Protocol Number: WQ21-2301

Guo's Aortic Arch Reconstruction: A Multicenter, Prospective Study of the Novel WeFlow-Tribranch Unique Embedded Aortic Triple-branch Arch Stent Graft System (GENIUS Study)

Trial Medical Device Name: WeFlow-Tribranch embedded aortic Triple-branch arch Stent Graft system

Model Specification: Refer to the protocol for specification details

Trial Medical Device Regulatory Classification:

Class III medical device requiring clinical trial approval Yes □ No ■

Protocol Version Number and Date: V1.0/20230830

Lead Unit: First Medical Center of The Chinese PLA General Hospital

Coordinating Investigator: Professor Guo Wei

Sponsor: Hangzhou Endonom Medtech Co., Ltd.

Trial Protocol Summary

Name of the Trial	Guo's Aortic Arch Reconstruction: A Multicenter, Prospective Study of the Novel WeFlow-Tribranch Unique Embedded Aortic Triple-branch Arch Stent Graft System (GENIUS Study)
Sponsor	Hangzhou Endonom Medtech Co., Ltd.
Trial Objective	The purpose of this clinical trial is to evaluate the safety and efficacy of the WeFlow-Tribranch embedded aortic Triple-branch arch Stent Graft system developed and manufactured by Hangzhou Endonom Medtech Co.; Ltd. in the treatment of patients with aortic arch aneurysm
Trial Equipment	WeFlow-Tribranch embedded aortic Triple-branch arch Stent Graft system
Sample Size	Considering a dropout rate of 20%, the planned enrollment is 90 subjects.
Sample Size Calculation	[redacted]
Follow-Up Period	After surgery, each subject will require 60 months of follow-up.
Patient Inclusion/ Exclusion Criteria	**Inclusion Criteria** 1. Patients aged 18 to 80 years old 2. Patients diagnosed with aortic arch lesions requiring intervention, including true aortic arch aneurysms, pseudo-aortic arch aneurysms, and ulcers involving the aortic arch. 3. Patients showing a suitable vascular condition, including: • Ascending aorta length greater than 50 mm (from the aortic sinusoid junction to the proximal cardiac margin of the innominate artery). • Ascending aorta diameter ≥ 24 mm and ≤ 48 mm; • Proximal anchoring zone length ≥ 30 mm; • Innominate artery diameter ≤ 24 mm and ≥ 6 mm, length ≥ 20 mm ; • Suitable arterial access for endovascular interventional treatment ; 4. Patients able to understand the purpose of the trial, participate in the trial voluntarily with informed consent form signed by the subject

him/herself or his or her legal representative, and willing to complete follow-up visits as required under the protocol.

5. [redacted].

Exclusion Criteria

1. Patients that have experienced systemic infection during past three months;
2. Neck surgery was performed within three months;
3. Previous endovascular interventional treatment involving the aortic arch was performed;
4. Infectious aortic disease、Takayasu arteritis，Marfan syndrome (or other connective tissue diseases);
5. Patients with severe stenosis, calcification, thrombosis or tortuosity;
6. Heart transplant patients;
7. Patients that have suffered MI or stroke during past three months;
8. Patients with Class IV heart function (NYHA classification);
9. Active peptic ulcers or upper gastrointestinal bleeding occurring within the previous three months;
10. Hematological abnormality, defined as follows: Leukopenia (WBC < 3 × 10^9/L), acute anemia (Hb < 90 g/L); thrombocytopenia (PLT count < 50 × 10^9/L), history of bleeding or coagulopathy;
11. Patients with renal insufficiency， serum creatinine > 150 μmol/L, and/or end-stage renal disease requiring renal dialysis;
12. Patients that are pregnant or breastfeeding;
13. Patients with allergies to contrast agents;
14. Patients with a life expectancy of less than 12 months;
15. Patients currently participating in other drug or device research;
16. Any other disease or abnormality that the investigators believe may hinder endovascular interventional treatment.

Primary Endpoints	Rate of all-cause mortality and major stroke within 12 months after surgery. All-cause mortality includes cardiac mortality, non-cardiac mortality and mortality from unknown causes. Major stroke is defined as a modified Rankin score (mRS) ≥ 2 at 90 days following stroke onset (see Annex 2).
Secondary Efficacy Endpoints	1. Rate of immediate technical success following surgery. Immediate technical success is defined as successful delivery of the aortic and branching stent graft conveyors to their predetermined positions, accurate positioning and successful deployment of the stent, safe removal of the delivery device outside the body, and the absence of Type I and III endoleaks per imaging studies conducted at the end of the procedure with all branching stents patency. 2. Rate of aortic aneurysm progression under control. Maximum increase in the diameter of the aortic aneurysm was ≤ 5 mm when compared with preoperative aortic aneurysm as of a 12-month postoperative CTA review. 3. Incidence of Type I or Type III endoleak. Intraoperative, 1-month, 6-month, and 12-month DSA or CTA imaging studies showing endoleaks. Intraoperative endoleaks subject to adjuvant treatment are not recorded. Endoleaks occurring after the completion of the procedure followed by one or more endoleaks occurring in the same subject at different follow-up stages that were not treated are counted as a single instance. 4. Incidence of aortic covered stent graft displacement. CTA examination will be performed at 1, 6, and 12 months post operation to determine if the stent has migrated, and evaluations will be recorded for both the main and branch stents. Displacement is defined as a displacement of more than 10 mm in the aortic and branch stent grafts at follow-up time points compared with the 30-day postoperative reference imaging. 5. Postoperative branch vessel patency rate. CTA examinations will be performed at 1, 6, and 12 months post-operation to evaluate branch vessel reconstruction and assess for occlusion, stenosis, or in-stent thrombosis.
Secondary Safety Endpoints	1. Rate of conversion to thoracotomy or secondary intervention. Whether subjects require conversion to open thoracic surgery or secondary interventional procedures due to new-onset aortic dissection caused by

	the index procedure. 2. Rate of major adverse events occurring within 30 days after surgery. Refers to all-cause mortality, myocardial infarction, ischemic stroke or respiratory failure occurring within 30 days after surgery. More specifically, myocardial infarction refers to a drastic reduction or complete interruption of the coronary blood supply due to coronary artery disease, resulting in severe and prolonged acute ischemia of the corresponding myocardium, leading to necrosis of cardiomyocytes. Ischemic stroke refers to the end result of necrosis of brain tissue caused by narrowing or occlusion of the arteries supplying blood to the brain or insufficient blood supply to the brain. Respiratory failure is defined as a state resulting in significantly prolonged intubation, tracheotomy, deterioration of lung function, or other fatal outcomes. 3. Rate of aortic aneurysm-related mortality at 12 months post operation. Refers to mortality caused by a ruptured aortic aneurysm or endovascular interventional treatment. 4. Incidence of severe adverse events. Refers to an event that occurs during the clinical trial that results in mortality or serious deterioration in patient health, including a fatal illness or injury, a permanent defect in body structure or body function, or an event that requires medical or surgical intervention to avoid one or more permanent defects in body structure or body function. 5. Incidence of device-related adverse events. Device-related adverse events refer to an adverse medical event related to the use of a device that occurs during the course of the clinical trial. However, a distinction should be made with respect to normal postoperative stress response, such as fever and chest and back discomfort, which, in the judgment of the investigator, need not be recorded as an adverse event. Recording of device-related adverse events will be applicable for conditions that are deemed by the investigator to be definitely related, possibly related, or of indeterminate relationship, to the test device.
Trial Visitation Plan	➢ Visit 1: Screening period (Day -15 to 0) ➢ Visit 2: Day of Surgery (Intraoperatively, after completion of stent-graft deployment) (Day 0)

	➢ Visit 3: Before discharge ➢ Visit 4: 30-day (±7 days) postoperative visit ➢ Visit 5: 6-month (±30 days) postoperative visit ➢ Visit 6: 12-month (±30 days) postoperative visit ➢ Visits 7, 8, 9 and 10: 24 months (±30 days) after surgery, 36 months (±30 days) after surgery, 48 months (±30 days) after surgery, 60 months (±30 days) after surgery

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Full Trial Protocol Text

1. Sponsor Information

1.1. Sponsor Name

Hangzhou Endonom Medtech Co., Ltd.

1.2. Sponsor Address

[redacted]

1.3. Sponsor Contact Information

Company Phone Number: [redacted]

2. List of Clinical Trial Sites and Investigators:

For details, see Annex 3 of the Protocol.

3. Statistical Analysis

[redacted]

Address: [redacted]

4. Clinical Trial Objectives and Content

4.1. Objectives

The purpose of this clinical trial is to evaluate the safety and efficacy of the WeFlow-Tribranch embedded aortic Triple-branch arch Stent Graft system developed and manufactured by Hangzhou Endonom Medtech Co.; Ltd. in the treatment of patients with aortic arch aneurysms.

4.2. Content

This study will be conducted at qualified clinical research institutions. Investigators will perform endovascular treatment in patients with aortic arch lesions using the WeFlow-Tribranch embedded aortic Triple-branch arch Stent Graft system, developed and manufactured by Hangzhou Endonom Medtech Co.; Ltd. This is a prospective, multicenter, single-arm objective performance criterion clinical study. An internet-based registration system

will be used to enroll and document all study subjects. The study is planned to initiate in October 2023, with completion of 90 clinical implantations by December 2025. Clinical follow-up assessments will be performed before discharge, at 30 days, 6 months, 12 months, 24 months, 36 months, 48 months, and 60 months postoperatively. Computed Tomography Angiography (CTA) imaging follow-up will be conducted at 30 days, 6 months, 12 months, 24 months, 36 months, 48 months, and 60 months after the procedure.

The primary endpoint of this trial is the incidence of all-cause death or major stroke within 12 months after surgery. Effectiveness endpoints include the incidence of Type I or Type III endoleak, the incidence of aortic stent graft migration, postoperative branch vessel patency rate, and the rate of conversion to open thoracic surgery or secondary interventional procedures. Safety endpoints comprise all-cause mortality rate, aortic aneurysm-related mortality rate, the incidence of Serious Adverse Events (SAEs), and the incidence of device-related adverse events. After completion of the 12-month primary endpoint evaluation, the sponsor will finalize the clinical study report and submit it to the National Medical Products Administration (NMPA). Annual long-term follow-up will continue up to the fifth year to evaluate long-term clinical outcomes.

5. Background Information Pertaining to the Clinical Trial

Aortic aneurysm (AA) refers to the aneurysmal dilatation of the aorta, generally defined as a dilated diameter exceeding 1.5 times that of the normal vascular lumen. Thoracic aortic aneurysm (TAA) involves the ascending aorta, aortic arch, or descending thoracic aorta. The overall incidence of TAA is approximately 10.4 per 100,000 person-years, among which aortic arch aneurysms account for only about 10% of all TAA cases[1]. More than 70% of patients with untreated thoracic aortic aneurysms will eventually progress to aneurysm rupture, and over 90% of ruptures are fatal. The natural growth rate of thoracic aortic aneurysms averages 0.1 cm per year. Consensus recommendations indicate that symptomatic aneurysms or penetrating aortic ulcers (PAUs) should be treated regardless of lesion size[2].

Based on domestic and international clinical experience, for aortic aneurysms involving the ascending aorta or aortic arch, open surgical repair is conventionally required due to the lack of

adequate proximal landing zones. Open surgical reconstruction for ascending and aortic arch aneurysms relies on deep hypothermic circulatory arrest, with perioperative mortality ranging from 2% to 16.5% and stroke rates from 2% to 18%[3–4]. Hybrid arch procedures provide sufficient proximal landing zones for endovascular repair and eliminate the need for deep hypothermic circulatory arrest; however, perioperative mortality (0%–15%) and stroke rates (0%–11%) remain relatively high[5]. In particular, patients with high surgical risks or clear surgical contraindications related to advanced age or comorbidities can only receive conservative medical therapy. A meta-analysis published by Wee I in European Journal of Vascular and Endovascular Surgery in 2019[6] included 17 studies with a total of 6,894 patients receiving medical management due to advanced age, underlying diseases, controversial diagnoses, refusal of surgery, or insufficient institutional resources. The results demonstrated an in-hospital all-cause mortality rate as high as 39.1%.

