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Protocol for GUo's renovisceral Artery reconstruction-1: a prospective, multicentre, single-arm clinical trial to evaluate the safety and efficacy of a multibRANched sTEnt graft systEm for thoracoabdominal aortic aneurysm (GUARANTEE study)

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ABSTRACT

Introduction The multibranched off-the-shelf stent graft is a promising treatment option for thoracoabdominal aortic aneurysm (TAAA). A commercially available, multibranched, off-the-shelf endograft called the t-Branch stent graft has demonstrated favourable midterm outcomes. Another two investigational off-the-shelf endografts, the GORE EXCLUDER Thoracoabdominal Branch Endoprosthesis and E-nside multibranch stent graft system, are still being developed. However, these three endografts have an unsatisfactory anatomic feasibility rate in patients with TAAA. Based on the concept of Guo's renovisceral artery reconstruction-1, a novel, multibranched, off-the-shelf endograft with different configurations has been developed.

Methods and analysis This prospective, multicentre, single-arm, cohort study will enrol 73 patients with TAAA. Preoperative and postoperative clinical data, as well as CT angiography images at each follow-up timepoint, will be analysed to evaluate the safety and efficacy of this novel, multibranched, off-the-shelf endograft for the treatment of TAAA. The primary safety end point is the major adverse event rate within 30 days after index endovascular aortic repair, including all-cause death, hepatic failure, bowel necrosis, renal failure, stroke, permanent paraplegia, cardiac infarction and respiratory failure. The primary efficacy end point is the successful treatment rate within 12 months after procedure, which is a composite of immediate technical success and no secondary surgical intervention related to TAAA within 12 months after the procedure.

Ethics and dissemination The protocol has been reviewed and approved by the ethics committee of Chinese PLA General Hospital (reference number: 2021-NO.-007) and each participating hospital. The findings of this study will be disseminated through conference presentations, peer-reviewed journal publications and social media.

Trial registration number NCT05054985.

Strengths and limitations of this study

- This is a prospective, multicentre, single-arm study to evaluate the safety and efficacy of a novel mixed multibranched stent graft system for thoracoabdominal aortic aneurysm.
- Adverse events that occur within 60 months postoperatively will be monitored through clinical visits and CT angiography findings.
- The main limitation of this study is the single-arm design, which has an innate bias in assessing the outcomes of interest.

INTRODUCTION

The multibranched stent graft technique has evolved into an established invasive treatment option for thoracoabdominal aortic aneurysm (TAAA), since it was introduced two decades ago.[1] A multibranched off-the-shelf device has inherent advantages over both physician-modified and custom-made devices because it does not require modification or manufacturing time, which is especially important in an emergency setting.[2] The t-Branch endograft (Cook, Bloomington, Indiana, USA) is a unique, commercially available, multibranched, off-the-shelf device.[3] Another two off-the-shelf endografts, the GORE EXCLUDER Thoracoabdominal Branch Endoprosthesis (TAMBE; W. L. Gore & Associates, Flagstaff, Arizona, USA)[4] and E-nside multibranch stent graft system (Jotec, Hechingen, Germany),[5] are still in the research stage. The TAMBE and t-Branch endografts have demonstrated promising early and midterm results, respectively.[4 6 7]

Both the t-Branch and TAMBE endografts have an outer branch design with one and two available configurations, respectively, while the E-nside endograft has an inner branch design with four available configurations. One critical issue with these three endografts is the suboptimal anatomic feasibility rate in real-life cohorts of patients with TAAA. When using any of the three off-the-shelf devices, the overall treatment feasibility rate is 58%,[8] suggesting the need for configuration improvement and size optimisation.

In collaboration with Lifetech Scientific (Shenzhen, China), we developed a novel multibranched thoracoabdominal stent graft system that consists of a multibranched endograft, self-expanding bridging stent graft, tubular or bifurcated abdominal stent graft and iliac limb extensions. The multibranched endograft is a mixed branch design with two inner branches for the visceral arteries and two outer branches for the bilateral renal arteries. Another feature of this multibranched endograft is the variations in the main body diameter, length and branch size, introducing diversified configurations that accommodate more anatomic conditions. The aim of the GUARANTEE study is to evaluate the safety and efficacy of this novel multibranched stent graft system for TAAA endovascular repair.

METHODS AND ANALYSIS

The GUARANTEE study was designed in accordance with the Standard Protocol Items: Recommendations for Interventional Trials statement,[9] and is registered with the US National Institute of Health (table 1). The actual study start date was 12 November 2021, and the estimated study completion date is 31 December 2028.

