fixed in 2.5% glutaraldehyde electron microscopy fixative for subsequent analysis.

6.5 Pharmacotherapy

Patients undergoing perioperative medication therapy, including traditional Chinese medicine or adjunctive devices, require documentation of the following: generic name, brand name, dosage and administration, frequency of administration, duration of use, purpose of medication, drug cost, and reason for medication change. As surgical management is process-oriented, medication therapy should be categorized according to clinical practice (admission, preoperative, intraoperative, postoperative, discharge) and summarized in a master table. Reasons for medication adjustments must be recorded. Poor efficacy: Determined based on surgical outcome, e.g., non-healing incision. Significant medical events/adverse events/adverse reactions: Gastrointestinal reactions; edema; weight gain; changes in liver/kidney function; allergies; other discomforts. Researcher-initiated adjustments, patient-initiated adjustments (specific reasons).

6.6 Adverse Event (AE)/Serious Adverse Event (SAE):

This project reports adverse events/serious adverse events as specified in the protocol. All adverse reaction events must be collected and reported, regardless of whether they are related to these products. Since surgical management is process-based, AEs/SAEs are categorized and summarized by clinical pathway in the master table.

6.7 Follow-up Period Data Collection

Follow-up: Post-discharge follow-up schedule, conducted as outpatient visits.

Follow-up content includes: General patient status, including physical examination and necessary laboratory tests, required imaging studies, and relevant scale assessments, including neuropsychiatric scoring. If the patient undergoes secondary surgery or is readmitted during follow-up, corresponding records must be documented. If additional laboratory tests are performed during follow-up, copies of the original reports must be filed in the medical record. The patient's current medical history, hospitalization details, medication status — particularly reasons for medication changes, dosages, and efficacy—must be documented. Investigators must enter laboratory test data into the eCRF (electronic Case Report Form) and retain the original test reports. Investigators must also provide assessments of laboratory test results as normal/abnormal and reference ranges.

7. Research time frame

This study will be conducted in the following two phases:

1) Study Preparation: This phase includes developing materials (CRF, EDC), Informed Consent Forms (ICF), selecting and evaluating study sites, obtaining ethics committee approval, developing the EDC system, and initiating the protocol and study sites. This phase is expected to take 2 months.

2) Patient enrollment, testing, follow-up, and data analysis completion: Estimated at 16 months.

The total duration of this study, from initiation to completion of the final study report, is projected to be 18 months.

Statistical Analysis Plan (SAP)

Study approval and patient consent

The study protocol was approved by the Institutional Review Committee of Tangdu Hospital (approval no. 202501-03) and conducted in accordance with the ethical principles for medical research involving human subjects described in the Declaration of Helsinki. All patients were informed of the trial objectives and methodology upon recruitment and informed consent was obtained prior to inclusion in this study.

Study design

This multicenter, cohort clinical study was conducted across six hospitals in China (Supplementary Protocol) from January 2024 to July 2025. The protocol in the supplementary documents provides detailed information on the rationale, design, and methodology of the study. Of 353 potential participants, 55 refused to undergo screening and 98 did not meet the inclusion criteria, resulting in the collection of plaques from 200 patients who met the inclusion criteria.

Plaque samples were collected via carotid endarterectomy, immediately rinsed with physiological saline to remove residual blood, and then placed in cryovials, which were sealed with parafilm and stored at -80°C for subsequent analysis. Bacteria in the plaque samples were identified via 5R 16S rRNA gene sequencing and validated by transmission electron microscopy (Supplementary Material). All analyses were conducted in a blinded manner.

Study cohort

The study cohort included 200 patients (age, 18–90 years) who were clinically diagnosed with moderate to severe carotid stenosis, met the inclusion criteria, and scheduled to undergo carotid endarterectomy. The study cohort also included patients with a history of stroke, who were required to have a preoperative modified Rankin Scale score of 0–2 and preoperative National Institutes of Health Stroke Scale score of 0–20. The exclusion criteria included any history of a brain tumor, refractory HTN, severe or acute heart failure, acute myocardial infarction or severe arrhythmia, severe liver function abnormalities, or known severe renal insufficiency. Patients with a history of severe infection (within the past 3 months), recent solid organ surgery, biopsy, or any active or recent bleeding (e.g., gastrointestinal, urinary), as well as those with both HTN and DM, were also excluded. Details of the inclusion and exclusion criteria are provided in the supplementary protocol.

Randomization and masking

Baseline clinical examinations were conducted and electronic health records were retrieved to

collect demographic and clinical data. Unscheduled routine follow-up examinations were conducted. Participants who did not undergo a follow-up examination were considered lost to follow-up (Supplementary Protocol). Postoperative adverse events were identified through review of electronic health records by independent investigators who were unaware of the 5R 16S rRNA gene sequencing results and the group assignments. The Data Safety Monitoring Board was responsible for overseeing the safety, ethics, and implementation of the study protocol. An independent statistician was responsible for the accuracy of the statistical analysis.

Outcomes

Primary endpoints include: (1) elucidating differences in bacterial composition within plaques collected from patients with distinct disease types; (2) analyzing plaque-associated bacterial types linked to adverse events. Secondary endpoints include: (1) identifying bacterial species within plaques and their localization; (2) determining the potential functions of identified bacteria.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows (version 24.0; IBM Corporation, Armonk, NY, USA). Based on data normality, comparisons between two groups were performed using the Student's *t*-test or Wilcoxon rank-sum test. Multiple comparisons of pathways retrieved from the Kyoto Encyclopedia of Genes and Genomes (KEGG) were adjusted by probability (*p*) values corrected for the false discovery rate. Clinical data are presented as the mean ± standard deviation or the median and interquartile range. For data with normal distribution and homogeneous variance, one-way analysis of variance (ANOVA) was used to test differences among multiple groups; otherwise, the Kruskal–Wallis test was applied. Count data are reported as frequencies (percentages). Logistic regression analysis was conducted to assess the association between bacteria and target outcome events. A p value < 0.05 was considered statistically significant.

Bacteria in Atherosclerotic plaques and adverse events
Case Report Form

Site ID: _____

Patient ID: _____

Patient Initials: _____

ClinicalTrials.gov ID： NCT06935279

Date: 01 Jan 2024

Instructions for Completion

1. Complete the Case Report Form for eligible participants;
2. Complete clearly using a blue-black or black pen; do not write in shaded areas;
3. This CRF must be used exclusively for the same subject throughout the entire trial;
4. The investigator must sign the CRF as required;
5. To avoid questioning each missing data point, every "□" or "○" must be filled in. Leaving a space indicates "not selected." If an item is "Not Done," enter "ND"; for "Unknown," enter "UK"; for "Not Available" or "Not Applicable," enter "NA." A "0" does not indicate missing information but represents a meaningful numerical value;
6. All numerical fields in the CRF are formatted as "□□□ ". Enter single-digit values in the rightmost space. If spaces remain to the left, fill them with "0". Example: For a subject with blood pressure of 120/80 mmHg, enter "Blood Pressure:□□□ /□□□ mmHg";
7. All dates on forms, including the subject's date of birth, are expressed in "Year/Month/Day" format. If the exact date is unknown, use "UK" and enter the date as "Year/Month/UK". Provide the full date whenever possible. All times are recorded using the 24-hour clock.

Case Report Form

Part 1. Planned Visits

Screening and Enrollment

O1. Onset Time
O2. Inclusion Criteria
O3. Exclusion Criteria
O4. Informed Consent and Enrollment

O1 Onset Date

O1. Date of Onset:□□□□ Year□□ Month□□ Day, Time□□ Hour□□ Minute (24-hour format)

O2 Inclusion Criteria	
□	1. Patients clinically diagnosed with moderate-to-severe carotid artery stenosis
□	2. Age 18 ≤ age ≤ 90
□	3. Patients undergoing carotid endarterectomy (CEA)
□	4. Preoperative mRS score for stroke patients:0-2
□	5. Preoperative NIHSS score for stroke patients: 0–20
□	6. Patient's Glasgow Coma Scale (GCS) score upon admission: 8-15 points
□	7. No fever or evidence of infection at admission
□	8. Informed consent signed by the subject or their legal representative
□	9. Good compliance with follow-up visits

*** Onset time refers to "the time when symptoms first appeared," defined as "the last time the subject appeared normal."**

O3 Exclusion Criteria	
□	1. Brain tumor (presence of mass effect)
□	2. Patient Glasgow Coma Scale (GCS) score < 8
□	3. Refractory hypertension unresponsive to medication (defined as sustained systolic blood pressure >185 mmHg or diastolic blood pressure >110 mmHg)
□	4. History of severe infection within the past three months
□	5. Severe or acute heart failure
□	6. Acute myocardial infarction or severe arrhythmia
□	7. Undergone major organ surgery or biopsy within the past month
□	8. Any active bleeding or recent bleeding (gastrointestinal, urinary tract, etc.) within the past month

□	9. Currently undergoing hemodialysis or peritoneal dialysis; known severe renal impairment (glomerular filtration rate < 220 mmol/L (2.5 mg/dL))
□	10. Concurrent malignant tumors, severe cardiopulmonary disease, or other conditions rendering the patient unable to tolerate surgery
□	11. Has participated in other interventional clinical studies that may influence the outcome assessment.
□	12. Severe liver function abnormalities.
□	13. Other circumstances deemed by the investigator to make participation in this study inappropriate or pose significant risk to the patient (e.g., inability to understand and/or comply with study procedures and/or follow-up due to psychiatric, cognitive, or emotional disorders)
□	14. Currently receiving immunosuppressive agents or undergoing immunotherapy
□	15. Severe chest or abdominal trauma requiring surgery、Severe Traumatic Brain Injury
□	16. Infectious Diseases such as Syphilis, AIDS, Hepatitis, and Tuberculosis
□	17. Patients with both hypertension and diabetes

O4 Informed Consent and Enrollment

O4.1 Has the patient or their legal representative signed the informed consent form?

○1 -No ○2 -Yes

O4.2 Date of informed consent signature by patient or legal representative (enrollment date):

□□□□ Year□□ Month□□ Day □□ Hour□□ Minute (24-hour format)

O4.3 Was a copy of the informed consent form provided to the patient or their legal representative?

○1 -No ○2 -Yes

Investigator's Declaration: I confirm that this patient meets the inclusion criteria and should be enrolled in this study. All information provided herein is true and reliable.