In recent years, the development of fenestrated and branched stent grafts has provided novel devices and approaches for aortic arch pathologies[7–9], substantially reducing the high mortality associated with open surgery (14% vs. 8%) [7,10–13]. Endovascular intervention features minimal trauma, fewer complications, lower mortality, and faster postoperative recovery, enabling active treatment for elderly patients or those with cardiac, pulmonary, hepatic, or renal insufficiency. Currently, endovascular repair has become the first-line treatment for anatomically suitable patients with arch disease who are ineligible for open surgery. In routine clinical practice, due to the lack of mature, widely applicable multi-branched endovascular grafts for aortic arch reconstruction, off-label techniques such as parallel stent grafting and fenestration are commonly adopted to treat aortic arch lesions with standard aortic stent grafts. The parallel stent technique preserves branch perfusion and extends the landing zone by deploying small parallel stents (chimney stents) at the junction of arch branch vessels and the main aortic stent graft; nevertheless, gaps between the main graft and chimney stents carry a long-term risk of endoleak. Fenestration can be performed via in-vitro or in-situ approaches. In-vitro fenestration suffers from inaccurate alignment, while in-situ fenestration avoids positioning errors but still has limitations, including the risk of embolic debris from

fenestration and inapplicability to severely tortuous anatomies. With continuous technological innovation, branched stent graft technology—especially multi-branched endovascular aortic arch reconstruction—has emerged as the future direction, owing to its conformity to physiological anatomy and hemodynamics[14–18].

Globally, research on multi-branched stent grafts remains in the early stage. For instance, the NEXUS aortic stent graft system by Endospan adopts a modular design for thoracic aortic lesions involving the aortic arch; however, it only reconstructs the brachiocephalic trunk, while the left common carotid artery and left subclavian artery require two additional bypass procedures to maintain cerebral perfusion. Further studies are needed to verify whether the single arterial diameter can fully satisfy perfusion demands of all arch vessels[19]. This device has obtained CE (Conformité Européenne) certification and is currently undergoing pivotal clinical investigations under the FDA (Food and Drug Administration) regulatory framework. The Multi-branch dual in-branched stent graft by COOK[13], the A-Branch triple in-branched stent graft system[20], and the RelayBranch stent graft by Terumo are also under feasibility evaluations[7,10,21–23]. Notably, RelayBranch received FDA Breakthrough Device Designation in March 2022; nevertheless, stroke risk remains a critical concern for such products.

Addressing the current limitations of clinical endovascular arch repair techniques and devices, the Modular Integrated Triple-Branched Aortic Arch Stent Graft System investigated in this study integrates in-branch and modular design concepts. The system consists of an integrated ascending aortic stent graft subsystem, an integrated arch stent graft subsystem, branched stent graft subsystems, and aortic extension stent graft subsystems. The integrated ascending aortic stent graft features two built-in branches for endovascular reconstruction of the innominate artery and left common carotid artery via matched branched subsystems, while the integrated arch stent graft reconstructs the left subclavian artery and connects with the ascending module to treat combined arch and descending aortic lesions, achieving total endovascular repair without debranching surgery. The modular integrated vascular design maintains uninterrupted cerebral perfusion during implantation, eliminates the need for deep hypothermic circulatory arrest and thoracotomy, reduces stroke risk, and provides an

innovative therapeutic alternative for patients.

The investigational device has completed registration testing with qualified results for all chemical and physical performance indicators. Preclinical animal studies and benchtop simulation tests have also been finalized, confirming that delivery system navigation, stent positioning, and deployment fully meet clinical operational requirements. Animal studies have verified favorable safety and feasibility. Additionally, comprehensive performance testing conducted by Hangzhou Endonom Medtech Co.; Ltd. has confirmed stable product performance and compliant quality. Accordingly, the investigational device satisfies all prerequisites for initiating clinical trials. This clinical trial application is submitted to validate the safety and efficacy of the WeFlow-Tribranch embedded aortic Triple-branch arch Stent Graft system.

6. Product Structural Composition, Working Principles, Mechanism of Action and Scope of Testing

6.1. Product Structural Composition, Working Principles and Mechanism of Action

The WeFlow-Tribranch embedded aortic Triple-branch arch Stent Graft system consists of an integrated ascending aortic stent graft subsystem, an integrated arch segment stent graft subsystem, an aortic extension stent graft subsystem, and a branched stent graft subsystem. The integrated ascending aortic stent graft subsystem is composed of an integrated ascending aortic stent graft and a delivery system, as shown in Figures 1 and 2.The integrated arch segment stent graft subsystem comprises an integrated arch segment stent graft and a delivery system, as shown in Figures 3 and 4.The aortic extension stent graft subsystem includes an aortic extension stent graft and a delivery system, as shown in Figures 5, 6 and 7.The branched stent graft subsystem consists of a branched stent graft and a delivery system, as shown in Figures 8 and 9. The integrated ascending aortic stent graft is equipped with two inner branches, which can reconstruct the innominate artery and the left common carotid artery via endovascular placement of the corresponding branched stent grafts. The integrated arch segment stent graft features one inner branch, enabling endovascular reconstruction of the left subclavian artery with the matching branched stent graft. Combined deployment of the integrated ascending

aortic stent graft, the integrated arch segment stent graft, and the aortic extension stent graft enables the treatment of lesions involving the aortic arch, as illustrated in Figure 10.

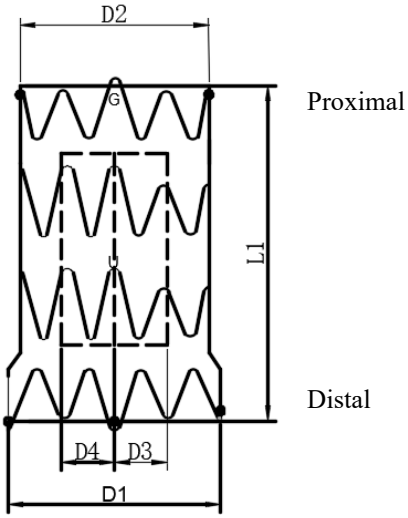

Figure 1 Embedded Ascending Aortic Stent Graft

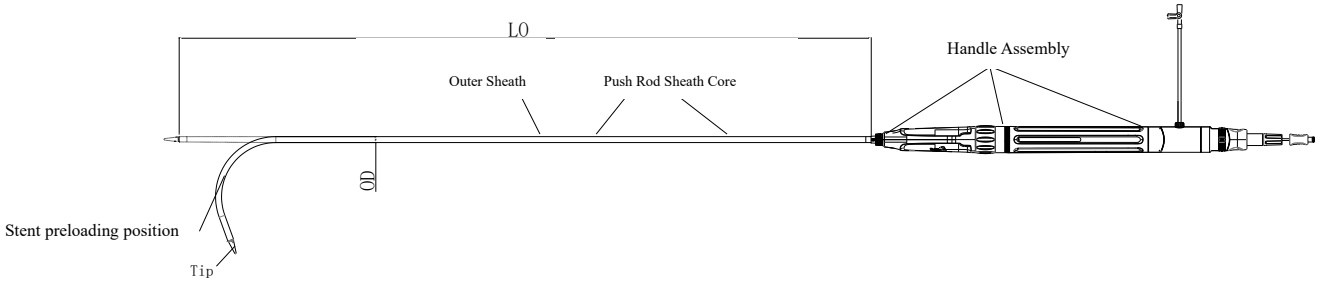

Figure 2 Delivery System for Embedded Ascending Aortic Stent Graft

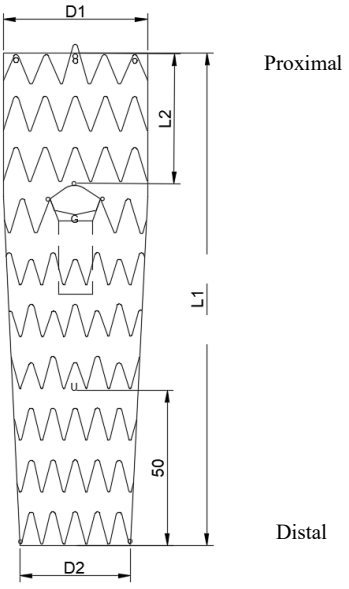

Figure 3 Embedded Aortic Arch Stent Graft

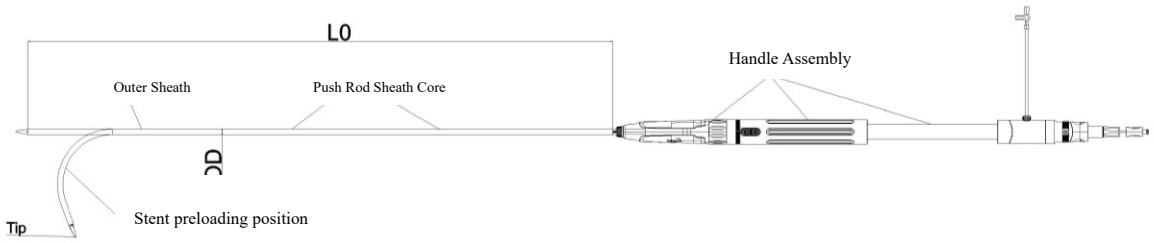

Figure 4 Delivery System for Embedded Aortic Arch Stent Graft

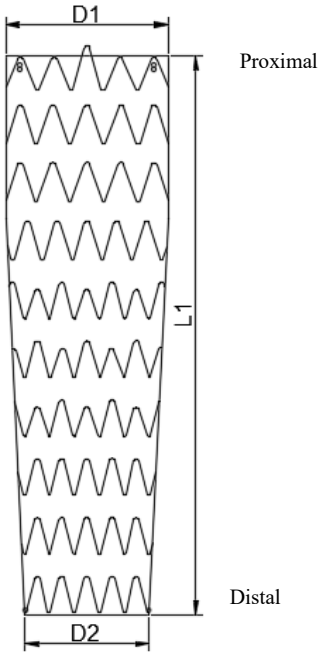

Figure 5 Aortic Extension Stent Graft

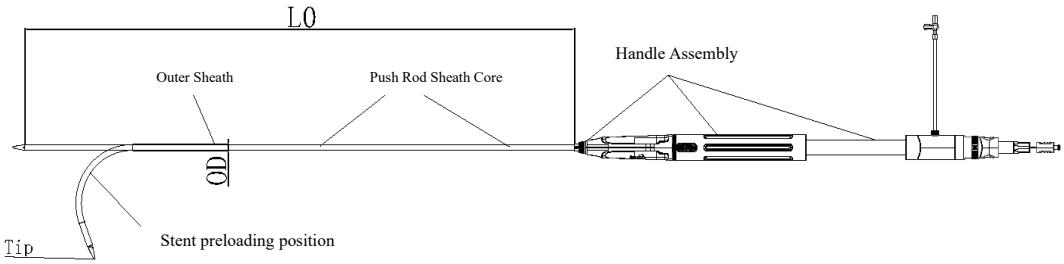

Figure 6 Aortic Extension Stent Graft Delivery System - S

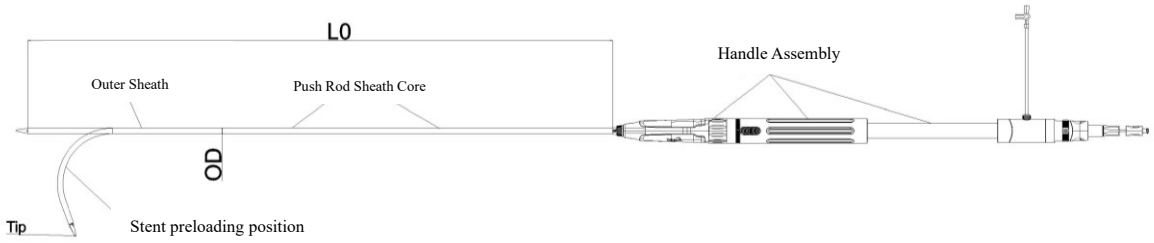

Figure 7 Aortic Extension Stent Graft Delivery System - L

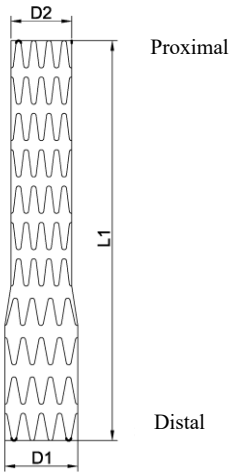

Figure 8: Branch Stent Graft

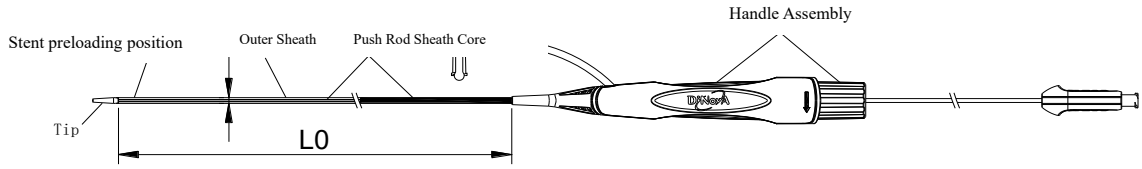

Figure 9 Delivery System for Branch Stent Graft

Figure 10 Modular Embedded Triple-Branch Aortic Arch Stent Graft System

6.2. Product Specifications

The product specification series of the Modular Embedded triple-branch aortic arch stent graft system are shown in Tables 1–6.：

Table 1: Specification Series of Modular Embedded Ascending Aortic Stent Graft Unit：mm