Study design

This prospective, multicentre, single-arm, cohort study will evaluate the safety and efficacy of a novel multibranched stent graft system for endovascular repair of TAAA. This study is being initiated by the Chinese PLA General Hospital and will involve patients from an additional 28 high-volume tertiary referral hospitals across all geographic areas of China (table 2). All participating hospitals have performed endovascular treatment in >50 patients with anatomically complex aortic aneurysms in the last 5 years.

Study end points

Primary safety end point

The primary safety end point is the major adverse event rate within 30 days after index endovascular aortic repair. Major adverse events include all-cause death, hepatic failure, bowel necrosis, renal failure, stroke, permanent paraplegia, cardiac infarction and respiratory failure.

Primary efficacy end point

The primary efficacy end point is the successful TAAA treatment rate at 12 months after the procedure.

Table 1 Trial registration data

Primary registry and trial identifying number	**ClinicalTrials.gov: NCT05054985**
Date of registration in primary registry	23 September 2021
Secondary identifying numbers	XJ-TAAA-01
Sources of monetary of material support	Lifetech Scientific (Shenzhen)
Primary sponsor	Lifetech Scientific (Shenzhen)
Secondary sponsor(s)	None
Contact for public queries	Wei Guo, Professor, email: pla301dml@vip.sina.com
Contact for scientific queries	Wei Guo, Professor
Brief title	Safety and Efficacy of a Multibranched Thoracoabdominal Stent Graft System for Thoracoabdominal Aortic Aneurysm
Official title	Guo's renovisceral artery reconstruction-1: a prospective, multicenter, single-arm clinical trial to evaluate the safety and efficacy of a multibranched stent graft system for thoracoabdominal aortic aneurysm (GUARANTEE study)
Countries of recruitment	China
Problem(s) studied	Endovascular treatment for TAAA
Intervention(s)	Multibranched thoracoabdominal stent graft system
Inclusion criteria	Age ≥18 and ≤80 years at the time of informed consent signature Maximum diameter of TAAA >50 mm, or rapid growth of sac >5 mm in diameter in the most recent 6 months, or rapid growth >10 mm in diameter within 1 year Proximal landing zone 17–36 mm in diameter and ≥25 mm in length If distal landing zone in abdominal aorta: Distal landing zone 12–36 mm in diameter and ≥20 mm in length If distal landing zone in iliac artery: Distal landing zone 7–25 mm in diameter and ≥15 mm in length Visceral vessel landing zone 6–13 mm in diameter and ≥15 mm in length Renal artery landing zone 4.5–9 mm in diameter and ≥15 mm in length Feasible iliofemoral artery and upper patent upper extremity access

Continued

Table 1 Continued

Primary registry and trial identifying number	ClinicalTrials.gov: NCT05054985
Exclusion criteria	Ruptured aortic aneurysm in unstable haemodynamic condition Aneurysmal aortic dissection Infected or mycotic aortic aneurysm Local or systemic infection that may result in endoprosthesis infection Occluded renovisceral artery Requiring simultaneous coverage or embolisation for bilateral internal iliac arteries Severe aortic stenosis, calcification or mural thrombus at stent-graft landing zone Diagnosis of acute coronary syndrome within the last 6 months Transient ischaemic attacks or stroke within the past 3 months Hepatic insufficiency comorbidity (ALT or AST ≥5 times the upper limit of normal value), or serum creatinine ≥150 µmol Severe pulmonary insufficiency inability to tolerate general anaesthesia Severe coagulation dysfunction Undergone major surgical or endovascular surgery within the last 30 days An allergic history for contrast agents, anticoagulants, antiplatelet drugs, stent graft or materials of delivery system Patients with connective tissue diseases or Takayasu arteritis Serious vital organ dysfunction or other serious diseases Patients participating in other clinical trials or not completed or withdrawn from other clinical trials within the last 3 months at the time of screening period Planning pregnancy, pregnancy or breast feeding Life expectancy <1 year Patients not appropriate for endovascular repair based on the investigators' clinical judgement
Study type	Interventional
Actual study start date	12 November 2021
Estimated study completion date	31 December 2028
Sample size	73
Recruitment status	Enrolling
Primary outcome(s)	Outcome: major adverse event. Time frame: 30 days after index endovascular procedure Outcome: immediate technical success and no reintervention-related TAAA within 12 months after index procedure. Time frame: within 12 months after index endovascular procedure
Secondary outcome(s)	Outcome: delivery system-related complications. Time frame: intraoperation and within 30 days after index procedure Outcomes: all-cause mortality, TAAA-related mortality, device-related adverse event and severe adverse events. Time frame: 6, 12 months, and 2–5 years after index procedure Outcomes: aneurysmal enlargement, type I/III endoleak, stent graft migration and renovisceral artery patency. Time frame: postoperative 6 and 12 months Outcomes: any reinterventions secondary to TAAA progression. Time frame: 6, 12 months, and 2–5 years after index procedure

ALT, alanine transaminase; AST, aspartate aminotransferase; TAAA, thoracoabdominal aortic aneurysm.