Investigator Signature:

Date of Signature:□□□□ Year□□ Month□□ Day

Visit 1: Baseline and Enrollment

Complete the following **within 8 hours of** patient **enrollment**:

A1. Basic Information
A2. Past Medical History
A3. Personal/Family History
A4. Medication History
A5. Clinical Examination
A6. Additional Tests

A1 Basic Information

A1.1 Preliminary Diagnosis: Moderate to Severe Carotid Artery Stenosis

A1.2 Outpatient ID: _____ Hospital ID: _____

A1.3 Gender: ○1- Male ○2- Female

A1.4 Age☐☐ years old **[Note: Participants under 18 or over 90 years old are ineligible for enrollment]**

A1.5 ID Number:☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

A1.6 Ethnicity: ○1- Han Chinese ○2- Other

A1.7 Contrast agent allergy

A1.8 Current Address: _____ Province, _____ City, _____ District/County

A1.9 Home Phone ☐☐☐☐ - ☐☐☐☐☐☐☐☐

A1.10 Mobile 1 ☐☐☐☐☐☐☐☐☐☐☐

A1.11 Mobile 2 ☐☐☐☐☐☐☐☐☐☐☐

A1.12 Mobile 3 ☐☐☐☐☐☐☐☐☐☐☐

A2 Medical History

A2.1 Onset Date:

☐☐☐☐Date:☐☐☐☐ Year:☐☐ Month:☐☐ Day: 24/01/2012 Time: 00:00:00 (24-hour format)

A2.2 Use of antiplatelet/anticoagulant drugs and intravenous thrombolysis after symptom onset:

☐ Yes - Drug name and dosage:☐ Aspirin☐ Clopidogrel bisulfate☐ Alteplase ☐ Rivaroxaban

☐ Other_____

☐ No

A3 Past Medical History

□**A3.1 Hypertension:**☐ Yes Hypertension present for☐☐ years

Highest blood pressure☐☐☐ /☐☐☐ mmHg;

Lowest blood pressure:☐☐☐ /☐☐☐ mmHg

☐ No

□**A3.2 Diabetes:**☐ Yes Diabetes diagnosed☐☐ years ago

Diabetes ○1- Type 1 ○2- Type 2

☐ No

□**A3.3 Hyperlipidemia:**☐ Yes, already diagnosed☐☐ Year

☐No

□**A3.4 Heart Disease**

□1 -Coronary Heart Disease: If "Coronary Heart Disease," select specific type:

□1 - Angina pectoris. If "Angina pectoris" is selected, indicate the time of last occurrence:

○1 - ≤30 days ○2 - >30 days

□2 - Myocardial infarction. If "Myocardial infarction" is selected, last occurrence date

○1 -≤30 days ○2 - > 30 days

□3 - Other

□2 - Arrhythmia: If "Arrhythmia," select specific type:

□1 - Atrial fibrillation

□2 -Atrial flutter

□3 - Conduction Disturbance (e.g., AV Block)

□4 - Sick sinus syndrome

□5 - Pacemaker Implantation

□6 - Other

□3 - Heart valve disease:

□4 - Heart valve replacement: Valve type ○1 - Bioprosthetic valve ○2 - Mechanical valve ○3 - Unknown

□5 - Cardiac dysfunction

□6- Nonbacterial thrombotic endocarditis

□7 - Dilated cardiomyopathy

□8 -Rheumatic heart disease

□**A3.4 Peripheral vascular disease:** □ Yes Last occurrence ○1 -≤30 days ○2 - > 30 days

□ No

□**A3.5 Transient ischemic attack:** □ Yes Last occurrence date ○1 -≤14 days ○2 - > 14 days

□ No

□**A3.6 Cerebral infarction:** □ Yes Date of most recent occurrence ○1 -≤6 months ○2 - > 6 months

□ No

□**A3.7 Cerebral hemorrhage** Last occurrence ○1 -≤6 months ○2 - > 6 months

□**A3.8 Intracranial Aneurysm Single/Multiple**

□**A3.9 Intracranial arteriovenous malformation**

□**A3.10 Malignant tumor**

□**A3.11 Severe hepatic impairment**

□**A3.12 Chronic renal insufficiency**

□**A3.13 Gastrointestinal Ulcer**

□**A3.14 Gastrointestinal bleeding**

□**A3.15 Chronic Obstructive Pulmonary Disease (COPD)**

□**A3.16 Sleep apnea**

□**A3.17 Mental Disorders**

□**A3.18 Traumatic brain injury**

A4 Personal/Family History

A4.1 Smoking:

○1 - Never smoked

○2 - Current smoker or quit within the past year

Daily Cigarette Consumption: ○1 - < 20 cigarettes ○2 -21-40 cigarettes ○3 - > 40 cigarettes

○3 - Former smoker, quit over 1 year ago

○4 -Unknown

A4.2 Alcohol consumption:

○1 - Never drinks alcohol

○2 -Previously drank, now abstinent

○3 - Currently drinks alcohol If selected, daily alcohol consumption:

○1 -Moderate drinking: <2 standard drinks per day

○2 - Moderate drinking: ≥2, <5 standard drinks per day

○3 -Heavy drinking: ≥5 standard drinks/day

○4 -Dose unknown

○4 -Unknown

(Note: 1 standard drink (drink) is equivalent to 100ml [2 liang] of wine, 360ml [1 can] of beer, or 50ml [approximately 1 liang] of high-proof spirits)

A5

(Note: Medication used continuously for more than 2 weeks within 6 months prior to onset)

□**A5.1 Antiplatelet Agents:**

If selected, specify type: □1- Aspirin □2 - Clopidogrel □3 - Ticagrelor □4 - Cilostazol □5 -Indomethacin □6 - Ozagrel □7 - Other_____ □8 Unknown

□**A5.2 Anticoagulants:**

If selected, specify type: □1 -Warfarin □2 -Low molecular weight heparin □3 -Unfractionated heparin □4 -Dabigatran

□5 -Rivaroxaban □6 -Apixaban □7 -Other_____ □8 -Unknown;

□**A5.3 Antihypertensive drugs:**

If selected, specify type: □1 -Calcium Channel Blockers (Calcium Channel Blockers: Amlodipine: Norvasc, Candesartan, Losartan) □2 -Angiotensin-Converting Enzyme Inhibitors (ACEI) (Fosinopril, Benazepril) □3 - Angiotensin II receptor blockers (ARBs) (Losartan: Cozaar,

Hypertension; Telmisartan; Irbesartan: Avandart) □4-Diuretics (Hydrochlorothiazide, Spironolactone, etc.) □5 -β-blockers (Bisoprolol) □6 -α-blockers □7 -α/β-blockers □8 -Other_____ □9 -Unknown;

□A5.4 Lipid-modifying drugs:

If applicable, please specify the type: □1 - Statins (Atorvastatin: □ Lipitor □ Atorvastatin; Rosuvastatin: □ Crestor □ Simvastatin) □2 - Niacin and its derivatives (Amoxicillin, etc.) □3 - Fibrates (Fenofibrate, Gemfibrozil, etc.) □4- Absorption inhibitors □5- Monoclonal antibodies (□ Iluostatin □ Alisertib) □6- Lipitor □7- Bile acid sequestrants (e.g., cholestyramine) □8- Other _____ □9- Unknown**;**

□A5.5 Antidiabetic drugs:

If applicable, specify type: □1- Insulin [IV or SC] (Humulin, Novolin) □2- Sulfonylureas (Glimepiride, Gliclazide, Glibenclamide) □3- Biguanides (Metformin) □ 4 - Alpha-Glucosidase Inhibitors (Acarbose: Glucobay, Capobay) □5 - Insulin Sensitizers □6 - Non-Sulfonylurea Insulin Secretagogues □7 - Other_____

□8 - Unknown**;**

□A5.6 Immunomodulatory drugs:

□A5.7 Traditional Chinese Medicines:

If applicable, please specify the type: □1- Dihydroergotamine ( ) □2- Xingnaojing ( ) □3- Ginkgo Biloba Leaf □4- Aescin

□5 - Asarum sieboldii □6 - Other_____ □7 - Unknown

A6 Clinical Examination

Physical Examination:

A6.1 Height□□□ (centimeters, cm)

A6.2 Weight□□□ (kilograms, kg)

A6.3 Waist Circumference□□□ cm (1 chi = 33.33 cm)

A6.4 Initial Heart Rate on Admission□□□ beats/min

A6.5 Initial pulse rate upon admission:□□□ beats/minute

A6.6 Initial blood pressure on the healthy side brachial artery (supine position):□□□ /□□□ mmHg

Clinical Scores

A6.7 mRS score prior to current episode: [Note: Patients with mRS > 2 based on pre-onset medical history are ineligible for enrollment]

○0 = Completely asymptomatic;

○1 = Symptoms present but no significant disability: Able to perform all usual duties and activities;

○2=Mild disability: Unable to perform all previously manageable activities, but capable of handling personal affairs without assistance;

○3=Moderate disability: Requires some assistance, but does not need help walking;

○4=Severe disability: Unable to walk without assistance and unable to care for personal bodily needs;

○5=Severe disability: Bedridden, incontinent, requiring constant nursing and care.

A6.8 NIHSS Score: [Range0-42Points; higher scores indicate more severe neurological impairment]

○0-1 points: Normal or near-normal;

○1–4 points: Mild stroke/mini-stroke;

○5–15 points: Moderate stroke;

○16-20: Moderate-severe stroke;

○21–42 points: Severe stroke.

A6.9 Mini-Mental State Examination (MMSE) Total Score☐☐ points

Item		Points					
Orientation (10 points)	1. What day of the week is today?					1	0
	What is today's date?					1	0
	What month is it now?					1	0
	What year is it?					1	0
	What season is it now?					1	0
	2. Where are you now?					1	0
	Which floor are you on?					1	0
	Which township (subdistrict) do you live in?					1	0
	Which county (district) do you live in?					1	0
	Which province do you live in?					1	0
Memory (3 points)	3. I will tell you three things. After I finish, please repeat them and remember them, as I will ask you again later (1 point each, total 3 points) Ball Flag Tree			3	2	1	0
Attention span and calculation skills (5 points)	4.100-7=? Subtract 5 times consecutively (93, 86, 79, 72, 65. 1 point each, total 5 points. If an answer is incorrect but the next one is correct, only one error is counted).	5	4	3	2	1	0
Memory (3 points)	5. Now, please tell me the things I just asked you to remember? Soccer ball, national flag, trees			3	2	1	0
Language Proficiency (9 points)	6. Naming Ability						
	Present a watch and ask, "What is this?"					1	0
	Present a pen and ask, "What is this?"					1	0
	7. Repetition Ability						
	I will now say a phrase. Please repeat it clearly after me: (Forty-four stone lions)!					1	0

	8. Reading Ability (Close your eyes) Please read this sentence aloud and follow the instructions above!					1	0
	9. Three-Step Command I will give you a piece of paper. Please follow my instructions: "Hold this paper with your right hand. Fold it in half with both hands. Place it on your left thigh." (1 point per action, 3 points total)			3	2	1	0
	10. Writing ability requires the subject to write a complete sentence.					1	0
	11. Structural Ability (Present the pattern) Please draw the pattern shown above!					1	0

A6.10 GCS Score: Total Score☐☐

Checklist	GCS Scoring Criteria	Score Assignment
Motor Response	6 - Normal (obeys commands); 5 - Can localize pain; 4 - Withdrawal response to pain; 3 - Decorticate response to pain; 2 - Decerebrate response to pain; 1 - No response	☐
Verbal Response	5 - Normal; 4 - Paraphrasing; 3 - Incoherent speech; 2 - Unintelligible; 1 - No speech	☐
Eye-opening response	4 - Spontaneous eye opening; 3 - Eye opening upon verbal cue; 2 - Eye opening upon painful stimulus; 1 - No eye opening to any stimulus	☐

A6.11 Preoperative Control of Nutritional Status (CONUT) Score

○0–1 points: Normal nutritional status;

○1–2 points: Indicates mild malnutrition;

○2–4 points: Moderate to severe malnutrition.

[Note: The CONUT score is a method for assessing patient nutritional status. It is calculated primarily by evaluating three indicators: serum albumin, total cholesterol, and lymphocyte count. 1. The normal range for serum albumin is 35–50 g/L. Values below this range indicate possible malnutrition; 2. Normal range for total cholesterol is 3.10–5.17 mmol/L. Values below this range indicate possible malnutrition; 3. Normal range for lymphocyte count is 1.0–3.5 × 10^9/L. Values below this range indicate possible malnutrition]

A6.12 Geriatric Nutritional Risk Index (GNRI)

GNRI ≥ 98: Good nutritional status, no nutritional risk;

92 ≤ GNRI < 98: Mild malnutrition, moderate nutritional risk;

82 ≤ GNRI < 92: Moderate malnutrition, moderate nutritional risk;

GNRI < 82: Severe malnutrition, high nutritional risk.