Specification	D1	D2	D	D4	L	Delivery System Specification
28	28	[redacted]	[redacted]	[redacted]		22F
30	30	[redacted]	[redacted]	[redacted]	[redacted]	22F
32	32	[redacted]	[redacted]	[redacted]	[redacted]	22F
34	34	[redacted]	[redacted]	[redacted]	[redacted]	22F
36	36	[redacted]	[redacted]	[redacted]	[redacted]	22F
38	38	[redacted]	[redacted]	[redacted]	[redacted]	24F
40	40	[redacted]	[redacted]	[redacted]	[redacted]	24F
42	42	[redacted]	[redacted]	[redacted]	[redacted]	24F
44	44	[redacted]	[redacted]	[redacted]	[redacted]	24F
46	46	[redacted]	[redacted]	[redacted]		24F

Specification	D1	D2	D	D4	L	Delivery System Specification
48	48	[redacted]	[redacted]	[redacted]		24F
50	50	[redacted]	[redacted]	[redacted]		24F
52	52	[redacted]	[redacted]	[redacted]		24F

Table 2: Specification Series of the Modular Embedded Aortic Arch Stent Graft (I) Unit：mm

Specification	D1	D2	D3	L1	Delivery System Specification
26	26	[redacted]	[redacted]	[redacted]	22F
28	28				22F
30	30				22F
32	32				22F
34	34				22F
36	36				22F
38	38				22F
40	40				24F
42	42				24F
44	44				24F
46	46				24F
48	48				24F
50	50				24F

Table 3: Fenestration Distance List of Modular Embedded Aortic Arch Stent Graft (II) Unit: mm

L1	L2
[redacted]	[redacted]

Table 4: Specification Sheet of Aortic Extension Stent Graft Unit：mm

Specification	D1	D2	L1	Delivery System Specification
26	26	[redacted]	[redacted]	20F
28	28			20F

Specification	D1	D2	L1	Delivery System Specification
30	30	[redacted]	[redacted]	20F
32	32	[redacted]	[redacted]	20F
34	34	[redacted]	[redacted]	22F
36	36	[redacted]	[redacted]	22F
38	38	[redacted]	[redacted]	22F
40	40	[redacted]	[redacted]	22F
42	42	[redacted]		22F
44	44	[redacted]		22F
46	46	[redacted]		22F
48	48	[redacted]		22F
50	50	[redacted]		22F

Table 5: Specification Series of Branch Stent Graft Unit：mm

Specification	D1	D2	L1	Delivery System Specification
7	7			10F
8	8			10F
9	9	[redacted]	[redacted]	10F
10	10	[redacted]	[redacted]	10F
11	11	[redacted]	[redacted]	10F
12	12	[redacted]	[redacted]	10F
13	13	[redacted]	[redacted]	10F
14	14	[redacted]	[redacted]	12F
16	16	[redacted]	[redacted]	12F
18	18	[redacted]	[redacted]	12F
20	20	[redacted]	[redacted]	12F
22	22	[redacted]	[redacted]	14F
24	24			14F
26	26			14F

Table 6: Delivery System Specifications Unit：mm

Specification	Type	OD	L0
22F	Modular Embedded Ascending	[redacted]	[redacted]
24F	Aortic Stent Graft System	[redacted]	[redacted]
22F	Modular Embedded Aortic Arch	[redacted]	[redacted]

Specification	Type	OD	L0
24F	Stent System	[redacted]	[redacted]
20F	Aortic Extension Stent Graft	[redacted]	[redacted]
22F	System	[redacted]	[redacted]
10F		[redacted]	[redacted]
12F	Branch Stent Graft System	[redacted]	[redacted]
14F		[redacted]	[redacted]

6.3. Trial Scope

This trial will be conducted at multiple domestic clinical centers, enrolling subjects from vascular surgery wards, cardiac surgery wards, emergency departments and other relevant settings. All subjects shall have a definitive preoperative diagnosis of aortic arch lesions, including true aortic arch aneurysm, pseudo-aortic arch aneurysm, and penetrating aortic ulcer.

7. Product Indications, Contraindications and Precautions

7.1. Indications

Applicable to lesions of the aortic arch, including true aortic arch aneurysm, pseudo-aortic arch aneurysm, and aortic arch ulcer.

7.2. Contraindications

(1) Patients with acute systemic infection.

(2) Patients with contraindications to antiplatelet and anticoagulant medications.

(3) Patients with allergies to contrast agents, anesthetic drugs, or materials of the stent and delivery system.

(4) Patients with vascular morphology unsuitable for endovascular repair.

7.3. Caution

(1) Prior to using this device, physicians must receive specialized professional training and maintain a thorough understanding of the principles, clinical applications, complications, adverse reactions, and potential risks of aortic stent graft procedures.

(2) This procedure typically involves the combined use of one integrated ascending aortic stent graft, one integrated aortic arch segment stent graft, and three branched stent grafts. Implantation of an additional aortic extension stent graft may be determined based on the patient's vascular anatomy. To effectively prevent endoleak, appropriate specifications and models for the

integrated ascending aortic stent graft, integrated aortic arch segment stent graft, aortic extension stent graft, and branched stent grafts shall be selected preoperatively.

(3) During advancement and positioning of the integrated ascending aortic stent graft system, positioning shall be guided by the proximal and distal radiopaque markers on the main stent graft, as well as the radiopaque markers at the integrated branch regions, to align these markers with the predetermined optimal deployment position.

(4) During advancement and positioning of the branched stent graft systems for the innominate artery and left common carotid artery, the positional relationship between the proximal radiopaque markers and the proximal radiopaque rings of the integrated branches within the lumen of the main integrated ascending aortic stent graft shall be considered; meanwhile, the positioning of the distal radiopaque markers within the corresponding branch arteries shall be ensured.

(5) During advancement and positioning of the integrated aortic arch segment stent graft system, the positional relationship between its proximal radiopaque markers and the previously deployed proximal segments of the innominate and left common carotid branched stent grafts shall be considered; the fenestration radiopaque markers shall be aligned with the orifice of the left subclavian artery.

(6) During advancement and positioning of the branched stent graft system for the left subclavian artery, the positional relationship between its proximal radiopaque markers and the distal radiopaque rings of the integrated branches within the lumen of the main integrated aortic arch segment stent graft shall be considered; meanwhile, the positioning of the distal radiopaque markers within the left subclavian artery shall be ensured.

(7) During advancement and positioning of the aortic extension stent graft system, the positional relationship between its proximal radiopaque markers and the distal radiopaque markers of the previously deployed integrated aortic arch segment stent graft shall be considered.

(8) After accurate positioning of the integrated ascending aortic stent graft, integrated aortic arch segment stent graft, aortic extension stent graft, and branched stent grafts, the handle position shall remain stationary until full deployment of all stent grafts; otherwise, inaccurate stent

positioning may occur.

(9) When the proximal or distal end of the integrated ascending aortic stent graft is adjacent to critical arterial branches (e.g., coronary arteries, innominate artery, etc.), angiography or other imaging modalities may be used to assist positioning and prevent coverage or occlusion of vital branch vessels by the graft fabric.

(10) Once the integrated aortic arch segment stent graft system contacts the integrated ascending aortic stent graft during advancement, no further upward pushing of the delivery system shall be attempted for positional adjustment; otherwise, severe consequences such as migration of the integrated ascending aortic stent graft, vascular injury, or stent deformation may occur.

(11) During selective catheterization of the two integrated branches of the integrated ascending aortic stent graft, full confirmation that the guidewire passes entirely through the integrated branch lumens is mandatory.

(12) This device consists of the integrated ascending aortic stent graft system, integrated aortic arch segment stent graft system, aortic extension stent graft system, and branched stent graft system. Each component is preloaded in its dedicated delivery system and individually packaged.

(13) The Modular Integrated Triple-Branched Aortic Arch Stent Graft System is sterilized with ethylene oxide prior to factory release.

(14) This device is intended for single-use only. The manufacturer assumes no liability for cross-infection or adverse outcomes resulting from unauthorized reuse of any stent graft, delivery system, or component of this device. Do not use the product if the sealed packaging is damaged prior to opening.

8. Overall Design

8.1. Trial Design

8.1.1. Trial Objectives

This study is a pre-market clinical trial of the WeFlow-Tribranch embedded aortic Triple-branch arch Stent Graft system. It aims to evaluate the safety and efficacy of the system, developed and manufactured by Hangzhou Endonom Medtech Co.; Ltd., in the endovascular interventional treatment of patients with aortic arch aneurysms, to provide clinical evidence for

the official domestic application of the device.

8.1.2. Trial Methodology and Rationale

This trial is designed as a prospective, multicenter, single-arm objective performance criterion clinical study.

Multicenter design: The trial will be conducted at multiple qualified domestic clinical centers. A multicenter approach facilitates patient enrollment, promotes benign competition among sites, and accelerates achievement of enrollment objective performance criterion. In addition, since subject data are collected from different regions and multiple centers by independent investigators, the final conclusions will be broadly representative.

Single-arm objective performance criterion design: Endovascular repair has become the preferred treatment for Stanford Type B thoracic aortic dissection; however, the management of lesions involving the ascending aorta or aortic arch remains challenging. Open surgery is the standard treatment for such diseases, yet it is associated with substantial surgical trauma, deep hypothermic circulatory arrest, antegrade/retrograde cerebral perfusion, and significantly elevated perioperative mortality and stroke rates. Patients enrolled in this trial generally present with aortic arch disease, advanced age, severe comorbidities, and are defined as high-risk individuals unsuitable for open surgery. Although existing thoracic aortic endovascular products can be modified and used off-label for aortic arch lesions, such structural adjustments lack adequate validation and carry potential safety and efficacy risks. Furthermore, no commercially available domestic device enables dual- or triple-branch reconstruction for supra-aortic arch vessels. Conservative medical treatment yields limited efficacy, and a more proactive intervention strategy is recommended for patients meeting intervention criteria. Setting a medical therapy control group would result in an extreme imbalance in risk–benefit profiles between the two arms. Therefore, a single-arm objective performance criterion design is adopted in this trial: a clinically meaningful objective performance criterion is predefined, and the safety and efficacy of the investigational device are evaluated without a parallel control group. The Guidelines for Clinical Trials of Transcatheter Implantable Artificial Aortic Valves issued by the NMPA recommend selecting clinically meaningful primary endpoints, with the 12-month cumulative all-cause mortality commonly proposed for sample-size estimation.

Considering the high clinical risk associated with ascending aortic and aortic arch diseases, and the anatomical proximity of the implant site to the aortic valve, the Guidelines for the Design of Medical Device Clinical Trials emphasize that primary endpoints should directly reflect clinical benefits and safety of the device. Accordingly, the primary endpoint of this trial is defined as the 12-month composite incidence of all-cause death or major stroke. In reference to the Guidelines for Clinical Trials of Aortic Stent Graft Systems, efficacy endpoints include the incidence of Type I or Type III endoleak, aortic stent graft migration rate, postoperative branch vessel patency rate, and conversion rate to open thoracic surgery or secondary interventional procedures. Safety endpoints comprise all-cause mortality, the incidence of serious adverse events, and the incidence of device-related adverse events. The objective performance criterion is established based on comprehensive, scientifically robust evidence from comparable marketed devices, while taking technological progress into account to ensure prospective rationality.

Medical records from five major hospitals in Honolulu, Hawaii, covering 1969 to 1977, reported 76 patients with atherosclerotic aortic aneurysms (including 10 involving the ascending aorta or aortic arch and 66 descending thoracic aortic aneurysms), with a mean age of 69 years and an estimated natural annual mortality of approximately 35%[24]. A 2002 database from Yale University documented the natural history of 1,600 patients with thoracic aortic aneurysms: once the thoracic aortic diameter reached 6 cm, 31% of patients experienced aortic rupture or dissection; when the descending aortic diameter reached 7 cm, the risk of rupture or dissection increased to 43%[11], with a mortality rate of up to 90% for such events. Prognoses are even poorer for surgically high-risk patients with arch-located aneurysms. Regarding penetrating aortic ulcers (PAU), the Chinese Expert Consensus on the Diagnosis and Management of Acute Aortic Syndromes (2021 Edition) recommends proactive surgical or endovascular repair for symptomatic PAUs, or those with a diameter > 20 mm or depth > 10 mm, due to the high risk of progression to pseudoaneurysm or rupture[25]. Published literature reports a natural annual mortality of 26.7% among patients with penetrating aortic ulcers[26]. The European Association for Cardio-Thoracic Surgery (EACTS) and the European Society for Vascular Surgery (ESVS) acknowledge that stroke remains a major complication during aortic arch endovascular repair, with reported rates up to 14%[27–29].

[redacted]

Measures to Reduce and Eliminate Bias

1) The clinical trial will be conducted in accordance with the trial protocol, national medical device clinical trial regulations and GCP principles as well as the company's standard operating procedures (SOP).