Successful TAAA treatment is a composite index that meets all of the following criteria: immediate technical success (successful delivery of the system to a predetermined location, successful deployment of the system and safe withdrawal of the delivery system from the body, with no type I/III endoleak), no secondary surgical intervention related to TAAA within 12 months after the procedure (due to aneurysm rupture, continuous enlargement, stent displacement, type I/III endoleak and branch stenosis or occlusion).

Secondary safety end points

The following secondary safety end points will be evaluated: delivery system-related complications during the procedure and within 30 days postoperatively, including conversion to open surgery, and any haemorrhage, haematoma or pseudoaneurysm of the arterial access; all-cause mortality at 6 months, 12 months and 2–5 years postoperatively; TAAA-related mortality at 6 months, 12 months and 2–5 years postoperatively; device-related adverse events at 6 months, 12 months and 2–5 years postoperatively; severe adverse events resulting in death or serious deterioration of health at 6 months, 12 months and 2–5 years postoperatively.

Secondary efficacy end points

The following secondary efficacy end points will be evaluated: aneurysmal enlargement at 6 and 12 months postoperatively (defined as a maximum aortic diameter increase of >5 mm relative to preoperative CT angiography (CTA)); type I/III endoleak at 6 and 12 months postoperatively; stent graft migration at 6 and 12 months postoperatively (defined as radiological evidence of stent graft displacement exceeding 10 mm); renovisceral artery patency rate at 6 and 12 months postoperatively (branch vessel patency is defined as stenosis of ≤50%); reintervention

Table 2 Trial centres

Centre	Geographic region
Chinese PLA General Hospital	North China
Beijing Anzhen Hospital, Capital Medical University	North China
Zhongshan Hospital, Fudan University	East China
The Second Xiangya Hospital of Central South University	Central China
People's Hospital of Xinjiang Uygur Autonomous Region	Northwest China
The First Hospital of China Medical University	Northeast China
Peking University People's Hospital	North China
West China Hospital of Sichuan University	West China
The First Affiliated Hospital, Sun Yat-Sen University	South China
Nanjing Drum Tower Hospital	East China
The First Affiliated Hospital, Zhejiang University	East China
The Second Affiliated Hospital of Harbin Medical University	Northeast China
Fuwai Central China Cardiovascular Hospital	Central China
The First Affiliated Hospital of Fujian Medical University	South China
Jiangsu Province Hospital	East China
The First Affiliated Hospital of Zhengzhou University	Central China
The First Affiliated Hospital of Chongqing Medical University	Southwest China
Shandong Provincial Hospital	North China
The First People's Hospital of Yunnan Province	Southwest China
Peking Union Medical College Hospital	North China
Shanghai Ninth People's Hospital	East China
Tianjin Medical University General Hospital	North China
Xijing Hospital	Northwest China
The Second Affiliated Hospital of Nanchang University	East China
Qilu Hospital of Shandong University	North China
First Affiliated Hospital of Kunming Medical University	Southwest China
Yan'an Hospital of Kunming City	Southwest China
The First Affiliated Hospital of Harbin Medical University	Northeast China
The First Hospital of Lanzhou University	Northwest China

secondary to TAAA progression at 6 months, 12 months and 2–5 years postoperatively.

Patient recruitment

We intend to recruit 73 patients between 18 and 80 years of age who are diagnosed with TAAA. To expedite patient recruitment, a competitive enrolment strategy will be used. In addition, any one of the 29 participating centres shall not recruit >36 patients (ie, one-half of the total planned enrolment).

Table 1 gives a detailed overview of the inclusion and exclusion criteria. Vascular specialists, including vascular surgeons and interventional radiologists, will determine patient eligibility in accordance with the inclusion and exclusion criteria. Engineers from Lifetech Scientific will provide on-site guidance regarding device manipulations for the early cases treated in participating hospitals.