[Note: GNRI calculation formula: GNRI = [1.489 × Appetite Score + 41.7 × (Actual Weight / Ideal Weight)] / Serum Albumin (g/L). The Appetite Score is based on the elderly individual's appetite status, while Ideal Weight is calculated using the individual's height and age.]

A7

A7.1 Pre-enrollment Laboratory Tests

Blood Collection Date:☐☐☐☐ Year☐☐ Month☐☐ Day Time:☐☐ Hour☐☐ Minute

Reference values		Count	
WBC - White Blood Cell		PSA-Prostate-Specific	
LYMPH# - Absolute		PCA - Protein C activity	
MONO# - Absolute		NT-proBNP - N-terminal	
NEUT# - Absolute		cTnI - Cardiac Troponin	
EO# - Eosinophil Absolute		MYO - Myoglobin	
BASO# - Basophil		AST - Aspartate	
PLT-Platelet Count		ALT - Alanine	
PDW-Platelet Distribution		AST/ALT	
MPV - Mean Platelet		TP - Total Protein	
P-LCR-Large Platelet		ALB-Albumin	
PCT - Prothrombin Time		GLO - Globulin	
RBC-Red Blood Cell		A/G Ratio	
HGB - Hemoglobin		TBIL - Total Bilirubin	
HCT-Hematocrit		D-BIL - Direct Bilirubin	
MCV - Mean Corpuscular		I-BIL - Indirect Bilirubin	
MCH - Mean Corpuscular			
MCHC - Mean		ALP - Alkaline	
RDW%-Red Cell		Na - Sodium	
PT - Prothrombin Time		CL - Chloride	
APTT - Activated Partial		Ca - Calcium	
Fib-Fibrinogen level		CO2-Carbon Dioxide	
TT-Thrombin Time		Carbon Dioxide Binding	
FDP-Fibrin(ogen)		cys-c (cystatin C)	
D-D (D-dimer)		BUN-Blood Urea	
TM		Cr-Creatinine	
TAT		eGFR (CKD)	
PIC		UA-Uric Acid	

Reference values		Count	
tPAI-C (tissue-type		UREA-Urea	
ATA-Antithrombin III		CK-Creatine Kinase	
LDH-Lactate		VB12-Vitamin B12	
		Folate	
TC-Total Cholesterol		R (R-value)	
TG-Triglycerides		Angle-Angle	
HDL-C - High-Density		MA-MA value	
LDL-C-Low-Density		CI-CI Score	
APOA-Apolipoprotein A1		LY30-LY30 value	
APOB-Apolipoprotein B		EPL-EPL value	
Lp(a) - Lipoprotein(a)		PAI-1 (PAI-1 rs1799889	
HCY-Homocysteine		CYP2C19 (Clopidogrel)	
HbA1c - Glycated		APOE (ApoE gene	
GLU - Fasting Blood		ABO	
CRP - C-reactive protein			

A7.2 ECG Findings ○1 -Normal ○2 -Abnormal*

*If "Abnormal", please select:

□1 -Atrial/Ventricular Fibrillation □2- Atrial/Ventricular Flutter

□3 - Sick sinus syndrome □4 -Second- or third-degree atrioventricular block

□5 -Sinus bradycardia or heart rate <50 bpm □99 - Other

A7.3 Preoperative Imaging Studies

A7.3.1 Preoperative head CT or MRI examination

Date:□□□□ Year:□□ Month:□□ Day: Time:□□ Hour:□□ Minute:

A7.3.2 Infarction Types and Recovery Levels

Infarction Type: ☐ Complete anterior circulation infarction ☐ Partial anterior circulation infarction ☐ Posterior circulation infarction ☐ Focal infarction

Recovery Status: Infarct shrinkage or disappearance ☐ Yes ☐ No

Cerebral Function Recovery: mRS Score Improvement ☐ Yes ☐ No

[Note: 1. Complete anterior circulation infarction: Manifested as triad symptoms, i.e., complete middle cerebral artery syndrome; Higher-level cerebral dysfunction (consciousness disturbance, aphasia, acalculia, spatial disorientation, etc.); homonymous hemianopia, and severe motor and/or sensory deficits in three contralateral areas (face, upper limb, lower limb). Most cases involve occlusion of the proximal trunk of the middle cerebral

artery, with a minority caused by occlusion of the internal carotid artery siphon segment, resulting in extensive cerebral infarction. 2. Partial anterior circulation infarction: Presents with two of the above triad features, or solely higher-level neurological impairment, or sensory-motor deficits more localized than in complete anterior circulation infarction. Indicates infarction in the distal trunk, branches, or small-to-medium vessels of the middle cerebral artery, or occlusion of branches associated with anticardiolipin antibodies. 3. Posterior circulation infarction: Manifested as vertebrobasilar syndrome of varying severity; may present as ipsilateral cranial nerve palsy with contralateral sensory-motor deficits; bilateral sensory-motor deficits; binocular coordination and cerebellar dysfunction without long tract signs or visual field defects. Caused by occlusion of the vertebral-basilar arteries and their branches, resulting in brainstem and cerebellar infarcts of varying sizes. 4. Lacunar infarction: Manifested as lacunar syndrome, such as pure motor hemiparesis, pure sensory stroke, ataxic hemiparesis, or clumsy hand-dysarthria syndrome. Most cases involve small lacunar lesions caused by lesions in the basal ganglia or small perforating vessels of the pons.

A7.3.3 Assessment of Vascular Stenosis Severity and Location

Assess the degree of cervical vascular stenosis via CTA, MRA, DSA, or US:

☐Mild ☐Moderate ☐Severe

Narrow section: ☐ Carotid artery ☐ Vertebral artery ☐ Intracranial arteries ☐ Subclavian artery

☐Bilateral ☐ Left ☐Right

☐Multiple ☐Isolated

A7.3.4 Preoperative Magnetic Resonance Cerebral Perfusion Imaging Evaluation

TTP (Normal/Prolonged) MTT (Normal/Prolonged) rCBF (Normal/Prolonged) rCBV (Normal/Prolonged)

[Note: 1. Time to peak (TTP)**:** The time from when the contrast agent reaches the main artery supplying the imaged brain region until it reaches its maximum concentration (s); 2. Mean transit time (MTT)**:** The time required for the contrast agent to traverse from the arterial to the venous side within the cranium, averaged across all transit times (s); 3. Cerebral Blood Flow (CBF)**:** Blood flow in milliliters per minute per 100 g of brain tissue [ml/(100g·min)]. In humans, gray matter is approximately: 80 ml/(100g·min); white matter: 20 ml/(100g·min); 4. Cerebral blood volume (CBV): Blood volume per 100 g of brain tissue [ml/100g]. Normal adult values range from approximately 4 to 5 ml.

A7.3.5 Preoperative Carotid Ultrasound Examination

Patch characteristics: Soft patch □ Fibrous patch □ Calcified patch □ Mixed patch □ Other □

Plaque Echo: Hypoechoic □ Isoechoic □ Hyperechoic □ Mixed Echo □

A7.3.6 Bubble test Positive □ Negative □

A7.4 Preoperative Chest CT Scan (within 24 hours of onset)

A7.4.1 Preoperative Chest CT Scan

Date□□□□ □□ □□ , Time□□ □□ (24-hour format)

A7.4.2 Presence of shadow, infiltration, or cavity: ○1 -No ○2 -Yes

A7.4.3 Location of lesion:

□1 - Left upper lobe □2 - Left lower lobe □3 - Right upper lobe □4 - Right middle lobe □5 - Right lower lobe

A7.4.4 Lesion cross-section Length□□□ .□□ cm Width□□□ .□□ cm

Number of layers□□□ .□□ layers Layer thickness□□□ .□□ cm

Lesion volume□□□ .□□ cm³/ml

A7.4.5 Has the lesion enlarged since the previous examination? (This item may be left blank for the initial chest CT): ○1 - No ○2 - Yes

A7.4.6 Is the lesion associated with pleural effusion? ○1 - No ○2 - Yes

Schedule next follow-up: ≤6 hours post-surgery

Visit 1 Completed Physician Signature: _____

Signature Date:□□□□ Year□□ Month□□ Day

Visit 2: ≤ 6 hours post-op

You must complete the following within 6 hours post-surgery:

B1. Visit Time
B2. Operating Room Care
B3. Anesthesia Management
B4. Intraoperative Medical Management
B5. Adverse Events

B1 Visit Date

B1. Visit Date□□□□ □□ □□ □□

B2. Operating Room Nursing

B 2.1 Operating Room Parameters

Room Temperature: ℃ Humidity: %.

B 2.2 Room Entry/Exit Times:

Entry: □□ :□□ ;

Departure: □□ hours□□ minutes;

Total time:□□ hours□□ minutes

B 2.3 Surgery Duration:

Start: □□ :□□ ;

End: □□ hours□□ minutes;

Total Duration:□□ hours□□ minutes

B 2.4 State of Consciousness Upon Entry:

Aware ○ Drowsy ○ Comatose ○ Superconscious ○

Consciousness upon discharge:

Alert ○ Drowsy ○ Comatose ○ Mildly Comatose ○

B2.5 Psychological State

Tense○ Anxious○ Calm○ Indifferent○

B2.6 Catheterization Method

Post-anesthesia ○ Pre-anesthesia ○

B2.7 Antibiotic Prophylaxis Status:

If selected, specify type: □1 - First/second-generation cephalosporins (Cefazolin, Cefuroxime)

□2 - Third-generation cephalosporins (Ceftriaxone) □3 - Other_____

B2.8 Infusion Reaction:

○ Smooth, no adverse infusion reactions ○ With _____

B2.9 Hypothermia Prevention:

Body Temperature: Upon Entry: ℃; Maintained: <36℃□ 36-37℃□ >37℃□

Heated Blanket: Present □ Absent □ Temperature ℃

B2.10 Pressure Ulcer Prevention:

Intraoperative Position: Supine Position□ Lateral Position□ (Left□ Right□)

Pressure Point Care: □ Head (Pillow.Ears.Eyes) □ Torso (Shoulders.Iliac Crests.Sacrococcyx) □ Limbs (Elbows.Knees.Heels.Toes)

Care Frequency: 1-2 times/day □ 3-4 times/day □ 5-6 times/day □ 7-8 times/day □ 9-10 times/day □ >10 times/day

B3 Anesthesia Management

B 3.1 Anesthesia Duration and Method:

Start: ☐☐ :00☐☐ :00;

End: ☐☐ hours☐☐ minutes;

Total Duration:☐☐ hours☐☐ minutes

Anesthesia method: Intravenous☐ Inhalation☐ Combined☐

B 3.2 Anesthesia Monitoring Parameters:

☐ ☐ ☐ ☐ Arterial Blood Gas ☐

Pre-induction blood pressure:☐☐☐ /☐☐☐ mmHg

Intraoperative Circulatory Status:☐ Stable ☐ Hypoperfusion: Duration: minutes

Fluid output: Blood loss ml; Urine output ml; Total: ml

Fluid Replacement Volume: Crystalloid ml; Colloid ml; Total: ml

Transfusion Volume:☐ None ☐ Yes: Red Blood Cells Units; Plasma ml; Cryoprecipitate Units