2) This clinical trial is a single-arm objective performance criterion study conducted simultaneously at multiple clinical centers across China. Subjects will be enrolled in accordance with the inclusion and exclusion criteria specified in the protocol. The enrolled study population shall maintain consistency with those investigated in previous studies, to minimize selection bias caused by incomparable baseline populations to the greatest extent possible.

3) Patients will be enrolled sequentially at each participating center and registered accordingly. A rigorous follow-up mechanism will be established, with sufficient communication maintained with the subjects to ensure high-quality follow-up, and to minimize missing data and participant dropout to the greatest extent possible.

4) The sponsor will provide training regarding the study protocol and the operation of the trial device to the investigators of this study to ensure that the investigators are fully aware of the study procedures and instructions regarding the proper use of the trial device.

5) The company will appoint qualified clinical trial investigators (CRAs) to visit and monitor the research center on a regular basis in order to maintain quality control and monitoring records, and to promptly communicate with the investigators regarding any problems found during the monitoring process.

6) They will furthermore be required to maintain and organize data and when data-related issues are found. Data analysts will check and confirm the data using a data challenge form to avoid

potential recording errors.

8.1.3. Trial Medical Device

Device Name: WeFlow-Tribranch embedded aortic Triple-branch arch Stent Graft system

Manufacturer: Hangzhou Endonom Medtech Co., Ltd.

8.1.4. Subject Selection

8.1.4.1. Selection Criteria (All of the following conditions must be met prior to enrollment)

1. Patients aged 18 to 80 years old
2. Patients diagnosed with aortic arch lesions requiring intervention, including true aortic arch aneurysms, pseudo-aortic arch aneurysms, and ulcers involving the aortic arch.
3. Patients showing a suitable vascular condition, including:
   - Ascending aorta length greater than 50 mm (from the aortic sinusoid junction to the proximal cardiac margin of the innominate artery).
   - Ascending aorta diameter ≥ 24 mm and ≤ 48 mm;
   - Proximal anchoring zone length ≥ 30 mm;
   - Innominate artery diameter ≤ 24 mm and ≥ 6 mm, length ≥ 20 mm；
   - Suitable arterial access for endovascular interventional treatment ;
4. Patients able to understand the purpose of the trial, participate in the trial voluntarily with informed consent form signed by the subject him/herself or his or her legal representative, and willing to complete follow-up visits as required under the protocol.
5. [redacted].

8.1.4.2. Exclusion Criteria (Enrollment will not be allowed if any of the following criteria are met)

1. Patients that have experienced systemic infection during past three months;

2. Neck surgery was performed within three months;

3. Previous endovascular interventional treatment involving the aortic arch was performed;

4. Infectious aortic disease、Takayasu arteritis，Marfan syndrome (or other connective tissue diseases);

5. Patients with severe stenosis, calcification, thrombosis or tortuosity;

6. Heart transplant patients;

7. Patients that have suffered MI or stroke during past three months;

8. Patients with Class IV heart function (NYHA classification);

9. Active peptic ulcers or upper gastrointestinal bleeding occurring within the previous three months;

10. Hematological abnormality, defined as follows: Leukopenia (WBC < 3 × 109/L), acute anemia (Hb < 90 g/L); thrombocytopenia (PLT count < 50 × 109/L), history of bleeding or coagulopathy;

11. Patients with renal insufficiency， serum creatinine > 150 μmol/L, and/or end-stage renal disease requiring renal dialysis;

12. Patients that are pregnant or breastfeeding;

13. Patients with allergies to contrast agents;

14. Patients with a life expectancy of less than 12 months;

15. Patients currently participating in other drug or device research;

16. Any other disease or abnormality that the investigators believe may hinder endovascular interventional treatment.

8.1.4.3. Dropout Criteria

All subjects who completed an informed consent form and were screened for entry into the clinical trial and who later withdrew, regardless of when and for what reason (excluding those who met the primary endpoint), will be counted as dropouts.

1) Subjects who withdraw themselves from the experiment for various reasons;
2) The ethics committee considers discontinuation of the study necessary for ethical and moral reasons due to one or more adverse events, especially serious adverse events;

3) The investigators consider it medically necessary for the subject to withdraw for the study;
4) There is a serious deviation from the trial protocol;
5) Subjects who are lost to follow up due to changes in work or living conditions or an accident, but for patients who are lost to follow up due to accidents such as traffic accidents, death, fractures, etc., a follow-up should be conducted promptly to determine whether or not there exists causal relationship with the trial device;
6) Subjects who are required to stop the trial for other reasons.

Notes: When a subject drops out due to a subject-related reason, the investigators should use all available avenues to contact the subject in order to inquire after the reason; if the subject drops out due to an adverse event, and the follow-up ultimately determines that there is a causal relationship with the trial device, the event must be recorded in the eCRF and the sponsor should be notified accordingly. All original data and source documents, i.e., retention files, which are also required for an intention-to-treat analysis (ITT Analysis), should be retained for all subjects who are enrolled and have entered the trial, regardless of whether they drop out.

8.1.4.4. Standards and Procedures for Stopping the Trial

Trial discontinuation refers to a situation in which the clinical study is not completed according to the protocol and all related clinical studies are stopped midway through the trial. Under all of the following conditions, with the exception of 5), will trigger mutual discussion between the sponsor and the investigator to determine whether or not to terminate the trial.

1) In the event that a serious safety concern arises during the course of the clinical trial the trial should be promptly terminated;
2) The trial should be discontinued when significant errors in the protocol are identified during the course of clinical studies, or when serious deviations in the implementation of the protocol make it difficult to evaluate the efficacy of the product;
3) The trial should be discontinued if the product is found to show sub-par efficacy or even complete inefficacy and is determined to be of no clinical value during the course of clinical research.
4) The trial is terminated upon the sponsor's request (e.g., due to funding issues, administrative reasons, etc.);
5) The trial is ordered to be terminated by the National Medical Products Administration

(NMPA) for any relevant reasons.

Early discontinuation of the trial must be agreed upon in writing by the principal investigator and the sponsor, and all trial data should be retained for reference purposes.

8.1.4.5. Enrollment Timetable

A subject may be enrolled upon obtaining confirmation that a signed informed consent form has been obtained, that the subject meets all entry criteria, and that the subject does not meet any exclusion criteria.

8.1.4.6. Expected Overall Duration of the Clinical Trial and Underlying Reasoning

In accordance with the relevant NMPA regulations on medical devices, this clinical study is scheduled to be conducted simultaneously at multiple qualified investigational centers across mainland China. Considering the patient volume at each center, the feasibility of implementing the protocol's inclusion and exclusion criteria, and the0 complexity of obtaining informed consent, the enrollment period is estimated to be 20 months. Mandatory CTA imaging follow-up will be performed at 30 days, 6 months, and 12 months post-operatively. A clinical summary will be prepared upon completion of the 12-month follow-up, and the 1-year clinical results will be submitted to the NMPA for review. Long-term follow-up will then continue from the 2nd to the 5th year; each subject will be followed for a total duration of 60 months. It is projected that the first subject will be enrolled in April 2024, and the final subject will be enrolled in December 2025. The overall study will be completed upon finalizing the 60-month follow-up of the last enrolled subject, which is estimated to occur in December 2030.

8.1.4.7. Expected Duration of Participation for Each Subject

For each subject, it is expected to take 60 to 62 months from the time of screening to performance of the procedure and the end of postoperative follow-up.

8.1.4.8. Number of Subjects Required for the Clinical Trial

The targeted number of valid cases for this study is 72. Considering a dropout rate of 20%, the total sample size is set at 90.

8.1.5. Primary Endpoints

Rate of all-cause mortality and major stroke within 12 months after surgery. All-cause mortality includes cardiac death, non-cardiac death, and death of unknown cause. Major stroke

is defined as a modified Rankin Scale (mRS) score ≥ 2 at 90 days after stroke onset (see Appendix 2).

Calculation formula:(Number of cases with all-cause mortality or major stroke at 12 months postoperatively / Total number of treated subjects) × 100%

8.1.6. Secondary Efficacy Endpoint

(1) Rate of immediate technical success following surgery. Immediate technical success is defined as successful delivery of the aortic and branching stent graft conveyors to their predetermined positions, accurate positioning and successful deployment of the stent, safe removal of the delivery device outside the body, and the absence of Type I and III endoleaks per imaging studies conducted at the end of the procedure with all branching stents patency.

(2) Rate of aortic aneurysm progression under control. Maximum increase in the diameter of the aortic aneurysm was ≤ 5 mm when compared with preoperative aortic aneurysm as of a 12-month postoperative CTA review.

(3) Incidence of Type I or Type III endoleaks. Intraoperative, 1-month, 6-month, and 12-month DSA or CTA imaging studies showing endoleaks. Intraoperative endoleaks subject to adjuvant treatment are not recorded. Endoleaks occurring after the completion of the procedure followed by one or more endoleaks occurring in the same subject at different follow-up stages that were not treated are counted as a single instance.

(4) Incidence of aortic covered stent graft displacement. CTA examination will be performed at 1, 6, and 12 months post operation to determine if the stent has migrated, and evaluations will be recorded for both the main and branch stents. Displacement is defined as a displacement of more than 10 mm in the aortic and branch stent grafts at follow-up time points compared with the 30-day postoperative reference imaging.

(5) Postoperative branch vessel patency rate. CTA examinations will be performed at 1, 6, and 12 months post-operation to evaluate branch vessel reconstruction and assess for occlusion, stenosis, or in-stent thrombosis.

8.1.7. Secondary Safety Endpoints

(1) Rate of conversion to thoracotomy or secondary intervention. Whether subjects require

conversion to open thoracic surgery or secondary interventional procedures due to new-onset aortic dissection caused by the index procedure.

(2) Rate of major adverse events occurring within 30 days after surgery. Refers to all-cause mortality, myocardial infarction, ischemic stroke or respiratory failure occurring within 30 days after surgery. More specifically, myocardial infarction refers to a drastic reduction or complete interruption of the coronary blood supply due to coronary artery disease, resulting in severe and prolonged acute ischemia of the corresponding myocardium, leading to necrosis of cardiomyocytes. Ischemic stroke refers to the end result of necrosis of brain tissue caused by narrowing or occlusion of the arteries supplying blood to the brain or insufficient blood supply to the brain. Respiratory failure is defined as a state resulting in significantly prolonged intubation, tracheotomy, deterioration of lung function, or other fatal outcomes.

(3) Rate of aortic aneurysm-related mortality at 12 months post operation. Refers to mortality caused by a ruptured aortic aneurysm or endovascular interventional treatment.

(4) Incidence of severe adverse events. Refers to an event that occurs during the clinical trial that results in mortality or serious deterioration in patient health, including a fatal illness or injury, a permanent defect in body structure or body function, or an event that requires medical or surgical intervention to avoid one or more permanent defects in body structure or body function.

(5) Incidence of device-related adverse events. Device-related adverse events refer to an adverse medical event related to the use of a device that occurs during the course of the clinical trial. However, a distinction should be made with respect to normal postoperative stress response, such as fever and chest and back discomfort, which, in the judgment of the investigator, need not be recorded as an adverse event. Recording device-related adverse events will be applicable for conditions that are deemed by the investigator to be definitely related, possibly related, or of indeterminate relationship, to the test device.

8.1.8. Standardization of Subject Screening and Selection Panel

Selection of subjects should be based on strict adherence to screening criteria at each test

center. Two vascular surgeons at each center need to clearly document the medical reasons for reaching their conclusions and additionally identify corresponding risks for each patient.

8.1.9. Imaging Examinations

Imaging studies will include echocardiography and angiography, and CT imaging should be standardized in terms of measurement methods used, such as the angle of measurement, data to be collected, reporting modalities, etc. CT scans must be used to provide information on vascular anatomy and potential lesions. The evaluation of the examination data, a qualified third-party core laboratory should be selected to evaluate imaging data.

8.2. Trial Procedure

1) Signing of informed consent;
2) Patient screening: Patients will be screened according to the inclusion criteria and exclusion criteria;
3) Patient enrollment;
4) Selection of trial products: Investigators determine the product specifications required by each subject, and the sponsor provides the corresponding product free of charge;
5) Performance of surgery: Surgery will be completed by the investigator;
6) Postoperative follow-up: Investigators are required to perform clinical follow-ups after surgery and prior to discharge, and on Day 30 and Months 6, 12, 24, 36, 48, and 60 following surgery, with CTA follow-up required on Day 30 and Months 6 and 12 following surgery, at the sponsor's expense;
7) Data analysis summary: The sponsor will collect all relevant data and information and commission a third party to evaluate and manage as well as statistically and analytically summarize the data.