Multibranched stent graft system design

The concept of Guo's renovisceral artery reconstruction-1 is to revascularise the renovisceral arteries using a mixed multibranched stent graft with two proximal inner branches for the coeliac trunk (CT) and superior mesenteric artery (SMA), and two distal outer branches for the bilateral renal arteries. An advantage of the inner branch design for the two proximal branches is that the stent graft segment where the inner branches are longitudinally attached can be used as landing zone, avoiding extensive stent graft coverage of healthy aorta, especially for TAAA with a limited extent. Based on the concept of Guo's renovisceral artery reconstruction-1, we collaborated with Lifetech Scientific to jointly develop a multibranched stent graft system for TAAA. This multibranched stent graft system is an off-the-shelf, multicomponent system composed of a multibranched endograft, self-expandable bridging stent graft for renovisceral artery reconstruction, tubular or bifurcated abdominal stent graft and iliac limb extensions (figure 1A).

The multibranched stent graft is named the G-Branch endograft, which consists of an upper part, a tapered portion (termed the waist) where the four branches arise, and a lower part that has a smaller diameter than the upper part. The waist has two longitudinally parallel inner branches to reconstruct the CT and SMA, and two outer branches for bridging the bilateral renal arteries (figure 1B,C). A radiopaque figure-of-8 marker and an 'o' marker are respectively fixed at the 3 and 9 o'clock positions of the proximal end to allow accurate positioning. The outlets and inlets of the four branches are outlined by circular markers to facilitate cannulation. Two radiopaque markers are positioned in the proximal and intermediate parts of the lower portion of the G-Branch to identify the overlapping length with distal extension. An 'o' marker is placed at the distal end to indicate the distal landing position.

The upper part of the G-Branch has a diameter of 24–40 mm (4 mm increments) and lengths of 40 and 70 mm. The longitudinal length of the waist is fixed at 10

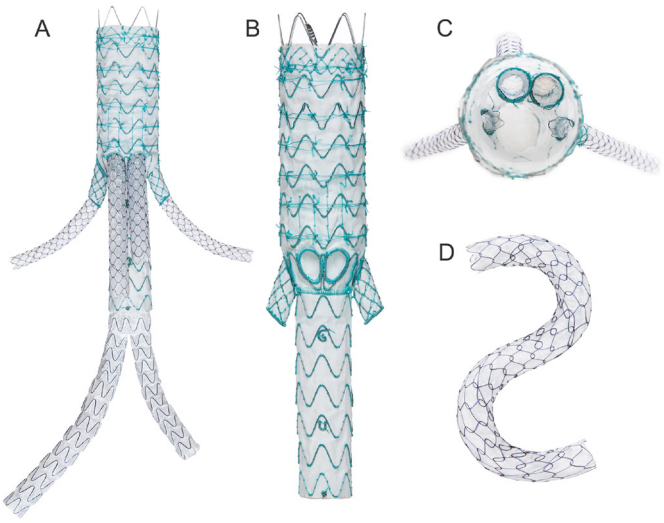

Figure 1 Photographs of the novel, off-the-shelf, multibranched stent graft system (Lifetech Scientific, Shenzhen, China). (A) Overview of this multibranched stent graft system comprising a multibranched endograft, self-expanding bridging stent graft, tubular or bifurcated abdominal stent graft and iliac limb extensions. (B) The G-Branch endograft has a mixed branch configuration, with two inner branches for the coeliac trunk and superior mesenteric artery and two outer branches for the bilateral renal arteries. (C) Internal view showing the structures of the four branches. (D) Self-expanding bridging stent graft (SilverFlowPV; Lifetech Scientific) constructed by a unique interwoven nitinol wire sandwiched by two layers of expanded polytetrafluoroethylene.

mm. The two inner branches are sewn to the internal face of the upper part of the G-Branch endograft, with the inlet of the left inner branch 3 mm higher than the right one; however, the outlets are designed at the same level, orientated at approximately 11 and 1 o'clock, respectively. The inner branches have two diameters available, 8 and 10 mm, with fixed lengths of 23 and 20 mm, respectively, for the left and right inner branches. The two outer branches are orientated at 3 and 9 o'clock, respectively, with an angle of deviation from the long axis of the G-Branch endograft of no larger than 30°. The outer branches have a fixed length of 15 mm, with a fixed diameter of 7 mm. The lower part of the stent graft is 70 mm in length and 14–18 mm in diameter (2 mm increments). A total of 26 types of G-Branch endografts are available, all of which require a 22F inner diameter femoral sheath introducer, regardless of the stent graft size. To facilitate visceral artery cannulation, the delivery system of the G-Branch endograft has two preloaded guidewires for the two inner branches.