Transfusion Reaction:☐ None ☐ Yes

B 3.3 Post-anesthesia assessment:

Level of Consciousness Scale: Level 0☐ Level 1☐ Level 2☐ Level 3☐ Level 4☐

Steward Score: Total Score☐ = Level of Consciousness☐ + Respiration☐ + Motor Response☐

Level of Consciousness: 2 points, fully alert; 1 point, responsive to stimulation; 0 points, unresponsive to stimulation;

Airway patency: 2 points, coughs on command; 1 point, spontaneously maintains airway patency; 0 points, requires airway support

Limb Activity: 2 points, conscious limb movement; 1 point, unconscious limb movement; 0 points, no movement

Extubation before leaving the operating room: Yes☐ With spontaneous breathing but not extubated☐ Without spontaneous breathing☐

B4 Intraoperative Medical Management

B 4.1 Surgical Duration and Approach:

Start: ☐☐ hours☐☐ minutes;
End: ☐☐ hours☐☐ minutes;
Total Duration:☐☐ hours☐☐ minutes
Carotid Endarterectomy (Plaster Removal): Left☐ Right☐
Surgical Incision Local Anesthesia: None☐ Yes☐ Drug: Lidocaine☐ Ropivacaine☐ Other:

B 4.2 Intraoperative Monitoring Parameters: (Post-anesthesia induction)

Blood pressure monitoring:

Initial Surgical Blood Pressure: ☐☐☐ /☐☐☐ mmHg

End of surgery blood pressure: ☐☐☐ /☐☐☐ mmHg

Blood pressure at vascular occlusion initiation:☐☐☐ /☐☐☐ mmHg

Blood pressure at end of vascular occlusion:☐☐☐ /☐☐☐ mmHg

Cerebral Oxygen Monitoring:

Pre-operative cerebral oxygenation: ☐☐ %

Cerebral oxygen monitoring at end of surgery: ☐☐ %

Cerebral Oxygen Monitoring at the Start of Vascular Occlusion:☐☐ %

End of cerebral oxygen monitoring after vascular occlusion:☐☐ %

Electrophysiological Monitoring:

Motor Evoked Potentials (MEPs) Alert ☐ Normal ☐

Somatosensory Evoked Potentials (SSEPs) Alert ☐ Normal ☐

Electroencephalogram (EEG) Alert ☐ Normal ☐

TCD Monitoring (Transcranial Doppler Ultrasound)

PSV EDV_____MFV_____

Intraoperative arterial clamping time:☐☐ minutes

B 4.2 Intraoperative Medical Management:

Intraoperative Microscope Use:

Drainage tube placement: Extra-carotid sheath☐ Intra-carotid sheath☐

Drainage tube removal time: <24h☐ 24-48h☐ >48h☐

Drainage volume:☐☐☐ ml

Arterial sheath suturing: Absorbable suture☐ Non-absorbable suture☐ (Tight☐ Loose ☐)

Subcutaneous Suture: Absorbable suture☐ Non-absorbable suture☐ (Interrupted☐ Continuous☐)

Skin Suturing: Absorbable sutures☐ Non-absorbable sutures☐ (Interrupted☐ Subcutaneous☐)

Skin incision length: cm

B5 Adverse Events

B5.1 Have any adverse events occurred since enrollment? ○1- No ○2- Yes

If "No" is selected, no further completion is required.

B5.2 In the event of an adverse event, please select:

For any adverse event/serious adverse event, please complete the Adverse Event/Serious Adverse Event Report Form (see attachment).

1. Date of death☐☐☐☐ ☐☐ ☐☐ , Time☐☐ ☐☐ (24-hour format)

Cause of Death:

○1-Vascular Cause of Death

○1 - Death due to ischemic stroke

○2 - Death from hemorrhagic stroke

○3 - Sudden cardiac death

○4 - Death from Acute Myocardial Infarction

○5 - Death from congestive heart failure

○6 - Pulmonary embolism

○7-Death from cardiovascular/cerebrovascular intervention or surgery (unrelated to acute myocardial infarction)

○8 - Other vascular-related deaths

○2-Non-vascular cause death

○3-Unknown cause

2. New-onset postoperative cerebral infarction Yes ○ No ○

First event date:

Date:□□□□ Year□□ Month□□ Day,□□ Hour□□ Minute (24-hour format)

Infarction location_____ Infarction area_____

Does it cause corresponding symptoms? ○1 -No ○2 -Yes If yes: Please describe symptoms

Determination of cervical vascular stenosis severity via CTA, MRA, DSA, or US (Mild □ ; Moderate □; Severe □ ; Total occlusion □)

3. Re-bleeding Time□□ Hours□□ Minutes (24-hour format)

3.1 Completed cranial imaging studies**:** □1CT □2MRI

3.2 Type and location

Subdural hematoma: Left Right Bilateral Subpial

Epidural hematoma: Left Right Bilateral Subdural;

Intracerebral hematoma: Left Right Bilateral Subtentorial

Subarachnoid hemorrhage: Basal cistern Lateral fissure Interpeduncular cistern Others

Ventricular hemorrhage: Left ventricle Right ventricle Third ventricle Fourth ventricle

Does it cause corresponding symptoms? ○1 -No ○2 -Yes If yes: Please describe the symptoms

Has it penetrated the ventricle? ○1 -No ○2 -Yes

Does it rupture into the subarachnoid space: ○1 -No ○2 -Yes

Midline shift: ○1 -No ○2 -Yes

Is cerebral herniation present: ○1 -No ○2 -Yes

4. Coagulation Abnormalities Time□□ hours□□ minutes (24-hour format)

4.1 Abnormal Coagulation Markers:

□1 -PT ○1 -Elevated ○2 -Decreased; □2 - INR ○1 -Elevated ○2 -Decreased;□3 - APTT ○1 - Elevated ○2 - Decreased; □4 - Fbg ○1 - Elevated ○2 - Decreased;

□5 - TT ○1 - Elevated ○2 - Decreased; □6 - FDP ○1 - Elevated ○2 - Decreased;

□7 - DD ○1 - Elevated ○2 - Decreased

5. Abnormal Absolute Platelet Count Time□□ Hours□□ Minutes (24-hour format)

5.1 Absolute Platelet Count:□□□ 10^9/L

6. Bleeding from Various Organs Time☐☐ H☐☐ Min (24-hour format)

6.1 Bleeding site: □1 - Gastrointestinal tract □2 - Respiratory tract □3 - Urinary tract □4 - Other organs □5 - Other □6 - Unknown

7. Abnormal Liver Function Time☐☐ Hours☐☐ Minutes (24-hour format)

8. Renal Function Abnormalities Time☐☐ Hours☐☐ Minutes (24-hour format)

9. Infection Time☐☐ Hour☐☐ Minute (24-hour format)

Site of Infection: □1 - Gastrointestinal Tract □2 - Respiratory Tract □3 - Urinary Tract □4 - Other □5 - Unknown

10. Myocardial infarction Time☐☐ Time☐☐ Minutes (24-hour format)

11. Lower Extremity Venous Thrombosis Time☐☐ Hours☐☐ Minutes (24-hour format)

12. Pulmonary embolism Time☐☐ hours☐☐ minutes (24-hour format)

13. Hyperlipidemia Time☐☐ Hours☐☐ Minutes (24-hour format)

14. Bradycardia Time☐☐ H☐☐ M (24-hour format)

15. Rash/Drug Allergy Time☐☐ H☐☐ M (24-hour format)

16. Diarrhea Time☐☐ hours☐☐ minutes (24-hour format)

17. Elevated blood sugar Time☐☐ Hours☐☐ Minutes (24-hour format)

18. Other Name: _____; Time☐☐ Hours☐☐ Minutes (24-hour format)

Next Visit Scheduled: 72±12 hours post-surgery

Visit 2 Completed Physician Signature: _____

Signature Date:☐☐☐☐ Year☐☐ Month☐☐ Day

Visit 3: 72 ± 12 hours post-op

You must complete the following within 72 ± 12 hours post-surgery:

C1. Visit Time
C2. Adverse events
C3. Clinical Examination
C4. Imaging studies
C5. Concomitant Medications

C1 Visit Date

C1. Visit Date□□□□ □□ □□

C2 Adverse Events

C2.1 Have any adverse events occurred since enrollment? ○1 -No ○2 -Yes

If "No" is selected, proceed directly to Section C3.

C2.2 If an adverse event occurred, please select:

If any adverse event/serious adverse event has occurred, complete the Adverse Event/Serious Adverse Event Report Form (see attachment).

1. Date of Death□□□□ □□ □□ , Time□□ □□ (24-hour format)

Cause of Death:

○1-Vascular Cause Death

○1 - Death due to ischemic stroke

○2 - Death from hemorrhagic stroke

○3 - Sudden cardiac death

○4- Death from Acute Myocardial Infarction

○5 - Death from congestive heart failure

○6 - Pulmonary embolism

○7 - Death from cardiovascular/cerebrovascular intervention or surgery (unrelated to acute myocardial infarction)

○8 - Other vascular-related deaths

○2-Non-vascular cause death

○3-Unknown cause

2. New-onset postoperative cerebral infarction Yes ○ No ○

First event date:

Date:□□□□ Year:□□ Month:□□ Day:□□ Hour:□□ Minute (24-hour format)

Infarction location_____ Infarction area_____

Caused corresponding symptoms ○1 -No ○2 -Yes If yes: Please describe symptoms

3. Re-bleeding Time□□ hours□□ minutes (24-hour format)

3.1 Completed cranial imaging studies**:** □1CT □2MRI

3.2 Type and location

Subdural hematoma: Left Right Bilateral Subpial

Epidural hematoma: Left Right Bilateral Subdural;

Intracerebral hematoma: Left Right Bilateral Subtentorial

Subarachnoid hemorrhage: Basal cistern Lateral fissure Interpeduncular cistern Others

Ventricular hemorrhage: Left ventricle Right ventricle Third ventricle Fourth ventricle

Does it cause corresponding symptoms? ○1 -No ○2 -Yes If yes: Please describe the symptoms

Has it penetrated the ventricle? ○1 -No ○2 -Yes

Does it rupture into the subarachnoid space: ○1 -No ○2 -Yes

Midline shift: ○1 -No ○2 -Yes

Brain herniation: ○1 -No ○2 -Yes

4. Coagulation Abnormalities Time☐☐ hours☐☐ minutes (24-hour format)

4.1 Abnormal Coagulation Markers:

□1 -PT ○1 -Elevated ○2 -Decreased; □2 - INR ○1 -Elevated ○2 -Decreased;

□3 - APTT ○1 - Elevated ○2 - Decreased; □4 - Fbg ○1 - Elevated ○2 - Decreased;

□5 - TT ○1 - Elevated ○2 - Decreased; □6 - FDP ○1 - Elevated ○2 - Decreased;

□7 - DD ○1 - Elevated ○2 - Decreased

5. Abnormal Absolute Platelet Count Time☐☐ Hours☐☐ Minutes (24-hour format)

5.1 Absolute Platelet Count:☐☐☐ 10^9/L

6. Bleeding from various organs Time☐☐ hours☐☐ minutes (24-hour format)

6.1 Site of bleeding: □1 - Digestive tract □2 - Respiratory tract □3 - Urinary tract □4 - Other organs □5 - Other

□6 - Unknown

7. Abnormal Liver Function Time☐☐ Hours☐☐ Minutes (24-hour format)

8. Renal Function Abnormalities Time☐☐ Hours☐☐ Minutes (24-hour format)

9. Infection Time☐☐ Hours☐☐ Minutes (24-hour format)

Site of Infection: □1 - Gastrointestinal Tract □2 - Respiratory Tract □3 - Urinary System