8.2.1. Trial Procedure Chart

Trial Procedure	**Screening Period**	**procedure**	**Follow-Up**				
Visit	V1	V2	V3	V4	V5	V6	V7-10
Days	-15~0d	0	Discharge	30 ± 7 days after	6 months ± 30 days	12 months ± 30 days	Annually ±30 days from Year

				surgery	after surgery	after surgery	2 to Year 5 post-procedure
Signing of Informed Consent Form	X						
Inclusion/Exclusion Criteria	X						
Medical History/ Demographic data	X						
Pregnancy Test	X						
Physical Examination	X	X	X				
Blood Panel	X		X				
Urine Panel	X		X				
Coagulation Function	X		X				
Liver and Kidney Function	X		X				
Clinical Symptom Assessment (Modified Rankin Scale, mRS)	X		X	X	X	X	
12-Lead ECG	X		X				
Echocardiography	X						
Aortic CTA	X			X	X	X	X
Cerebral CTA	X						

or MRA							
DSA		X					
Surgical Records		X					
Medication Records	X	X	X	X	X	X	X
Adverse Event Records		X	X	X	X	X	X

Notes:

- Pregnancy Test: Women of childbearing age as well as women who are suspected of being pregnant during the trial will be subject to this test.
- Physical Examination: Heart rate, respiration, blood pressure and body temperature.
- Blood Panel: Erythrocytes, leukocytes, platelet count and hemoglobin.
- Urine Panel: pH, leukocytes, erythrocytes and proteins.
- Liver and Kidney Function: Creatinine (Cr), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL) and direct bilirubin (DBIL)
- Coagulation Function Testing: Activated partial thromboplastin time (APTT), prothrombin time (PT), internationalized standard ratio (INR), fibrinogen (FIB), thromboplastin time (TT) and D-dimer
- Data pertaining to past medication and past medical history for the three months preceding the date on which informed consent is obtained will be collected
- The CTA measurement data obtained during the screening period shall be reviewed and confirmed by the lead investigational site before subject enrollment can be initiated.
- Before discharge (Visit 3): Refers to a visit from the postoperative to a day before discharge, and the results of the last laboratory examination before discharge are collected;
- CTA data obtained prior to surgery and at 30 ± 7 days after surgery, 6 months ± 30 days after surgery and 12 months ± 30 days after surgery will be collected;

- Concomitant medication records: medications relevant to the evaluation of the investigational device (including anticoagulants, antiplatelet agents, antihypertensives, lipid-lowering drugs, hypoglycemic drugs, antibiotics, etc.); and medications administered for underlying diseases, concomitant diseases, or adverse events.
- Adverse event records: all adverse events starting from Visit V2.
- In the event of a stroke in a subject, the modified Rankin Scale (mRS) score shall be collected at 90 days after the stroke onset.
- If feasible, laboratory data obtained within 15 days prior to subject enrollment (before signing the informed consent form), as well as aortic CTA, cerebral CTA or Magnetic Resonance Angiography (MRA), echocardiography, and 12-lead ECG data obtained within 30 days prior to signing the informed consent form, may be used for baseline assessment without repeat testing.
- Long-term follow-up CTA data shall be collected at postoperative Years 2, 3, 4 and 5 (±30 days), with records of adverse events and concomitant medications related to adverse events.*Relevant examinations and data collection shall be performed only in patients randomized to the test group.

8.2.2. Trial Conduct

1) Visit 1: Screening Period (Day -15 to 0)

After the subject signs the informed consent form, baseline information and baseline examinations shall be collected, and screening shall be performed according to the inclusion and exclusion criteria. Eligible screened subjects will complete enrollment registration. The specific collected items are as follows:

- Demographic information, including age, gender, height, weight
- Physical examination data, including heart rate, respiration, blood pressure and body temperature
- Family history and previous medical history, including surgical history, concomitant diseases, concomitant medications and medical treatments
- Routine laboratory testing:
  - Blood panel: Erythrocytes, leukocytes, platelet count and hemoglobin

- Urine panel: pH, leukocytes, erythrocytes and proteins
- Liver and kidney function: Creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL) and direct bilirubin (DBIL)
- Coagulation function: Activated partial thromboplastin time (APTT), prothrombin time (PT), internationalized standard ratio (INR), fibrinogen (FIB), thromboplastin time (TT) and D-dimer

- Pregnancy test (for female patients of childbearing age)
- Clinical Symptom Assessment (Modified Rankin Scale, mRS)
- 12-Lead ECG
- CTA angiography
- Cerebral CTA or MRA
- Echocardiography examination
- Concomitant medications

2) Visit 2: Intraoperative (0 day)

Record the procedural details; the specific collected items are as follows:

- Physical examination data
- DSA imaging data
- Surgery-related records (selection of stent type, arterial access, deployment, Interventional operation time (the time the sheath enters the body to the time the sheath is pulled out of the body), immediate success, etc.)
- Concomitant medications
- Adverse events
- Device defects

3) Visit 3: Before discharge

- Physical examination
- Blood panel: Erythrocytes, leukocytes, platelet count and hemoglobin
- Urine panel: pH, leukocytes, erythrocytes and proteins
- Liver and kidney function: Creatinine, alanine aminotransferase (ALT), aspartate

aminotransferase (AST), total bilirubin (TBIL) and direct bilirubin (DBIL)

- Coagulation function: Activated partial thromboplastin time (APTT), prothrombin time (PT), internationalized standard ratio (INR), fibrinogen (FIB), thromboplastin time (TT) and D-dimer
- Clinical Symptom Assessment (Modified Rankin Scale, mRS)
- 12-Lead ECG
- Concomitant medications
- Adverse events
- Device defects

4) Visit 4: (30 ± 7 days after surgery)

This visit will be a post-discharge follow-up visit with the following information collected from the subject:

- Clinical Symptom Assessment (Modified Rankin Scale, mRS)
- Concomitant medications
- CTA angiography (aortic diameter, thrombosis status, branch vessel patency, arterial perfusion, etc.)
- Adverse events
- Device defects

5) Visit 5: (6 months ± 30 days after surgery)

This visit will be a post-discharge follow-up visit with the following information collected from the subject:

- Clinical Symptom Assessment (Modified Rankin Scale, mRS)
- CTA angiography (aortic diameter, thrombosis status, branch vessel patency, arterial perfusion, etc.)
- Concomitant medications
- Adverse events
- Device defects

6) Visit 7, 8, 9, 10: (24 to 60 months ±30 days after the procedure)

This visit will be a post-discharge follow-up visit with the following information collected from the subject:

- CTA angiography (aortic diameter, thrombosis status, branch vessel patency, arterial perfusion, etc.)
- Adverse events and concomitant medications related to adverse events

8.3 Device Usage Specification

After obtaining approval from the Ethics Committee, the Sponsor shall be responsible for providing the investigational medical devices to the clinical trial institutions and investigators, and determining the transportation conditions, storage conditions, storage duration, shelf life, etc.

The investigational medical devices shall be qualified in quality, with easy identification, proper coding, and affixed with the special label “For Clinical Trial Use Only”. They shall be properly packaged and stored in accordance with the requirements of the clinical trial protocol.

The Sponsor shall be responsible for the safety of the investigational medical devices during the clinical trial. When the Sponsor becomes aware of any issues that may affect the safety of subjects or that may alter the Ethics Committee’s approval for the continuation of the trial, it shall immediately notify all clinical trial institutions and investigators and take appropriate measures.

8.4. Monitoring Plan

In accordance with the requirements of the Medical Device Clinical Trial Quality Management Regulations, the sponsor will select inspectors who meet relevant requirements to perform inspection duties at all participating institutions. The number of supervisors and the frequency of supervision will be confirmed with the supervisor in accordance with the specific visit requirements and test procedures. Specific responsibilities shall include:

1) Confirm prior to the trial that clinical trial institutions are sufficiently equipped, including staffing and training, laboratories are fully equipped and in good working condition, there are enough subjects to participate in the trial and researchers are familiar with the trial requirements;
2) Monitor clinical trial institutions and researchers before, during, and after the trial to determine whether or not they are compliant with relevant regulations, the Medical Device Clinical Trial Quality Management Regulations and the clinical trial protocol;

3) Confirm that each subject signs an informed consent form prior to participating in the clinical trial, and understands the state of subject enrollment and trial progress; ascertain and record instances of failure to follow-up, perform testing or perform examinations by the investigators as well as whether or not such errors were subject to correction; and ensure that patients who have yet to complete the trial procedure and who are affected by revisions to the informed consent form re-sign the form;
4) Confirm that all case report forms are correctly filled out and consistent with the original data; all errors or omissions have been corrected or noted, and signed and dated by the investigator; and the disease type, total number of cases and the gender, age, and treatment efficacy pertaining to each case are confirmed and recorded;
5) Confirm that subject withdrawal from the clinical trial or failure to comply with the requirements specified in the informed consent form are recorded, and discusses the situation with an investigator;
6) Confirm that all adverse events, complications and device defects are recorded, and serious adverse events and device defects that may cause serious adverse events are reported and recorded by the appropriate deadlines;
7) Monitor the provision, use, maintenance, transportation, receipt, storage, distribution, processing, and recycling of trial medical devices;
8) Supervise regular maintenance and calibration of related equipment during the clinical trial;
9) Ensure that all clinical trial related documents received by investigators are current;
10) The monitor should issue a written report to the sponsor after each monitoring session; the report shall include the name of the monitor, the date of the monitoring session, the time of the monitoring session, the location of the monitoring session, the content of the monitoring session, the names of any related investigators, the completion status of the project, existing problems, a conclusion, and corrections, etc. to any errors or omissions.

9. Statistical Considerations

9.1. Sample Size Calculation

9.1.1. Total Sample Size

[redacted]

After accounting for a 20% dropout rate, the total sample size is determined to be 90 subjects. The sample size calculation formula is presented below:.

$$n = \frac{\left[Z_{1-\alpha/2}\sqrt{P_0(1-P_0)} + Z_{1-\beta}\sqrt{P_T(1-P_T)}\right]^2}{(P_T - P_0)^2}$$

Where: P_T denotes the expected event rate of the investigational device, and P_0 denotes the objective performance criterion.

9.1.2. Number of Clinical Trial Subjects per Disease and Basis for the Determination Thereof

This study does not address issues of multimorbidity, so only the total number of clinical trial subjects is subject to requirements.

9.1.3. Minimum and Maximum Number of Subjects per Clinical Trial Institution and Corresponding Reasoning

This trial will be conducted simultaneously at multiple qualified clinical trial institutions in China. In principle, the number of enrolled subjects will be distributed as evenly as possible across each center to ensure sufficient center representativeness. However, considering feasibility and enrollment progress, adjustments to the number of enrollments will be made based on actual conditions to maintain a relatively balanced enrollment size per center. The final enrollment size of any given single center shall not exceed 50% of the total number of subjects.

9.2. Analysis Sets

The trial's statistical analysis will be conducted on the basis of the following analyzed populations,

which need to be clearly defined before the statistical analysis begins, and in this trial they include:

1. Full Analysis Set (FAS): Refers to the subject set that is as close as possible to intention-to-treat (ITT) principles, which is derived from all randomized subjects with minimal and reasonable censoring, and contains all subjects who have been subject to randomization and have previously used an investigational device. The FAS will be used for the evaluation of primary and secondary indicators.

2. Per Protocol Set (PPS): All patients showing good compliance with the trial protocol, good adherence, completion of the treatment specified in the trial protocol and no deficiencies in key efficacy indicators. The PPS will be used for the evaluation of primary and secondary indicators.

3. Safety Set (SS): All subjects who used an investigational device following randomization and underwent a safety evaluation. The SS will be is used for an analysis of safety indices.

9.3. Elimination Criteria

Prior to the statistical analysis of data, the principal investigator, sponsor, and statistical analysis institution shall assess whether an individual subject meets any of the following conditions. The principal investigator shall comprehensively determine whether to eliminate the subject from the analysis sets based on factors including the subject's completion of the trial, reasons for trial, and shall issue a relevant written explanation for the elimination. A subject shall be considered for elimination if any of the following criteria is met:

1) The subject was enrolled in violation of the inclusion/exclusion criteria and should not have been admitted to the trial.
2) During the trial, the investigator determined that the subject had other factors precluding continued trial participation, and the subject's trial participation was formally terminated.
3) Major protocol deviations occurred during the implementation of the clinical trial protocol, including subjects whose treatment regimen were modified during the trial.
4) The subject failed to comply with the trial plan with poor compliance, which has impaired the efficacy or safety evaluation. Examples include: never used the investigational medical device, failure to collect data required for efficacy and safety evaluation in accordance with the trial protocol, and absence of any observation data.

9.4. Statistical Design, Methodology and Analytical Procedures

9.4.1. Statistical Design

This clinical trial adopts a prospective, multi-center, superiority, randomized controlled trial design to evaluate the efficacy and safety of the investigational device.

9.4.2. Statistical Methodology and Analysis

1) General Principles

For quantitative variables, mean, standard deviation, median, minimum, maximum, lower quartile (Q1), and upper quartile (Q3) will be calculated. For categorical variables, the number and percentage of subjects in each category will be presented.

Comparison of general characteristics between the two groups will be analyzed using appropriate methods according to the type of variables. Between-group comparisons of quantitative data will be performed using the independent samples t-test (for homogeneous variance and normal distribution) or the Wilcoxon rank-sum test, depending on the data distribution. Categorical data will be analyzed using the chi-square test or Fisher's exact test (if the chi-square test is not applicable). Ordinal data will be analyzed using the Wilcoxon rank-sum test or the CMH test.

2) Completion Status and Demographic Analysis

The number of enrollments and completions for each center will be summarized and a list of fallout cases as well as a detailed list of reasons for non-completion will be created. Patients' demographic characteristics (age, sex, etc.), relevant medical history treatment, etc. will be described. A demographic analysis will be performed based on an FAS analysis set.

3) Primary Endpoints

Primary Endpoint: The incidence of all-cause death or major stroke within 12 months after the procedure. All-cause death includes cardiac death, non-cardiac death, and death of unknown cause. Major stroke is defined as a modified Rankin Scale (mRS) score ≥ 2 assessed at 90 days after stroke onset. The hypothesis testing is specified as follows:

Null Hypothesis: H0: $P_T - P_C \leq \Delta$

Alternative Hypothesis: H1: $P_T - P_C > \Delta$

$\alpha = 0.025$ (single tail)

At the significance level of $\alpha = 0.025$ (one-sided) and statistical power of $1-\beta = 0.8$, the incidence rate of all-cause mortality or major stroke within 12 months post-procedure shall be statistically described, and its two-sided 95% confidence interval (95% CI) shall be estimated. The upper limit of the 95% CI

shall be compared with the Objective Performance Criteria (OPC). Statistical conclusions will then be drawn accordingly. If the upper limit of the 95% CI is lower than the objective performance criterion P_0, the primary endpoint shall meet the trial requirements, and the investigational device can be considered to satisfy the requirements for clinical application.

4) Secondary Endpoints

Technical success immediately post-procedure, aortic aneurysm progression control rate, incidence of Type I or Type III endoleak, incidence of aortic stent graft migration, postoperative patency rate of branch vessels, incidence of conversion to open thoracic surgery or secondary interventional procedure, major adverse event rate within 30 days post-operation, aortic aneurysm-related mortality at 12 months post-operation, incidence of serious adverse events, and incidence of device-related adverse events.

Statistical description shall be performed for secondary efficacy indicators, with frequencies and percentages calculated. FAS (Full Analysis Set) and PPS (Per Protocol Set) analyses shall also be conducted.

Statistical description shall be performed for secondary safety indicators, with frequencies and percentages calculated. The SS (Safety Set) analysis shall be adopted as the primary approach.

The Kaplan-Meier method shall be used to estimate the survival rate and its 95% confidence interval, with Kaplan-Meier curves plotted accordingly.

Descriptive statistical analysis shall be performed for the changes of all laboratory parameters before and after the trial. All adverse events occurring during the trial shall be recorded in detail; descriptive statistical analysis of adverse events shall be conducted with a list attached.

In addition to the above statistical methods, detailed and additional exploratory analyses may be required, which shall be confirmed in the Study Report and Statistical Analysis Plan (SAP)..

9.5. Statistical methods for all data, including the handling of missing, unused or erroneous data (including premature discontinuation and withdrawal) and inconsistent data.

A Statistical Analysis Plan (SAP) shall be developed prior to study initiation. After database lock, statistical analysis shall be performed in accordance with the SAP, and a statistical analysis report shall be generated based on the results.

（1）Handling of missing data: Missing data shall be handled according to the analysis set in which they are included. Missing data for the primary endpoint in the Full Analysis Set (FAS) shall be classified by reason as follows:

Missing data clearly due to unsatisfactory efficacy: loss to follow-up or missing primary efficacy data resulting from adverse events, death, etc., related (or possibly related) to the investigational device or aortic dissection.

Missing data not attributable to unsatisfactory efficacy: loss to follow-up, failure to complete assessments, or other reasons such as force majeure (e.g., epidemic restrictions) resulting from adverse events, death, etc., unrelated to the investigational device or aortic dissection.

For the first category of missing data, worst-case imputation shall be used in both the FAS and Per Protocol Set (PPS), treated as “12-month postoperative failure”. For the second category of missing data, three imputation methods shall be applied separately, followed by sensitivity analysis:

1)Best-case imputation: all treated as “12-month postoperative success”; 2)Worst-case imputation: all treated as “12-month postoperative failure”; 3)Tipping-point analysis: the imputation proportions of success and failure in the two groups shall be varied iteratively to comprehensively demonstrate whether the study meets the statistical hypothesis under different scenarios and to identify the tipping point at which the conclusion changes.

No statistical imputation shall be used for missing data of other endpoints.

（2）Handling of inconsistent data: During data management, logical checks shall be performed on the database. Inconsistent data shall be queried via data query forms sent to investigators. Inconsistent data shall be resolved based on written responses from investigators. The database shall not be locked until all inconsistent data has been resolved.

（3）Handling of erroneous data: During data management, quality control should be conducted on the database. Erroneous data shall be identified and queried via data queries (Query). Errors shall be corrected based on investigators’ responses, and queries shall be closed only after confirmation from investigators. The database shall not be locked until all erroneous data has been corrected.

9.6. Deviations from the Original Statistical Plan

Changes to the original statistical analysis plan due to changes to the protocol should be agreed

upon among multiple parties, including the sponsor, investigators, data management and statistical analysis staff, and ethics staff and should be made in strict compliance with clinical trial operating regulations and procedures, and changes will not be made lightly otherwise.

10. Data Management

10.1. Data Management System

The data collection/management system used for this trial corresponds to an electronic data capture (EDC) system. An EDC system that has been systematically validated and has trace management and user rights management has been selected.

10.2. eCRF Design

The data manager will design the eCRF according to the needs of the protocol and each eCRF will contain all the data points specified in the protocol, excluding external data. eCRFs will be directly exported from the corresponding EDC system (in PDF format).

10.3. Data Management Plan

The data manager will draft a DMP based on the finalized protocol, project requirements, etc. It will furthermore be determined after discussion by all parties involved in the clinical trial.

10.4. Data Verification Plan

The data manager will draft a data verification plan based on the clinical trial protocol and eCRFs. It will furthermore be determined after discussion by all parties involved in the clinical trial.

10.5. Electronic Database Construction and Testing

A database builder will construct the database, including configuring logical verification rules, system function settings, etc.; a data administrator will manage rights according to each user's job role(s). Database testing will include entry, export, logical verification, eCRF interface, and system functionality testing.

10.6. Database Training and Formal Launch

Prior to the official launch of the trial database, the data manager will train relevant personnel. The training will include: System operation skill training and/or project requirement training. The specific nature of the training will depend on each participant's responsibilities and previous experience. Database launch: Once the database passes testing and all other preparatory work is

completed and following confirmation by the sponsor, the database will be officially launched.

10.7. Data Verification

Data verification includes source data verification (SDV) conducted by monitors through comparing electronic Case Report Forms (eCRF) with source documents, logical review by the medical team in accordance with the Medical Review Plan, and verification by the data management team in accordance with the verification rules specified in the Data Review Plan. In case of any queries, the personnel responsible for queries may directly issue manual queries in the database. If data violates the system verification rules configured by the data management team in the database, the system will generate automated queries. After the data entry personnel confirm the source data and clarify the queries, the personnel responsible for queries shall confirm the data status and clarification description and may close the query only after confirmation of correctness. This process may be repeated until no data queries remain. The generation and resolution of all queries, as well as all data updates and modifications, will be automatically saved in the system audit trail for reference.

10.8. Medical Coding

Medical terminology included in clinical trial data must be standardized prior to carrying out statistical analysis. Medical codes need to be created systematically or manually, based on a medical code dictionary that is in common use in the field of clinical trials. Data that do not meet the requirements of the selected medical coding dictionary or for which there exist unresolved questions need to be confirmed with a clinical investigator in the form of a data query. Medical coding content may include: Past medical history, concomitant medications and adverse events. The specific requirements for coding are defined in the Data Management Plan.

10.9. External Data Management

When external data exists for the clinical trial, the data manager must develop an external data management plan and plan out the entire process for managing external data during the clinical trial in advance.

10.10. Data Backup

The system will be automatically backed up daily on a data management cloud server.

10.11. Data Review

Data generated during the course of a clinical trial may violate the clinical trial protocol, requiring a clinical data review at the general trial level. Problems identified in the data review can be addressed by taking appropriate measures, such as revising the clinical trial protocol and censoring subject data.

10.12. Locking of Data

At the end of the study, once the database lock list has been reviewed, the principal investigator, sponsor, statisticians, data managers, supervisors, and other relevant personnel will jointly authorize locking of the database. When data errors are discovered after the database is locked, the potential impact of these data errors on the safety and efficacy analyses will be assessed jointly by the principal investigator, sponsor, statisticians, data managers, and related personnel. If there is a significant impact on the above, the stakeholders will co-sign to unlock the database after which data corrections can be made; if there is no significant impact, the errors in question will be documented in corresponding statistical analysis and clinical summary reports.

10.13. Data Management Reports

The data manager will summarize the process by which data management work was performed as well as operational specifications and management quality and thereby draft a data management report.

11. Feasibility Analysis

11.1. Probability of Success Analysis

The investigational device will be manufactured in accordance with the requirements of the medical device quality management system. The trial device was analyzed and evaluated for physical, chemical and biological properties as well as associated risks, and the results of the analysis demonstrated the feasibility and safety of the product; furthermore, all risks were identified as within acceptable limits, with potential clinical benefits outweighing the risks of use and the device was determined to be more beneficial to subjects' health, with the potential to improve their quality of life.

This trial device was tested on animals and complete experimental data were obtained during the animal testing process, with no adverse events reported in animal test results, demonstrating that the product is safe and effective (refer to the Animal Studies Report).

11.2. Probability of Failure Analysis

- Subjects experienced serious adverse events and an excessive level of dropouts;

- Information provided on the label does not effectively provide guidance to the operator;
- Too many subjects were lost to follow-up;

However, the above factors remain under control, and assuming training can improve the level and proficiency of operation, the investigators have also developed a complete test protocol accounting for the specific nature of the trial.

In addition, the clinical institutions undertaking the trial are well endowed with equipment and technical resources, and the clinical trial leadership has excellent clinical experience, so the likelihood of trial failure is low.

12. Clinical Trial Quality Control

In order to ensure the accuracy and completeness of the data in each eCRF, the implementing institution or a designated supervisor must monitor the research center on a regular basis. During each monitoring visit, the data submitted by the center needs to be compared with corresponding raw data. Investigators' compliance with appropriate regulations and research guidelines will also be assessed.

Researchers must ensure that medical documentation is kept properly and remains intact. Research documents should be subject to inspection by the implementing organization and/or regulatory authorities. Supervisors need to confirm that the rights and welfare of subjects are protected, that the research adheres to GCP guidelines, and that the trial protocol is followed.

13. Clinical Trial Ethical Issues and Informed Consent

13.1. Ethical Considerations

This clinical trial is conducted in compliance with the Declaration of Helsinki and applicable national regulations. The investigator is responsible for submitting the clinical trial protocol, informed consent form, and informational materials provided to subjects to the Ethics Committee, in order to obtain an independent approval document for the conduct of the clinical trial. Approval from the Ethics Committee must be obtained before initiation of the clinical trial. Written approval from the Ethics Committee shall be issued to the investigator, who shall then provide a copy of the approval document to the study sponsor. The Ethics Committee’s approval document shall be accompanied by a list of all committee members involved in the review and approval, together with their respective roles.

During the clinical study, any issues related to the safety of the clinical study, such as amendments to the clinical trial protocol or the informed consent form, and serious adverse events occurring during the study also must be promptly reported to the Ethics Committee. The completion or early termination of the clinical study must also be reported to the Ethics Committee.

13.2. Trial Protocol Approval

Prior to the clinical study, the investigator shall submit the clinical study protocol, informed consent form and other relevant documents to the Medical Ethics Committee of the hospital where the institution of the clinical study responsible is located. The clinical study may only commence after obtaining approval from the Ethics Committee. Any amendments to the study protocol shall be implemented only after approval by the Ethics Committee. Serious adverse events during the clinical study shall be reported in a timely manner in accordance with GCP requirements.

13.3. Informed Consent Process

It is the responsibility of the investigators to explain the purpose, methods, benefits, and potential risks of the clinical trial to each subject and to obtain an informed consent form signed by each subject of the clinical trial. Informed consent must be obtained from the subject prior to the commencement of any operational procedures associated with the clinical trial. For those subjects who, for any reason, are unable to sign an informed consent form themselves, their guardian or witness must sign the informed consent form. By signing an informed consent form, the subject shall authorize the clinical study monitor/auditor/health investigation organization to verify raw data that has been obtained from the clinical study to determine the reliability of the clinical study data.

14. Provisions for Reporting Adverse Events and Device Defects

14.1. Adverse Events

An adverse medical event that occurs during the conduct of a clinical trial of a medical device, regardless of whether it is related to the investigational medical device.