□4 - Other □5 - Unknown

10. Myocardial infarction Time☐☐ Hours☐☐ Minutes (24-hour format)

11. Lower Extremity Venous Thrombosis Time☐☐ hours☐☐ minutes (24-hour format)

12. Pulmonary embolism Time☐☐ Hours☐☐ Minutes (24-hour format)

13. Hyperlipidemia Time☐☐ Hours☐☐ Minutes (24-hour format)

14. Bradycardia Time☐☐ H☐☐ M (24-hour format)

15. Rash/Drug Allergy Time☐☐ H☐☐ M (24-hour format)

16. Diarrhea Time☐☐ hours☐☐ minutes (24-hour format)

17. Hyperglycemia Time☐☐ Hours☐☐ Minutes (24-hour format)

18. Other Name: _____; Time☐☐ :☐☐ (24-hour format)

C3 Clinical Examination

Physical Examination:

C3.1 72±12-hour follow-up visit Heart rate:☐☐☐ beats/min

C3.2 72±12-hour follow-up visit Pulse rate:☐☐☐ beats/min

C3.3 72±12-hour follow-up

Systolic Blood Pressure 1 (Supine Position, Systolic Reading):☐☐☐ /☐☐☐ mmHg

Systolic Blood Pressure 2 (Supine Position, Systolic Reading):☐☐☐ /☐☐☐ mmHg

Diastolic Blood Pressure 1 (Supine Position, Systolic Priority):☐☐☐ /☐☐☐ mmHg

Diastolic Blood Pressure 2 (supine position, systolic measurement):☐☐☐ /☐☐☐ mmHg

C3.4 72±12-hour follow-up visit

Highest respiratory rate within 24 hours:☐☐☐ breaths/min

Highest body temperature within 24 hours:☐☐ .☐☐ °C

Sputum characteristics:☐ purulent sputum ☐ clear sputum ☐ no sputum

Cough:☐ Yes ☐ No

Shortness of breath (wheezing, labored breathing):☐ Yes ☐ No

Lung auscultation:☐ Rales ☐ Wet rales ☐ Bronchial breath sounds ☐ Other:_____**;**

Nasal endotracheal intubation:☐ Yes ☐ No

Endotracheal intubation:☐ Yes ☐ No

Date of intubation: Date☐☐☐☐ Year☐☐ Month☐☐ Day, Time☐☐ Hours☐☐ Minutes (24-hour format)

Ventilator-assisted ventilation:☐ Yes ☐ No

Ventilator-assisted ventilation start time: Date☐☐☐☐ Year☐☐ Month☐☐ Day, Time☐☐ Hour☐☐ Minute (24-hour format)

Ventilator oxygen concentration fraction (FiO2 = 0.21 + oxygen flow rate / 25):☐☐ .☐☐ %

Arterial Blood Gas Partial Pressure of Oxygen (PaO_2):☐☐☐ .☐☐ mmHg

Clinical Scores

C3.2 NIHSS Score: [Range0-42Points; higher scores indicate more severe neurological impairment]

- ○0-1 points: Normal or near-normal;
- ○1-4 points: Mild stroke/mini-stroke;
- ○5–15 points: Moderate stroke;
- ○16–20: Moderate-to-severe stroke;
- ○21–42 points: Severe stroke.

C3.3 mRS Score [Note: Score based on condition at the time of this visit]

- ○0=Completely asymptomatic;
- ○1=No significant disability despite symptoms: Able to perform all duties and activities previously undertaken;
- ○2 = Mild disability: Unable to perform all previously undertaken activities, but able to manage personal affairs without assistance;
- ○3 = Moderate disability: Requires some assistance, but does not need help walking;
- ○4=Severe disability: Unable to walk without assistance and unable to care for personal bodily needs;
- ○5=Severe disability: Bedridden, incontinent, requiring constant nursing and care.

C4 Imaging Studies

C4.1 Postoperative Cranial CT or MRI

Date:☐☐☐☐ Year:☐☐ Month:☐☐ Day:☐☐ Time:☐☐

Type of Infarction and Recovery Status

Ischaemic Type: √ Complete anterior circulation ischaemia √ Partial anterior circulation

ischaemia √ Posterior circulation ischaemia √ Focal ischaemia

Recovery Level: Infarct shrinkage or disappearance ☐ Yes ☐ No

Cerebral Function Recovery: mRS Score Improvement ☐ Yes ☐ No

[Note: 1. Complete anterior circulation infarction: Manifested as triad symptoms, i.e., complete middle cerebral artery syndrome; Higher-level cerebral dysfunction (consciousness disturbance, aphasia, acalculia, spatial disorientation, etc.); homonymous hemianopia, and severe motor and/or sensory deficits in three contralateral areas (face, upper limb, lower limb). Most cases involve occlusion of the proximal trunk of the middle cerebral artery, with a minority caused by occlusion of the internal carotid artery siphon segment, resulting in extensive cerebral infarction. 2. Partial anterior circulation infarction: Presents with two of the above triad features, or solely higher-level neurological impairment, or sensory-motor deficits more localized than in complete anterior circulation infarction. Indicates infarction in the distal trunk, branches, or small-to-medium vessels of the middle cerebral artery, or occlusion of branches associated with anticardiolipin antibodies. 3. Posterior circulation infarction: Manifested as vertebrobasilar syndrome of varying severity; may present as ipsilateral cranial nerve palsy with contralateral sensory-motor deficits; bilateral sensory-motor deficits; binocular coordination and cerebellar dysfunction without long tract signs or visual field defects. Caused by occlusion of the vertebral-basilar arteries and their branches, resulting in brainstem and cerebellar infarcts of varying sizes. 4. Lacunar infarction: Manifested as lacunar syndrome, such as pure motor hemiparesis, pure sensory stroke, ataxic hemiparesis, or clumsy hand-dysarthria syndrome. Most cases involve small lacunar lesions caused by lesions in the basal ganglia or small perforating vessels of the pons.

C4.2 Postoperative Assessment of Revascularization

Is the surgical site patent? Yes☐ No☐

Determination of cervical vascular stenosis severity via CTA, MRA, DSA, or US (Mild ☐ ; Moderate ☐; Severe ☐ ; Total occlusion ☐)

C4.3 Follow-up chest CT scan without contrast (72±12 hours after onset)

B4.2.1 Follow-up chest CT scan (72±12 hours after onset)

Date☐☐☐☐ ☐☐ ☐☐ , Time☐☐ ☐☐ (24-hour format)

B4.2.2 Presence of shadows, infiltration, or cavities: ○1 -No ○2 -Yes

B4.2.3 Location of lesion:

□1 - Left upper lobe □2 - Left lower lobe □3 - Right upper lobe □4 - Right middle lobe □5 - Right lower lobe

B4.2.4 Lesion cross-section Length☐☐☐ .☐☐ cm Width☐☐☐ .☐☐ cm

Number of layers☐☐☐ .☐☐ layers Layer thickness☐☐☐ .☐☐ cm

Lesion volume☐☐☐ .☐☐ cm³/ml

B4.2.5 Has the lesion enlarged since the previous examination? (This item may be left blank for the initial chest CT): ○1 - No ○2 - Yes

B4.2.6 Is the lesion associated with pleural effusion? ○1- No ○2- Yes

C4.4 Laboratory Tests

Blood draw date:

☐☐☐☐ Year☐☐ Month☐☐ Day Time:☐☐ Hour☐☐ Minute (24-hour format)

Visits:			
WBC - White Blood Cell		PSA-Prostate-Specific	
LYMPH# - Absolute		PCA - Protein C activity	

Visits:			
MONO# - Absolute		NT-proBNP - N-terminal	
NEUT# - Neutrophil		cTnI - Cardiac Troponin	
EO# - Eosinophil Absolute		MYO-Myoglobin	
BASO# - Basophil		AST - Aspartate	
PLT-Platelet Count		ALT - Alanine	
PDW-Platelet Distribution		AST/ALT	
MPV - Mean Platelet		TP - Total Protein	
P-LCR-Large Platelet		ALB-Albumin	
PCT - Prothrombin Time		GLO-Globulin	
RBC-Red Blood Cell		A/G Ratio	
HGB - Hemoglobin		TBIL - Total Bilirubin	
HCT-Hematocrit		D-BIL - Direct Bilirubin	
MCV - Mean Corpuscular		I-BIL-Indirect Bilirubin	
MCH - Mean Corpuscular			
MCHC - Mean		ALP - Alkaline	
RDW%-Red Cell		Na - Sodium	
PT - Prothrombin Time		CL - Chloride	
APTT - Activated Partial		Ca - Calcium	
Fib-Fibrinogen level		CO2-Carbon Dioxide	
TT-Thrombin Time		Carbon Dioxide Binding	
FDP-Fibrin(ogen)		cys-c (cystatin C)	
D-D (D-dimer)		BUN-Blood Urea	
TM		Cr-Creatinine	
TAT		eGFR (CKD)	
PIC		UA-Uric Acid	
tPAI-C (tissue-type		UREA-Urea	
ATA-Antithrombin III		CK-Creatine Kinase	
LDH-Lactate		VB12-Vitamin B12	
		Folate	

Visits:			
TC - Total Cholesterol		R (R-value)	
TG - Triglycerides		Angle-Angle	
HDL-C-High-Density		MA-MA Value	
LDL-C - Low-Density		CI-CI value	
APOA-Apolipoprotein A1		LY30-LY30 value	
APOB-Apolipoprotein B		EPL-EPL value	
Lp(a) - Lipoprotein(a)		PAI-1 (PAI-1 rs1799889	
HCY-Homocysteine		CYP2C19 (Clopidogrel)	
HbA1c - Glycated		APOE (ApoE gene	
GLU - Fasting Blood		ABO	
CRP - C-reactive protein			

C5 Concomitant Medications

C5.1 Please complete medication consolidation

Schedule next visit: 30 days post-surgery

Visit 3 Completed Physician Signature: _____

Signature Date:☐☐☐☐ Year☐☐ Month☐☐ Day

Discharge Record

Please complete upon subject discharge

G1 Basic Discharge Information

1.1 Discharge Date:□□□□ -□□ -□□

1.2 Hospitalization ID

G2 Discharge Diagnosis

2.1 Final Diagnosis at Enrollment: Moderate to Severe Carotid Stenosis

F2.1.1 Degree of Stenosis:

F2.1.2 Site of Stenosis:

2.2 Other Diagnoses:

□ 1. Hypertension:

If "Hypertension," select type: ○1- Primary Hypertension ( ) ○2- Secondary Hypertension

Hypertension Grading:

○1 - Stage 1: Systolic blood pressure 140-159 mmHg and/or diastolic blood pressure 90-99 mmHg

○2 - Grade 2: Systolic blood pressure 160-179 mmHg and/or diastolic blood pressure 100-109 mmHg

○3 - Grade 3: Systolic blood pressure ≥180 mmHg and/or diastolic blood pressure ≥110 mmHg

□ 2. Diabetes

□ 3. Dyslipidemia

□ 4. Coronary heart disease

□ 5. Arrhythmia If "Arrhythmia" is selected, then:

□1 - Paroxysmal atrial fibrillation □2 - Persistent atrial fibrillation □3 - Permanent atrial fibrillation

□4 - Atrial flutter □5 - Frequent premature beats □6 - Other

□ 6. Respiratory System Diseases

If selecting "Respiratory System Diseases," please choose

○1 - Pulmonary infection ○2 - Pulmonary embolism ○3 - Asthma

○4 - COPD ○5 - Hemoptysis ○6 - Other

□ 7. Liver Disease

□1 -Abnormal liver function □2 -Viral carrier □3 -Cirrhosis

□4 -Liver surgery □5 -Other

□ 8. Urinary System Diseases

□1 - Chronic renal insufficiency □2 - Urinary tract infection □3 - Urinary tract hemorrhage □4- Other

□ 9. Digestive System Diseases

□1 - Digestive System Ulcers □2 - Digestive System Bleeding □3 - Other

□ 10. Peripheral Arterial Disease

□ 11. Deep Vein Thrombosis

□ 12. Cognitive Impairment

□ 13. Epilepsy

Discharge Information Collection

○1 -No ○2 -Yes

Photograph and upload discharge summary ○1 -No ○2 -Yes

mRS score at discharge: [Note: Based on pre-onset medical history assessment,

patients with mRS > 2 are ineligible for enrollment]

- ○0 = Completely asymptomatic;
- ○1=Symptoms present but no significant disability: Able to perform all previously engaged duties and activities;
- ○2 = Mild disability: Unable to perform all previously engaged activities, but can manage personal affairs without assistance;
- ○3 = Moderate disability: Requires some assistance, but can walk without help;
- ○4 = Severe disability: Unable to walk without assistance and unable to care for personal bodily needs;
- ○5=Severe disability: Bedridden, incontinent, requiring constant nursing and care.