Any pre-existing disease documented in medical history during the screening period shall not be considered an adverse event unless there is a change in its nature, severity, frequency, or required intervention.

14.1.1. Severity Assessment of Adverse Events

Mild: Symptoms are slight and do not interfere with normal daily activities, generally, no treatment is required, and symptoms are resolved spontaneously.

Moderate: Symptoms are sufficient to cause discomfort and interfere with normal daily activities; treatment may be required.

Severe: Symptoms result in significant discomfort; may lead to subject withdrawal from the trial; may result in discontinuation of treatment with the investigational device; specific treatment is required.

14.1.2. Causality Assessment between Adverse Event and Investigational Medical Device

1.Relatedness to the investigational product:

Related to the investigational medical device: (1) There is a reasonable temporal relationship. (2) The event is a known risk of the device or can be explained by its mechanism of action. (3) The injury improves or resolves after cessation of device use. (4) The injury recurs upon rechallenge with the device. (5) The event cannot be explained by other confounding factors. If all five criteria are met, the relationship is assessed as "Definite”; if at least two criteria are met, it is assessed as "Possible".

Not related to the investigational medical device: (1) There is no reasonable temporal relationship. (2) The event type cannot be caused by the investigational medical device. (3) The event can be explained by concomitant devices/medications, disease progression, or other therapeutic interventions. (4) Definitely Not Related: All 3 criteria are satisfied. (5) Probably Not Related: At least 1 criterion is satisfied.

2. Relatedness to the procedure:

Definitely related: The reaction is consistent with the known reaction profile of the procedure.

Probably related: The reaction is consistent with the known reaction profile of the procedure; the patient’s clinical condition or other treatments may also contribute to the reaction.

Probably unrelated: The reaction is poorly consistent with the known reaction profile of the procedure; the patient’s clinical condition or other treatments may account for the reaction.

Definitely unrelated: The reaction is inconsistent with the known reaction profile of the procedure; the patient’s clinical condition or other treatments can fully explain the reaction; the reaction resolves upon improvement of the underlying disease or discontinuation of other treatments,

and reappears following reintroduction of such other treatments.

14.2. Severe Adverse Events

A Serious Adverse Event refers to any untoward medical occurrence during a clinical trial of a medical device that results in death or severe deterioration of health status, including fatal disease or injury, permanent impairment of body structure or function, requirement for hospitalization or prolongation of hospitalization, medical intervention required to prevent permanent impairment of body structure or function, fetal distress, fetal death, congenital anomaly or congenital defect.

Planned hospitalization due to a pre-existing disease or surgery specified in the clinical trial protocol that does not cause severe deterioration of health status shall not be regarded as a Serious Adverse Event.

14.3. Device Defects

Device defects refer to unreasonable risks that may endanger human health and life during normal use of the medical device and may include label errors, quality problems, and other malfunctions.

14.4. Reporting Procedures

14.4.1. Adverse Events

Adverse event data will be collected throughout the study, and the investigators will record and monitor all adverse events in the appropriate eCRF until recovery or stabilization occurs.

14.4.2. Severe Adverse Events

If a serious adverse event occurs during the course of the trial, regardless of whether it is related to the study device, appropriate therapeutic measures must be taken immediately and reported in writing to the medical device management department of the corresponding clinical trial facility, and the sponsor must be notified. The medical device clinical trial management department shall report in writing to the corresponding institutional review board as well as the Food and Drug Supervision and Administration Department of the province, autonomous region or directly governed municipality where the clinical trial institution is located within 24 hours. The clinical trial institution and investigators should provide the corresponding institutional review board and sponsor with all needed information in the event of a subject death. The sponsor shall report to the competent Food and Drug Supervision and provincial Administration Department and Health and Family Planning Department

within 5 working days, and shall notify other clinical trial institutions and investigators participating in the trial, as well as notify the institutional review board of the clinical trial institution via the institution's medical device clinical trial management department.

14.4.3. Potential Adverse Events

Allergies, aortic dissection enlargement, aortic dissection rupture, arterial thrombosis, arterial injury, arterial perforation, arteriovenous fistula, pseudoaneurysm, hemorrhage/hematoma, bowel syndrome, pulmonary syndrome, heart failure/myocardial infarction, intermediate surgery, death, edema, sexual dysfunction, fever, renal insufficiency/failure, wound syndrome, air embolism and device complications, including: incorrect release position, stent migration, stent breakage, endoleak and coating rupture.

14.4.4. Device Defects

In the event that a device defect is found during the course of the clinical trial, the investigators should record all device defects discovered during the course of the clinical trial and analyze the cause of the incident alongside the sponsor to create a written analysis report which recommends whether to continue, suspend or terminate the trial, and the clinical trial institution's medical device clinical trial management department shall report said findings to the institutional review board for review.

For any device defect which may result in a serious adverse event, the sponsor shall report said event or defect to the competent Food and Drug Supervision and provincial Administration Department and Health and Family Planning Department within 5 working days after being informed of the event, and shall notify other clinical trial institutions and investigators participating in the trial, as well as notify the institutional review board of the clinical trial institution via the institution's medical device clinical trial management department.

15. Provisions Pertaining to Clinical Trial Protocol Deviations and Clinical Trial Protocol Revisions

15.1. Protocol Deviations

A protocol deviation refers to a case of non-compliance with protocol requirements, which in turn makes data unavailable or inaccessible.

Protocol deviations include, but are not limited to:

- An operation was not performed within the permitted follow-up window
- Required data was not obtained
- Follow-up procedures were conducted at an unapproved center

15.2. Protocol Violations

A protocol violation refers to a case of non-compliance with protocol requirements and/or regulatory guidelines. Protocol violations may affect the scientific validity of the study and/or the rights and safety of subjects.

Protocol violations include, but are not limited to:

- Failure to obtain informed consent
- Violations of the inclusion/exclusion criteria
- Violations of protocol requirements which affect the main objectives of the study design

In some cases, compliance issues may arise during the informed consent process. Investigators should try to obtain guidance from the ethics committee of the research center to ensure that subjects receive the appropriate information required to make a decision as to whether or not to participate in the trial. The investigators are obligated to take any measures that the EC deems necessary, including subject withdrawal. In the analysis of the study data, deviations from the consent process of subjects who were deemed by the EC to be available for continued participation in the study would be considered a protocol violation.

15.3. Provisions Governing Revision of the Clinical Trial Protocol

A clinical trial protocol for medical device testing should as a primary matter of principle provide the maximum protection possible of the rights, safety and health of subjects and should be jointly designed and formulated by the medical institution responsible for the clinical research as well as the sponsor, and implemented only after approval by an ethics committee; if there is any modification of the clinical trial protocol, informed consent, or case report form during the course of the trial, said modification must be approved by the ethics committee before continuing the clinical trial.

16. Direct Access to Source Data and Files

All clinical findings, observations, and other activities carried out throughout clinical study must be documented and maintained in the medical records of each enrolled subject, either in the original

records or in a copy that is consistent with the original. For data recorded on an eCRF, the corresponding medical records (source documents) must also show the same source data.

The medical records (source documents) must contain, but are not limited to contain, the following information:

- Date of informed consent
- The fact that the subject is participating in a clinical trial
- Demographic characteristics
- Dated discharge reports
- Medical history / surgical history records and previous medications
- Size and characteristics of blood vessels and lesions
- Description of device use (all materials used, intraoperative medications, dates, times, etc.)
- All adverse events (AEs, SAEs, ADEs and SADEs): Diagnosis and symptoms, start and end dates, severity, measures taken and outcome
- Concomitant medication
- Clinical trial outcome or withdrawal date

The following additional documents are considered source documents and must be filed with corresponding medical records / subject records:

- Serious adverse event reports

Clinical trial institutions should retain all clinical trial data for a period of 10 years after the end of the clinical trial. The sponsor should save clinical trial data until the medical device is no longer in use.

17. Financing and Insurance

The research funding required for this trial is being provided by Hangzhou Endonom Medtech Co., Ltd.; refers to the clinical study protocol for specific costs and details.

To ensure the rights and safety of subjects, the sponsor will purchase clinical trial insurance for subjects participating in this study, referring to the Insurance Policy for details and terms.

18. Content to be Covered in the Clinical Trial Report

After the completion of the clinical trial, the medical institution undertaking the clinical trial shall issue a clinical trial report in accordance with the requirements of the medical device clinical trial

protocol and corresponding prescribed format. The clinical trial report shall include the name and specifications of the trial device, a summary of the clinical protocol, a list of participating centers, a statistical analysis of the population, a record of adverse events occurring during the clinical trial and measures taken in response, an analysis of clinical trial results, product indications, contraindications and precautions, clinical trial conclusions and the opinions of the investigators and clinical trial management department of the clinical trial institution.

19. Confidentiality

The personal data of study participants enrolled in this clinical trial shall be kept confidential. However, the administrative department of the medical device clinical trial institution, the ethics committee, the drug regulatory authority, the health authority, as well as monitors and auditors, may access the participants' personal clinical trial data in accordance with prescribed procedures when necessary for their official duties.

20. Stipulations Governing the Publication of Trial Results

The sponsor and investigators should agree upon a final version of the trial report.

Hangzhou Endonom Medtech Co., Ltd. shall have the right to include the clinical trial report in any registration documents or registration declarations as well as in any information materials compiled for use by medical professionals.

Prior to publication of the entire multicenter clinical trial results, information from each center cannot be published separately, and all research papers must be reviewed by Hangzhou Endonom Medtech Co., Ltd.

All information pertaining to the trial device (e.g., patent applications, previously undisclosed manufacturing processes provided to the researcher by the sponsor, basic scientific data, etc.) is considered confidential and is the exclusive property of the sponsor. Investigators may not use the above information for other purposes without the express written permission of the sponsor.

21. Allocation of Responsibilities

21.1. Responsibilities of the Sponsor

(1) The sponsor shall be responsible for the authenticity and compliance of the medical device clinical trial. Where the sponsor is an overseas institution, it shall appoint a Chinese enterprise legal person as its legal agent in accordance with relevant laws and regulations to assist the sponsor in fulfilling its obligations.

(2) The sponsor's quality management system shall cover the entire process of the medical device clinical trial, including selection of clinical trial institutions and principal investigators, design of the clinical trial protocol, conduct of the clinical trial, documentation, reporting of results, and archiving of records. The sponsor's quality management measures shall be appropriate to the risks of the clinical trial.

(3) Before initiating a medical device clinical trial, the sponsor shall: (i) Ensure that the product design is finalized, and that pre-clinical studies of the investigational medical device have been completed, including performance verification and validation, product inspection reports based on the product technical requirements, risk-benefit analysis, etc., and that the results support the clinical trial; (ii) Select registered medical device clinical trial institutions, specialties, and principal investigators according to the characteristics of the investigational medical device; (iii) Be responsible for developing and providing the investigator's brochure, clinical trial protocol, informed consent form, case report form, standard operating procedures, and other relevant documents to the medical device clinical trial institutions and principal investigators.

(4) The sponsor shall sign a contract with the medical device clinical trial institutions and principal investigators to clarify the rights and obligations of all parties in the clinical trial.

(5) After the medical device clinical trial has been approved by the ethics committee and the contract with the clinical trial institution has been signed, the sponsor shall register the clinical trial with the drug regulatory authority of the province, autonomous region, or municipality directly under the Central Government where the sponsor is located.

(6) The medical device clinical trial institution may start informed consent and screening of the first subject only after completion of clinical trial registration.

(7) Before initiation of the medical device clinical trial, the sponsor shall organize training related to the clinical trial, including the working principle, intended use, product performance, operation method, installation requirements, technical specifications of the investigational medical device, as well as the clinical trial protocol, standard operating procedures, and other relevant documents.

(8) The sponsor shall provide the investigational medical device free of charge in compliance

with the Good Clinical Practice for Medical Devices (2022).

(9) The sponsor shall pay for expenses related to the medical device clinical trial for subjects. In the event of injury or death related to the medical device clinical trial, the sponsor shall bear the corresponding medical expenses, compensation, or indemnity, excluding injuries caused by negligence of the investigator and the clinical trial institution, or progression of the subject's underlying disease.

(10) The sponsor shall be responsible for the assessment and reporting of safety information during the medical device clinical trial.

(11) The sponsor shall assume responsibility for monitoring the medical device clinical trial, establish standard operating procedures for monitoring, and appoint monitors who meet the requirements of the Good Clinical Practice for Medical Devices (2022) to perform monitoring duties.

(12) To ensure the quality of the clinical trial, the sponsor may appoint auditors independent of the clinical trial, with appropriate training and experience, to conduct audits of the conduct of the clinical trial and assess compliance with the protocol, this regulation, and relevant laws and regulations.