NIHSS score at discharge: [Range0-42Points; higher scores indicate more severe neurological impairment]

- ○0-1 points: Normal or near-normal;
- ○1–4 points: Mild stroke/mini-stroke;
- ○5–15 points: Moderate stroke;
- ○16-20: Moderate-severe stroke;
- ○21–42 points: Severe stroke.

□□

Item		Score					
Orientation (10 points)	1. What day of the week is today? What is today's date? What month is it now? What year is it? What season is it now?					1 1 1 1 1	0 0 0 0 0
	2. Where are you now? Which floor are you on? Which township (subdistrict) do you live in? Which county (district) do you live in? Which province do you live in?					1 1 1 1 1	0 0 0 0 0
Memory (3 points)	3. I will tell you three things. After I finish, please repeat them and remember them, as I will ask you again later. (1 point each, total 3 points) Ball Flag Tree			3	2	1	0
Attention span and calculation skills (5 points)	4.100-7=? Subtract 5 five times consecutively (93, 86, 79, 72, 65. 1 point each, total 5 points. If an answer is incorrect but the next one is correct, only one error is counted)	5	4	3	2	1	0
Memory (3 points)	5. Now, please tell me the things I just asked you to remember? Soccer ball, national flag, trees			3	2	1	0
Language Proficiency (9 points)	6. Naming Ability Present a watch and ask, "What is this?" Present a pen and ask, "What is this?"					1 1	0 0
	7. Repetition Ability I will now say a phrase. Please repeat it clearly after me: (Forty-four stone lions)!					1	0

	8. Reading Ability (Close your eyes) Please read this sentence aloud and follow the instructions above!					1	0
	9. Three-Step Command I will give you a piece of paper. Please follow my instructions: "Hold this paper with your right hand. Fold it in half with both hands. Place it on your left thigh." (1 point per action, 3 points total)			3	2	1	0
	10. Writing ability requires the subject to write a complete sentence.					1	0
	11. Structural Ability (Present a pattern) Please draw the pattern shown above!					1	0

GCS Score: Total Score☐☐

Checklist	GCS Scoring Criteria	Score
Motor Response	6 - Normal (obeys commands); 5 - Can localize pain site; 4 - Avoidance response to pain; 3 - Decorticate response to pain; 2 - Decerebrate response to pain; 1 - No response	☐
Verbal Response	5 - Normal; 4 - Paraphrasing; 3 - Incoherent speech; 2 - Unable to understand; 1 - No speech	☐
Eye-opening response	4 - Spontaneous eye opening; 3 - Eye opening in response to verbal call; 2 - Eye opening in response to painful stimulus; 1 - No eye opening to any stimulus	☐

Visit 4: 30 ± 2 days post-op

You must complete the following within 30 ± 2 days post-surgery:

D1. Visit Time
D2. Adverse events
D3. Clinical examination
D4. Imaging studies
D5. Concomitant Medications

D1 Visit Date

D1. Visit Date□□□□ □□ □□

D2 Adverse Events

D2.1 Have any adverse events occurred since enrollment? ○1- No ○2- Yes

If "No" is selected, proceed directly to Section D3.

D2.2 If an adverse event occurred, please select:

For any adverse event/serious adverse event, complete the Adverse Event/Serious Adverse Event Report Form (see attachment).

1. Date of Death□□□□ □□ □□ , Time□□ □□ (24-hour format)

Cause of Death:

○1-Vascular Cause Death

○1 - Death due to ischemic stroke

○2 - Death from hemorrhagic stroke

○3 - Sudden cardiac death

○4- Death from Acute Myocardial Infarction

○5 - Death from congestive heart failure

○6 - Pulmonary embolism

○7 - Death from cardiovascular/cerebrovascular intervention or surgery (unrelated to acute myocardial infarction)

○8 - Other vascular-related deaths

○2-Non-vascular cause death

○3-Unknown cause

2. New-onset postoperative cerebral infarction Yes ○ No ○

First event date:

Date:□□□□ Year□□ Month□□ Day,□□ Hour□□ Minute (24-hour format)

Infarction location_____ Infarction area_____

Did it cause corresponding symptoms? ○1 -No ○2 -Yes If yes: Please describe symptoms

3. Re-bleeding Time□□ hours□□ minutes (24-hour format)

3.1 Completed cranial imaging studies**:** □1CT □2MRI

3.2 Type and location

Subdural hematoma: Left Right Bilateral Subpial

Epidural hematoma: Left Right Bilateral Subdural;

Intracerebral hematoma: Left Right Bilateral Subtentorial

Subarachnoid hemorrhage: Basal cistern Lateral fissure Interpeduncular cistern Others

Ventricular hemorrhage: Left ventricle Right ventricle Third ventricle Fourth ventricle

Does it cause corresponding symptoms? ○1 -No ○2 -Yes If yes: Please describe the symptoms

Has it penetrated the ventricle? ○1 -No ○2 -Yes

Does it rupture into the subarachnoid space: ○1 -No ○2 -Yes

Midline shift: ○1 -No ○2 -Yes

Brain herniation: ○1 -No ○2 -Yes

4. Coagulation Abnormalities Time□□ hours□□ minutes (24-hour format)

4.1 Abnormal Coagulation Markers: □1 -PT ○1 -Elevated ○2 -Decreased;

□2 - INR ○1 -Elevated ○2 -Decreased;

□3 - APTT ○1 - Elevated ○2 - Decreased; □4 - Fbg ○1 - Elevated ○2 - Decreased;

□5 - TT ○1 - Elevated ○2 - Decreased; □6 - FDP ○1 - Elevated ○2 - Decreased;

□7 - DD ○1 - Elevated ○2 - Decreased

5. Abnormal Absolute Platelet Count Time☐☐ Hours☐☐ Minutes (24-hour format)

5.1 Absolute Platelet Count:☐☐☐ 10^9/L

6. Bleeding from various organs Time☐☐ hours☐☐ minutes (24-hour format)

6.1 Site of bleeding: □1 - Digestive tract □2 - Respiratory tract □3 - Urinary tract □4 - Other organs □5 - Other

□6 - Unknown

7. Abnormal Liver Function Time☐☐ Hours☐☐ Minutes (24-hour format)

8. Renal Function Abnormalities Time☐☐ Hours☐☐ Minutes (24-hour format)

9. Infection Time☐☐ Hours☐☐ Minutes (24-hour format)

Site of Infection: □1 - Gastrointestinal Tract □2 - Respiratory Tract □3 - Urinary System □4 - Other □5 - Unknown

10. Myocardial infarction Time☐☐ Hours☐☐ Minutes (24-hour format)

11. Lower Extremity Venous Thrombosis Time☐☐ hours☐☐ minutes (24-hour format)

12. Pulmonary embolism Time☐☐ Hours☐☐ Minutes (24-hour format)

13. Hyperlipidemia Time☐☐ Hours☐☐ Minutes (24-hour format)

14. Bradycardia Time☐☐ H☐☐ M (24-hour format)

15. Rash/Drug Allergy Time☐☐ H☐☐ M (24-hour format)

16. Diarrhea Time☐☐ hours☐☐ minutes (24-hour format)

17. Hyperglycemia Time☐☐ Hours☐☐ Minutes (24-hour format)

18. Other Name: _____; Time☐☐ :☐☐ (24-hour format)

D3 Clinical Examination

Physical Examination:

3.1 Heart rate:☐☐☐ beats/min

3.2 Pulse rate:☐☐☐ beats/min

3.3 Systolic Blood Pressure 1 (Supine Position, Systolic Reading):☐☐☐ /☐☐☐ mmHg

Systolic Blood Pressure 2 (Supine Position, Systolic Reading):☐☐☐ /☐☐☐ mmHg **Diastolic Blood Pressure 1 (Supine Position, Systolic Reading):**☐☐☐ /☐

☐☐ mmHg **Diastolic Blood Pressure 2 (supine position, systolic measurement):**

☐☐☐ /☐☐☐ mmHg

3.4 Highest respiratory rate within 24 hours:☐☐☐ breaths/min

Highest body temperature within 24 hours:☐☐ .☐☐ °C

Sputum characteristics:☐ purulent sputum ☐ clear sputum ☐ no sputum

Cough:☐ Yes ☐ No

Shortness of breath (wheezing, labored breathing):☐ Yes ☐ No

Lung auscultation:☐ Rales ☐ Wet rales ☐ Bronchial breath sounds ☐ Other:__ _;

Nasal endotracheal intubation:☐ Yes ☐ No

Endotracheal intubation:☐ Yes ☐ No

Date of intubation: Date☐☐☐☐ Year☐☐ Month☐☐ Day, Time☐☐ Hours☐☐ Minutes

Ventilator-assisted ventilation:☐ Yes ☐ No

Ventilator-assisted ventilation start time: Date☐☐☐☐ Year☐☐ Month☐☐ Day, Time ☐☐ Hour☐☐ Minute

Ventilator oxygen concentration fraction (FiO_2 = 0.21 + oxygen flow rate / 25): ☐☐ .☐☐ %

Arterial blood gas partial pressure of oxygen (PaO_2):☐☐☐ .☐☐ mmHg

Clinical Score

3.5 NIHSS Score: [Range0-42Points; higher scores indicate more severe neurological impairment]

- ○0-1 points: Normal or near-normal;
- ○1–4 points: Mild stroke/mini-stroke;
- ○5–15 points: Moderate stroke;
- ○16–20: Moderate-to-severe stroke;
- ○21–42: Severe stroke.

3.6 mRS Score [Note: Scored based on condition at the time of this visit]

- ○0= Completely asymptomatic;
- ○1 = Symptoms present but no significant disability: Able to perform all previously engaged duties and activities;
- ○2 = Mild disability: Unable to perform all previously engaged activities, but can manage personal affairs without assistance;

○3 = Moderate disability: Requires some assistance, but can walk without help;

○4 = Severe disability: Unable to walk without assistance and unable to care for personal bodily needs;

○5=Severe disability: Bedridden, incontinent, requiring constant nursing and care.