(13) The sponsor shall ensure that the medical device clinical trial is conducted in accordance with the protocol. If the sponsor finds that the clinical trial institution or investigator fails to comply with the protocol, this regulation, or relevant laws and regulations, it shall promptly point out and correct the non-compliance. In case of serious or persistent non-compliance, the sponsor shall terminate the participation of such institution and investigator in the clinical trial and submit a written report to the drug regulatory authority of the province, autonomous region, or municipality directly under the Central Government where the clinical trial institution is located.

(14) The sponsor shall submit a written report to all principal investigators, the administrative department of the medical device clinical trial institutions, and the ethics committees within 10 working days after suspension, termination, or completion of the clinical trial.The sponsor shall report to the drug regulatory authority of the province, autonomous region, or municipality directly under the Central Government where the sponsor is located within 10 working days after termination or completion of the clinical trial.

21.2. Responsibilities of the Ethics Committee

(1) The Ethics Committee shall be responsible for protecting the legitimate rights, interests and safety of subjects, and safeguarding their dignity.

(2) The Ethics Committee shall comply with the ethical principles of the Declaration of Helsinki (World Medical Association) and relevant laws and regulations. The composition, operation and filing management of the Ethics Committee shall meet the requirements of the health administration department.

(3) All members of the Ethics Committee shall receive training in ethical knowledge, these Regulations and relevant laws and regulations, be familiar with the ethical principles and relevant laws and regulations for medical clinical trials and abide by the working procedures of the Ethics Committee.

(4) The Ethics Committee shall review the ethical acceptability and scientific validity of the medical device clinical trial.

(5) The Ethics Committee shall conduct follow-up oversight of the medical device clinical trial. If it finds that the rights, interests and safety of subjects cannot be guaranteed, it may require in writing the suspension or termination of the clinical trial at any time.

(6) The Ethics Committee shall review safety information such as serious adverse events occurring at the trial site reported by investigators, and safety information such as investigational device-related serious adverse events reported by the sponsor. The Ethics Committee may require amendments to the clinical trial protocol, informed consent form and other information provided to subjects, or suspend or terminate the clinical trial.

(7) The Ethics Committee shall review the potential impact of deviations from the clinical trial protocol on the rights, interests and safety of subjects, or on the scientific validity and integrity of the medical device clinical trial.

(8) During the medical device clinical trial, amendments to documents such as the clinical trial protocol and informed consent form, as well as resumption of a suspended clinical trial, may be implemented only after written approval has been obtained again from the Ethics Committee.

(9) The Ethics Committee shall retain all records of ethical review, including written review

records, member information, submitted documents, meeting minutes and relevant correspondence records.

21.3. Responsibilities of the Clinical Trial Institution

(1) The medical device clinical trial institution shall meet the filing requirements and establish a clinical trial management organizational structure and management system. The medical device clinical trial institution shall have a corresponding clinical trial management department responsible for the administration of medical device clinical trials.

(2) The management department of the medical device clinical trial institution shall be responsible for completing, managing and updating the filing information of the medical device clinical trial institution in the filing and management information system, including clinical trial specialties, principal investigators and other relevant information. It shall be responsible for submitting the annual work summary report of medical device clinical trials conducted in the previous year online via the filing system. Before the ethics committee reviews the medical device clinical trial, it shall organize the qualification assessment of the principal investigator of the clinical trial and complete the filing.

(3) The medical device clinical trial institution shall establish a quality management system covering the entire process of medical device clinical trial implementation, including training and assessment, conduct of clinical trials, management of medical devices, management of biological samples, handling of adverse events and device deficiencies, reporting of safety information, documentation, quality control and other systems, to ensure that the principal investigator fulfills his/her relevant clinical trial responsibilities, that subjects receive appropriate medical care, and that the data generated from the trial are authentic.

(4) Before undertaking a medical device clinical trial, the medical device clinical trial institution shall evaluate the relevant resources according to the characteristics of the investigational medical device to ensure that it has the appropriate qualifications, personnel, facilities and conditions.

(5) The medical device clinical trial institution and investigators shall cooperate with monitoring and audits organized by the sponsor, as well as inspections conducted by drug regulatory authorities and health administration departments.

(6) The medical device clinical trial institution shall properly keep clinical trial records and essential documents in accordance with relevant laws and regulations and the contract signed with the sponsor.

21.4. Responsibilities of Investigators

(1) The Principal Investigator responsible for the medical device clinical trial shall possess the qualifications and conditions required by Good Clinical Practice for Medical Devices (2022).

(2) The Principal Investigator shall ensure that the medical device clinical trial is conducted in compliance with the latest version of the clinical trial protocol approved by the Ethics Committee and shall conduct the trial within the agreed time limit in accordance with this regulation and relevant laws and regulations.

(3) The Principal Investigator may, as required by the medical device clinical trial, delegate qualified investigators who have received clinical trial-related training to conduct the following: subject recruitment, informed consent, screening and follow-up; management and use of the investigational medical device and control medical device (if applicable); management and use of biological samples (if applicable); handling of adverse events and device deficiencies; documentation of clinical trial data and completion of case report forms.

(4) Investigators participating in the medical device clinical trial shall possess the qualifications and conditions required by Good Clinical Practice for Medical Devices (2022).

(5) Investigators shall comply with the ethical principles of the Declaration of Helsinki (World Medical Association) and relevant ethical requirements and meet the informed consent requirements specified in the Good Clinical Practice for Medical Devices (2022).

(6) Investigators shall be responsible for the management of the investigational medical device and control medical device (if applicable) provided by the sponsor. They shall ensure that such devices are used only for subjects enrolled in the clinical trial, stored and kept as required during the trial, and disposed of after completion or termination of the trial in accordance with relevant laws and regulations and the contract with the sponsor.

(7) Investigators shall ensure that the collection, processing, storage, transportation, destruction, etc. of biological samples in the medical device clinical trial comply with the clinical trial protocol

and relevant laws and regulations.

(8) In the event of an adverse event during the medical device clinical trial, investigators shall provide adequate and timely treatment and management for the subject. If the subject develops concurrent diseases requiring treatment, investigators shall inform the subject promptly. Investigators shall document all adverse events and identified device deficiencies occurring during the medical device clinical trial.

(9) Investigators shall report safety information in the medical device clinical trial in a timely manner. The Principal Investigator shall promptly handle received safety information:(i) Upon receiving information related to the investigational medical device regarding serious adverse events and other safety information from the sponsor, the Principal Investigator shall acknowledge and review such information promptly, consider whether adjustments are needed for subject treatment, and communicate with subjects as early as necessary;(ii) Upon receiving notification from the sponsor or Ethics Committee to suspend or terminate the medical device clinical trial, the Principal Investigator shall notify subjects promptly and ensure that subjects receive appropriate treatment and follow-up.

(10) The Principal Investigator shall report the progress of the medical device clinical trial to the Ethics Committee on schedule, and promptly report events affecting the rights, interests and safety of subjects or deviations from the clinical trial protocol.

(11) If the sponsor seriously or persistently violates this regulation and relevant laws and regulations, or requests alteration of trial data or conclusions, the medical device clinical trial institution and investigators shall submit a written report to the drug regulatory authority of the province, autonomous region, or municipality directly under the Central Government where the sponsor is located.

Note: For other specific responsibilities of each party, please refer to the Clinical Trial Agreement and other relevant documents.

22. Abbreviations

AA	Aortic Aneurysm
ADE	Adverse Drug Event
AE	Adverse Event
CE	CONFORMITE EUROPEENNE
CRA	Clinical Research Associate
CRC	Clinical Research Coordinator
CTA	Computed Tomography Angiography
DMP	Data Management Plans
DVP	Data validation plan
EACTS	European Association for Cardio-Thoracic surgery
eCRF	Electronic Case Report Form
EC	Ethics Committee
ECG	Electrocardiogram
ESVS	European Society for Vascular Surgery
FAS	Full Analysis Set
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICF	Informed Consent Form
ITT	Intention-to-treat
MDR	Medical device regulation
MRA	Magnetic Resonance Angiography
mRS	Modified Rankin Scale
NMPA	National Medical Products Administration
NYHA	New York Heart Association
OPC	Objective Performance Criteria
PAU	Penetrating Aortic Ulcer
PI	Principal Investigator
PPS	Per Protocol Set
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
SS	Safety Set
TAA	Thoracic Aortic Aneurysm

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24. Investigator Declaration

I hereby agree to:

1) Conduct the clinical trial in strict accordance with the Helsinki Declaration, current Chinese regulations, and the trial protocol.
2) Accurately record all required data in the Case Report Form (CRF) and complete all clinical trial reports on time.
3) Allow the trial medical device to only be used in the clinical trial, and document completely and accurately the receipt and usage of the trial medical device during the clinical trial and keep corresponding records.
4) Allow any monitors or inspectors authorized by the sponsor, as well as all regulatory authorities to conduct monitoring and investigation of the clinical trial.
5) Strictly implement the terms of the clinical trial contract/agreement signed by the involved parties.

I have read the entire clinical trial protocol, including the above statement, and I agree with all the above.

Principal Investigator Signature (Year) (Month) (Day)

Medical Device Clinical Trial Institution Signed (Stamped) (Year) (Month) (Day)

Sponsor   Signed (Stamped) (Year) (Month) (Day)

Annex 1. The European System for Cardiac Operative Risk Evaluation (EuroSCORE)

Item	Score	Patients
Patient characteristics		
Age（Per 5 years or part thereof over the age of 60 years）	1	
Sex（female）	1	
Chronic pulmonary disease (Long-term use of bronchodilators or steroids for respiratory disease)	1	
Peripheral arteriopathy (Claudication, carotid stenosis ⩾50%, previous or planned intervention on the abdominal aorta, limb arteries, or carotid arteries.)	2	
Neurological dysfunction (Severely impaired mobility or activities of daily living.)	2	
Previous cardiac surgery (Previous pericardiotomy / previous opening of the pericardium)	3	
Serum creatinine: Preoperatively 200 μmol/L	2	
Active endocarditis (Antibiotic therapy at the time of surgery.)	3	
Critical preoperative state (Preoperative cardiac arrest, mechanical ventilation, renal failure, inotropic support, intra-aortic balloon pump (IABP) use, ventricular arrhythmia.)	3	
Cardiac-related factors		
Unstable angina (Rest pain requiring intravenous (IV) nitrates.)	2	
Left ventricular function: Moderate (30%–50%)	1	
Left ventricular function: Poor (＜30%)	3	
Recent Myocardial Infarction (MI): Within 90 days	2	
Pulmonary hypertension (Systolic pulmonary artery pressure ⩾ 60 mmHg)	2	

Operation-related factors		
Emergency operation	2	
Major cardiac procedure other than or in addition to CABG	2	
Surgery on the thoracic aorta	3	
Post-infarct septal rupture	4	

Annex 2. Modified Rankin Scale (mRS) Score Reference Table

Item	Content	Score
No symptoms at all		0
No significant disability despite symptoms	Able to carry out all usual duties and activities	1
Slight disability	Unable to carry out all previous activities, but able to look after own affairs without assistance	2
Moderate disability	Requiring some help, but able to walk without assistance	3
Moderately severe disability	Unable to walk without assistance and unable to attend to own bodily needs without assistance	4
Severe disability	Bedridden, incontinent and requiring constant nursing care and attention	5
Dead		6

Annex 3 List of Clinical Trial Institutions and Investigators

Site Code	Clinical Trial Institution Name	Principal Investigator
1	The First Medical Center of Chinese PLA General	Guo Wei
2	Zhongshan Hospital, Fudan University	Fu Weiguo
3	Guangdong Provincial Hospital of Chinese	Fan Xiaoping
4	The First Affiliated Hospital of Harbin Medical	Xie Baodong
5	The First Hospital of Jilin University	Gao Yongsheng
6	The Second Affiliated Hospital of Nanchang	Zhou Weimin
7	Nanjing First Hospital	Chen Xin
8	The First Affiliated Hospital of Nanjing Medical	Shao Yongfeng
9	The Affiliated Hospital of Qingdao University	Guo Mingjin
10	West China Hospital, Sichuan University	Hu Jia
11	Shandong Provincial Hospital	Wu Xuejun
12	Beijing Anzhen Hospital, Capital Medical	Chen Zhong
13	Shanghai Chest Hospital	Zhu Dan
14	Xiamen Cardiovascular Hospital, Xiamen	Wu Xijie
15	The First People's Hospital of Yunnan Province	Gong Kunmei
16	The First Affiliated Hospital of Air Force Military	Zuo Jian
17	The First Affiliated Hospital of China Medical	Xin Shijie
18	Xiangya Hospital, Central South University	Wang Wei
19	The First Affiliated Hospital of Sun Yat-sen	Chang Guangqi
20	The First Affiliated Hospital of Zhengzhou	Li Zhen

Note: The participating sites listed in the table above were screened at the initiation of the trial and may be adjusted according to trial progress. (Site ranking is sorted by the uppercase first letter of the Chinese pinyin of the institution names.)