D4 Imaging Studies

D4.1 Postoperative cranial CT or MRI scan

Date:□□□□ Year:□□ Month:□□ Day:□□ Time:□□

Type of Infarction and Recovery Status

Ischaemic Type: √ Complete anterior circulation ischaemia √ Partial anterior circulation ischaemia √ Posterior circulation ischaemia √ Focal ischaemia

Recovery Level: Infarct shrinkage or disappearance ☐ Yes ☐ No

Cerebral Function Recovery: mRS Score Improvement ☐ Yes ☐ No

[Note: 1. Complete anterior circulation infarction: Manifested as triad symptoms, i.e., complete middle cerebral artery syndrome; Higher-level cerebral dysfunction (consciousness disturbance, aphasia, acalculia, spatial disorientation, etc.); homonymous hemianopia, and severe motor and/or sensory deficits in three contralateral areas (face, upper limb, lower limb). Most cases involve occlusion of the proximal trunk of the middle cerebral artery, with a minority caused by occlusion of the internal carotid artery siphon segment, resulting in extensive cerebral infarction. 2. Partial anterior circulation infarction: Presents with two of the above triad features, or solely higher-level neurological impairment, or sensory-motor deficits more localized than in complete anterior circulation infarction. Indicates infarction in the distal trunk, branches, or small-to-medium vessels of the middle cerebral artery, or occlusion of branches associated with anticardiolipin antibodies. 3. Posterior circulation infarction: Manifested as vertebrobasilar syndrome of varying severity; may present as ipsilateral cranial nerve palsy with contralateral sensory-motor deficits; bilateral sensory-motor deficits; binocular coordination and cerebellar dysfunction without long tract signs or visual field defects. Caused by occlusion of the vertebral-basilar arteries and their branches, resulting in brainstem and cerebellar infarcts of varying sizes. 4. Lacunar infarction: Manifested as lacunar syndrome, such as pure motor hemiparesis, pure sensory stroke, ataxic hemiparesis, or clumsy hand-dysarthria syndrome. Most cases involve small lacunar lesions caused by lesions in the basal ganglia or small perforating vessels of the pons.

D4.2 Postoperative Assessment of Revascularization

Is the surgical site patent? Yes□ No□

Assess the degree of cervical vascular stenosis via CTA, MRA, DSA, and US (Mild □; Moderate □; Severe □ ; Total occlusion □)

D4.3 Repeat chest CT scan without contrast

1. Follow-up chest CT scan

Date:□□□□ Year□□ Month□□ Day, Time:□□ Hour□□ Minute (24-hour format)

2 Presence of shadows, infiltrates, or cavities: ○1 - No ○2 - Yes

3Location of lesion:

□1 - Left upper lobe □2 - Left lower lobe □3 - Right upper lobe

□4 - Right middle lobe □5 - Right lower lobe

4 Lesion cross-section Length□□□ .□□ cm Width□□□ .□□ cm

Number of layers□□□ .□□ layers Layer thickness□□□ .□□ cm

Lesion Volume□□□ .□□ cm^3/ml

5. Has the lesion enlarged since the previous scan? (Not applicable for initial chest CT):

○1 - No ○2 - Yes

6. Is there pleural effusion associated with the lesion? ○1 -No ○2 -Yes

4.4 Laboratory Tests

Blood draw date:

□□□□ Year□□ Month□□ Day Time:□□ Hour□□ Minute (24-hour format)

Visits:			
WBC - White Blood Cell		PSA-Prostate-Specific	
LYMPH# - Absolute		PCA - Protein C activity	
MONO# - Absolute		NT-proBNP - N-terminal	
NEUT# - Neutrophil		cTnI-Cardiac Troponin I	
EO# - Eosinophil Absolute		MYO-Myoglobin	
BASO# - Basophil		AST - Aspartate	
PLT-Platelet Count		ALT - Alanine	
PDW-Platelet Distribution		AST/ALT	

Visits:			
MPV - Mean Platelet		TP-Total Protein	
P-LCR-Large Platelet		ALB-Albumin	
PCT - Prothrombin Time		GLO - Globulin	
RBC-Red Blood Cell		A/G Ratio	
HGB - Hemoglobin		TBIL - Total Bilirubin	
HCT-Hematocrit		D-BIL - Direct Bilirubin	
MCV - Mean Corpuscular		I-BIL - Indirect Bilirubin	
MCH - Mean Corpuscular			
MCHC - Mean		ALP - Alkaline	
RDW%-Red Cell		Na - Sodium	
PT - Prothrombin Time		CL - Chloride	
APTT - Activated Partial		Ca - Calcium	
Fib-Fibrinogen level		CO2-Carbon Dioxide	
TT-Thrombin Time		Carbon Dioxide Binding	
FDP-Fibrin(ogen)		cys-c (cystatin C)	
D-D (D-dimer)		BUN-Blood Urea	
TM		Cr-Creatinine	
TAT		eGFR (CKD)	
PIC		UA-Uric Acid	
tPAI-C (tissue-type		UREA-Urea	
ATA-Antithrombin III		CK-Creatine Kinase	
LDH-Lactate		VB12-Vitamin B12	
		Folate	
TC-Total Cholesterol		R (R-value)	
TG - Triglycerides		Angle-Angle	
HDL-C-High-Density		MA-MA Value	
LDL-C - Low-Density		CI-CI value	
APOA-Apolipoprotein A1		LY30-LY30 value	
APOB-Apolipoprotein B		EPL-EPL value	

Visits:			
Lp(a) - Lipoprotein(a)		PAI-1 (PAI-1 rs1799889	
HCY-Homocysteine		CYP2C19 (Clopidogrel)	
HbA1c - Glycated		APOE (ApoE gene	
GLU - Fasting Blood		ABO	
CRP - C-reactive protein			

D5 Concomitant Medications

D5.1 Please complete concomitant medications

Schedule Next Visit: 90days post-surgery

Visit 4 Completed Physician Signature: _____

Signature Date:□□□□ -□□ -□□

Visit 5: 90 ± 2 days post-op

You must complete the following by 90 ± 2 days post-surgery:

E1. Visit Date
E2. Adverse Events
E3. Clinical Examination
E4. Imaging Studies
E5. Concomitant Medications

E1 Visit Date

1. Visit Date□□□□ □□ □□

E2 Adverse Events

2.1 Have any adverse events occurred since enrollment? ○1 -No ○2 -Yes

If "No" is selected, proceed directly to Section E3.

2.2 If an adverse event occurred, please select:

In the event of any adverse event/serious adverse event, please complete the Adverse Event/Serious Adverse Event Report Form (see attachment).

1. Date of death□□□□ □□ □□ , Time□□ □□ (24-hour format)

Cause of Death:

○1-Vascular Cause of Death

○1 - Death due to ischemic stroke

○2 - Death from hemorrhagic stroke

○3 - Sudden cardiac death

○4 - Death from Acute Myocardial Infarction

○5 - Death from congestive heart failure

○6 - Pulmonary embolism

○7 - Death from cardiovascular/cerebrovascular intervention or surgery (unrelated to acute myocardial infarction)

○8 - Other vascular-related deaths

○2-Non-vascular cause death

○3-Unknown cause

2. New-onset postoperative cerebral infarction Yes ○ No ○

First event date:

Date:□□□□ Year□□ Month□□ Day,□□ Hour□□ Minute (24-hour format)

Infarction location_____ Infarction area_____

Does it cause corresponding symptoms? ○1 -No ○2 -Yes If yes: Please describe symptoms

3. Re-bleeding Time□□ hours□□ minutes (24-hour format)

3.1 Cranial Imaging Completed: □1- CT □2- MRI

3.2 Type and location

Subdural hematoma: Left Right Bilateral Subpial

Epidural hematoma: Left Right Bilateral Subdural;

Intracerebral hematoma: Left Right Bilateral Subtentorial

Subarachnoid hemorrhage: Basal cistern Lateral fissure Interpeduncular cistern Others

Ventricular hemorrhage: Left ventricle Right ventricle Third ventricle Fourth ventricle

Does it cause corresponding symptoms? ○1 -No ○2 -Yes If yes: Please describe the symptoms

Has it penetrated the ventricles: ○1 -No ○2 -Yes

Does it rupture into the subarachnoid space: ○1 -No ○2 -Yes

Midline shift: ○1 -No ○2 -Yes

Brain herniation: ○1 -No ○2 -Yes

4. Coagulation Abnormalities Time□□ Hours□□ Minutes (24-hour format)

4.1 Abnormal Coagulation Markers:

□1 -PT ○1 -Elevated ○2 -Decreased;

□2 - INR ○1 -Elevated ○2 -Decreased;

□3 - APTT ○1 - Elevated ○2 - Decreased;

□4 - Fbg ○1 - Elevated ○2 - Decreased;

□5 - TT ○1 - Elevated ○2 - Decreased;

□6 - FDP ○1 - Elevated ○2 - Decreased;

□7 - DD ○1 - Elevated ○2 - Decreased

5. Abnormal Absolute Platelet Count Time□□ hours□□ minutes (24-hour format)

5.1 Absolute Platelet Count:□□□ 10^9/L

6. Bleeding sites: Time:□□ hours□□ minutes (24-hour format)

6.1 Bleeding site: □1- Gastrointestinal tract □2- Respiratory tract □3- Urinary tract □4- Other organs □5- Other □6 - Unknown

7. Abnormal Liver Function Time□□ Hours□□ Minutes (24-hour format)

8. Renal Function Abnormalities Time□□ Hours□□ Minutes (24-hour format)

9. Infection Time□□ Hours□□ Minutes (24-hour format)

Site of Infection: □1 - Gastrointestinal Tract □2 - Respiratory Tract □3 - Urinary System □4- Other □5- Unknown

10. Myocardial infarction Time□□ Hours□□ Minutes (24-hour format)

11. Lower Extremity Venous Thrombosis Time□□ hours□□ minutes (24-hour format)

12. Pulmonary embolism Time□□ Hours□□ Minutes (24-hour format)

13. Hyperlipidemia Time□□ Hours□□ Minutes (24-hour format)

14. Bradycardia Time□□ H□□ M (24-hour format)

15. Rash/Drug Allergy Time□□ H□□ M (24-hour format)

16. Diarrhea Time□□ hours□□ minutes (24-hour format)

17. Hyperglycemia Time□□ Hours□□ Minutes (24-hour format)

18. Other Name: _____; Time□□ :□□ (24-hour format)

E3 Clinical Examination

Physical Examination:

3.1 Heart rate:□□□ beats/min

3.2 Pulse rate:□□□ beats/min

3.3 Systolic Blood Pressure 1 (Supine Position, Systolic Reading):□□□ /□□□ mmHg

Systolic Blood Pressure 2 (Supine Position, Systolic Reading):□□□ /□□□ mmHg **Diastolic Blood Pressure 1 (Supine Position, Systolic Reading):**□□□ /□

☐☐ mmHg **Diastolic Blood Pressure 2 (supine position, systolic measurement):**

☐☐☐ /☐☐☐ mmHg

3.4 Highest respiratory rate within 24 hours:☐☐☐ breaths/min

Highest body temperature within 24 hours:☐☐ .☐☐ °C

Sputum characteristics:☐ purulent sputum ☐ clear sputum ☐ no sputum

Cough:☐ Yes ☐ No

Shortness of breath (wheezing, labored breathing):☐ Yes ☐ No

Lung auscultation:☐ Rales ☐ Wet rales ☐ Bronchial breath sounds ☐ Other:__ _;

Nasal endotracheal intubation:☐ Yes ☐ No

Endotracheal intubation:☐ Yes ☐ No

Date of intubation: Date☐☐☐☐ Year☐☐ Month☐☐ Day, Time☐☐ Hours☐☐ Minutes

Ventilator-assisted ventilation:☐ Yes ☐ No

Ventilator-assisted ventilation start time: Date☐☐☐☐ Year☐☐ Month☐☐ Day, Time ☐☐ Hour☐☐ Minute

Ventilator oxygen concentration fraction (FiO_2 = 0.21 + oxygen flow rate / 25): ☐☐ .☐☐ %

Arterial blood gas partial pressure of oxygen (PaO_2):☐☐☐ .☐☐ mmHg

Clinical Score

3.5 NIHSS score: [Range0-42Points; higher scores indicate more severe neurological impairment]

○0-1 points: Normal or near-normal;

○1–4 points: Mild stroke/mini-stroke;

○5–15 points: Moderate stroke;

○16–20: Moderate-to-severe stroke;

○21-42: Severe stroke.

3.6 mRS Score [Note: Score based on condition at the time of this visit]

○0=Completely asymptomatic;

○1=No significant disability despite symptoms: Able to perform all duties and activities previously undertaken;

○2 = Mild disability: Unable to perform all previously undertaken activities, but able to manage personal affairs without assistance;

○3 = Moderate disability: Requires some assistance, but does not need help walking;

○4=Severe disability: Unable to walk without assistance and unable to care for personal bodily needs;

○5=Severe disability: Bedridden, incontinent, requiring constant nursing and care.

E4 Imaging Studies

4.1 Postoperative Cranial CT or MRI

Date:□□□□ Year:□□ Month:□□ Day:□□ Time:□□

Ischaemic Type and Recovery Status

Ischaemic Type: √ Complete anterior circulation ischaemia √ Partial anterior circulation ischaemia √ Posterior circulation ischaemia √ Focal ischaemia

Recovery Level: Infarct shrinkage or disappearance □ Yes □ No

Cerebral Function Recovery: mRS Score Improvement □ Yes □ No

[Note: 1. Complete anterior circulation infarction: Manifested as triad symptoms, i.e., complete middle cerebral artery syndrome; Higher-level cerebral dysfunction (consciousness disturbance, aphasia, acalculia, spatial disorientation, etc.); homonymous hemianopia, and severe motor and/or sensory deficits in three contralateral areas (face, upper limb, lower limb). Most cases involve occlusion of the proximal trunk of the middle cerebral artery, with a minority caused by occlusion of the internal carotid artery siphon segment, resulting in extensive cerebral infarction. 2. Partial anterior circulation infarction: Presents with two of the above triad features, or solely higher-level neurological impairment, or sensory-motor deficits more localized than in complete anterior circulation infarction. Indicates infarction in the distal trunk, branches, or small-to-medium vessels of the middle cerebral artery, or occlusion of branches associated with anticardiolipin antibodies. 3. Posterior circulation infarction: Manifested as vertebrobasilar syndrome of varying severity; may present as ipsilateral cranial nerve palsy with contralateral sensory-motor deficits; bilateral sensory-motor deficits; binocular coordination and cerebellar dysfunction without long tract signs or visual field defects. Caused by occlusion of the vertebral-basilar arteries and their branches, resulting in brainstem and cerebellar infarcts of varying sizes. 4. Lacunar infarction: Manifested as lacunar syndrome, such as pure motor hemiparesis, pure sensory stroke, ataxic hemiparesis, or clumsy hand-dysarthria syndrome. Most cases involve small lacunar lesions caused by lesions in the basal ganglia or small perforating vessels of the pons.

4.2 Postoperative Assessment of Revascularization

Is the surgical site patent? Yes□ No□

Determination of cervical vascular stenosis severity via CTA, MRA, DSA, or US

(Mild □; Moderate □; Severe □ ; Total occlusion □)

4.3 Follow-up Chest CT Scan

B4.2.1 Follow-up Chest CT Scan

Date□□□□ □□ □□ , Time□□ □□ (24-hour format)

B4.2.2 Presence of shadows, infiltration, or cavities: ○1 -No ○2 -Yes

B4.2.3 Location of lesion:

□1 - Left upper lobe □2 - Left lower lobe □3 - Right upper lobe

□4 - Right middle lobe □5 - Right lower lobe

B4.2.4 Lesion cross-section Length□□□ .□□ cm Width□□□ .□□ cm

Number of layers □ □ □ . □ □ layers Layer thickness□□□ .□□ cm

Lesion volume□□□ .□□ cm³/ml

B4.2.5 Has the lesion enlarged since the previous examination? (This item may be left blank for the initial chest CT): ○1 - No ○2 - Yes

B4.2.6 Is the lesion associated with pleural effusion? ○1- No ○2- Yes

4.4 Laboratory Tests

Blood draw date:□□□□ Year□□ Month□□ Day Time:□□ Hour□□ Minute (24-hour format)

Visits:			
WBC - White Blood Cell		PSA-Prostate-Specific	
LYMPH# - Absolute		PCA - Protein C activity	
MONO# - Absolute		NT-proBNP - N-terminal	
NEUT# - Neutrophil		cTnI-Cardiac Troponin I	
EO# - Eosinophil Absolute		MYO-Myoglobin	
BASO# - Basophil		AST - Aspartate	
PLT-Platelet Count		ALT - Alanine	
PDW-Platelet Distribution		AST/ALT	

Visits:			
MPV - Mean Platelet		TP - Total Protein	
P-LCR-Large Platelet		ALB-Albumin	
PCT - Prothrombin Time		GLO - Globulin	
RBC-Red Blood Cell		A/G Ratio	
HGB - Hemoglobin		TBIL - Total Bilirubin	
HCT-Hematocrit		D-BIL - Direct Bilirubin	
MCV - Mean Corpuscular		I-BIL-Indirect Bilirubin	
MCH - Mean Corpuscular			
MCHC - Mean		ALP - Alkaline	
RDW%-Red Cell		Na - Sodium	
PT - Prothrombin Time		CL - Chloride	
APTT - Activated Partial		Ca - Calcium	
Fib-Fibrinogen level		CO2-Carbon Dioxide	
TT-Thrombin Time		Carbon Dioxide Binding	
FDP-Fibrin(ogen)		cys-c (cystatin C)	
D-D (D-dimer)		BUN-Blood Urea	
TM		Cr-Creatinine	
TAT		eGFR (CKD)	
PIC		UA-Uric Acid	
tPAI-C (tissue-type		UREA-Urea	
ATA-Antithrombin III		CK-Creatine Kinase	
LDH-Lactate		VB12-Vitamin B12	
		Folate	
TC-Total Cholesterol		R (R-value)	
TG - Triglycerides		Angle-Angle	
HDL-C-High-Density		MA-MA Value	
LDL-C - Low-Density		CI-CI value	
APOA-Apolipoprotein A1		LY30-LY30 value	
APOB-Apolipoprotein B		EPL-EPL value	

Visits:			
Lp(a) - Lipoprotein(a)		PAI-1 (PAI-1 rs1799889	
HCY-Homocysteine		CYP2C19 (Clopidogrel)	
HbA1c - Glycated		APOE (ApoE gene	
GLU - Fasting Blood		ABO	
CRP - C-reactive protein			

E5 Combination Medication

E5.1 Please complete combination therapy

Visit 5 Completed Physician Signature: _____

Signature Date: □□□□□□ □□

Combination Medication Chart

	Generic Name	Brand Name	Dosage		Administration Frequency	Route of Administration	Start Time	End Time	Remarks
			Quantity	Unit					
○1 **Anti-hypertensive drugs**				○μg ○mg ○g ○ml ○bag ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○ IM ○IV injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○Once per week ○Q8h ○Other: ____	○Oral ○Intramuscular injection ○Intravenous injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○ IM ○IV injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
○2 **Anti-diabetic drugs**				○μg ○mg ○g ○ml ○bag ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○Once per week ○Q8h ○Other: ____	○Oral ○Intramuscular injection ○Intravenous injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○ IM ○IV injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○Intramuscular injection ○Intravenous injection ○Intravenous infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
○3 **Lipid-regulating drugs**				○μg ○mg ○g ○ml ○bag ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○ IM ○IV injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	

				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○Intramuscular injection ○Intravenous injection ○Intravenous infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
○4 **Anti-platelet Agents**				○μg ○mg ○g ○ml ○bag ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○ IM ○IV injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○Intramuscular injection ○Intravenous injection ○Intravenous infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
○5 **Anticoagulants**				○μg ○mg ○g ○ml ○bag ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○ IM ○IV injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○Intramuscular injection ○Intravenous injection ○Intravenous infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
○6 **Traditional Chinese Medicines**				○μg ○mg ○g ○ml ○bag ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○Once per week ○Q8h ○Other: ____	○ Oral ○ IM ○IV injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○Intramuscular injection ○Intravenous injection ○Intravenous infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
○7 **Other medications**				○μg ○mg ○g ○ml ○bag ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○ IM ○IV injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	

				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○Intramuscular injection ○Intravenous injection ○Intravenous infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○ IM ○IV injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○ Intramuscular injection ○ Intravenous injection ○Intravenous infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	
				○μg ○mg ○g ○ml ○ bags ○ tablet ○Other: ____	○QD ○BID ○TID ○QOD ○1 time/week ○Q8h ○Other: ____	○ Oral ○ IM ○IV injection ○IV infusion ○Subcutaneous injection ○Topical ○Other	_____Year ____Month _____Day	_____Year ____Month _____Day	

Adverse Event Record Form

Please enter adverse events according to the codes provided below *. If no code exists, directly enter the adverse event name (using standard medical terminology in block letters). Record one adverse event per column; mark "√" in the corresponding "○" box.			
Name			
Start Date	_____Year_____Month _____Day	_____Year_____Month_ _____Day	_____Year_____Month_ _____Day
End Date	_____Year_____Month _____Day OR ○ Continues to exist	_____Year_____Month_ _____Day OR ○ Continues to exist	_____Year_____Month_ _____Day OR ○ Continues to exist
Severity	○1 ○2 ○3 ○4 ○5	○1 ○2 ○3 ○4 ○5	○1 ○2 ○3 ○4 ○5
Potentially Related Diseases or Medications			
Relevance Assessment	○1 Definitely related ○2 Highly likely ○3 Possibly related ○4 Likely unrelated ○5 Not related	○1 Definitely relevant ○2 Very likely related ○3 Possibly relevant ○4 May be irrelevant ○5 Not related	○1 Definitely relevant ○2 Very likely related ○3 Possibly relevant ○4 Possibly unrelated ○5 Not relevant
Clinical Measures			
Outcome	○1 Resolution/Recovery ○2 Improvement ○3 Unchanged ○4 Worsened ○5 Unable to track ○6 Other	○1 Resolution/Recovery ○2 Improvement ○3 Unchanged ○4 Worsened ○5 Unable to track ○6 Other	○1 Disappeared/Recovered ○2 Alleviated ○3 Unchanged ○4 Worsened ○5 Unable to track ○6 Other
Severity Adverse Event	○1 Yes (Reason) ○2 No	○1 Yes (Reason) ○2 No	○1 Yes (Reason) ○2 No
Remarks			