The bridging stent graft (SilverFlowPV; Lifetech Scientific) is a self-expandable, expanded polytetrafluoroethylene (ePTFE)-covered stent. This stent is constructed using a unique interwoven nitinol wire sandwiched by two thin layers of ePTFE, providing favourable flexibility, fracture resistance and lower-profile features (figure 1D). The SilverFlowPV has a tubular or tapered shape (usually from proximal to distal). The stent graft diameter is 5–12 mm at the proximal end and 5–14 mm at the distal end, while the stent graft length is 20–120 mm. An inner 6F, 7F or 8F introducer sheath is required, depending on the stent graft diameter.

The distal stent graft extensions (ie, tubular or bifurcated stent graft, and iliac limb extensions) are constructed by encapsulating a nitinol Z stent skeleton within two layers of ePTFE. The stent graft barbs are located in the second covered stent ring to preclude type IV endoleak. A variety of extension stent graft sizes are available to accommodate the different diameters of the G-Branch endograft and individual arterial anatomical variations.

Endovascular technique

Endovascular aortic procedures are performed in a hybrid operating room under fluoroscopic control with the patient under general anaesthesia. Prophylactic spinal drainage is used at the discretion of the operator. After surgical exposure of the axillary artery, intravenous heparin loading is started with a bolus of 100 IU/kg body weight to achieve an activated clotting time of at least 250 s. Activated clotting time is measured at 30 min intervals throughout the procedure. A subsequent dose of heparin will be administered if required. The axillary artery is directly punctured to establish the antegrade vascular access through which the thoracic descending aorta is catheterised. Two 8F long sheaths are introduced into the upper descending thoracic aorta. The bilateral common femoral artery is percutaneously punctured and a 5/6F sheath inserted. The femoral artery sheath is exchanged for a Perclose ProGlide device to provide a 'preclose' suture. Two ProGlides are used for the femoral artery where the G-Branch passes through, while one is used for the contralateral side.

A 22F DrySeal introducer sheath (W. L. Gore & Associates) is advanced through the iliac artery to establish the vascular access for the thoracoabdominal stent graft. In cases of Crawford extent I, II, or part of III TAAA, the proximal stent graft is deployed first. The G-Branch endograft is advanced into the lower portion of the thoracic aorta, with the outlet of the inner branch 10–30 mm proximal to the origin of the CT. The device allows stepwise deployment, enabling the upper part to be partially constrained while the lower part is completely constrained; at this point, the two outer branches can expand adequately, and the G-Branch position can be manually adjusted and precisely located in the target region using fusion imaging techniques or real-time angiography.

Once the G-Branch is semi-released, the preloaded SMA guidewire is advanced into the upper thoracic descending aorta. A gooseneck snare is advanced close to the preloaded guidewire through the 8F long sheath from the axillary access. The preloaded guidewire is then captured and exteriorised via the axillary approach to establish the axillofemoral access. A balloon catheter is loaded into the axillofemoral guidewire and advanced into the inner branch for the SMA. Once the balloon is

inflated, the 8F sheath from the axillary artery is advanced into the inner branch as the balloon is deflating under real-time fluoroscopy (ie, balloon-supported passage technique).[10] The same method is used to place another 8F long sheath into the inner branch for the CT. The SMA and CT are then sequentially catheterised with a 0.035-inch hydrophilic wire coupled with a 4F catheter through the two 8F long sheaths. The two preloaded guidewires are withdrawn from the delivery system, and the reducing ties of the upper part are released. Sequential stenting of the CT and SMA is performed using SilverFlowPV. The bridging stent graft is routinely ballooned, and selective angiography is used to identify endoleaks, stent graft migration, stenosis or occlusion. Relining bare metal stents are not routinely used unless stent graft compression is noted.

After visceral artery reconstruction, the bilateral outer branches are sequentially cannulated through the two 8F long sheaths. The technical challenge in renal artery revascularisation is the long sheath advancement into the renal artery, especially in patients with an upward oriented renal artery. In such cases, the sheath advancement can be facilitated by exchanging the 6/7F sheath with a more flexible dilator in the balloon-supported passage technique. For patients with extremely challenging renal artery anatomy, a crossed bridging stent graft with the left outer branch connecting the right renal artery and the right outer branch reconstructing the left renal artery is used because this contributes to a larger manipulating space and a smaller catheterisation angle, which facilitates the long sheath advancement. Following SilverFlowPV deployment for the bilateral renal arteries, stent ballooning and selective angiography are routinely performed. The G-Branch endograft is then released completely and endovascular repair is finished with the implantation of the distal components (tubular or bifurcated stent graft, and iliac limb extensions). After the completion of the endovascular procedure, heparin anticoagulation is antagonised by protamine in a dosage ratio of 2:1. Figure 2 shows a patient with type V TAAA performed accordingly to the above-mentioned technical protocol.

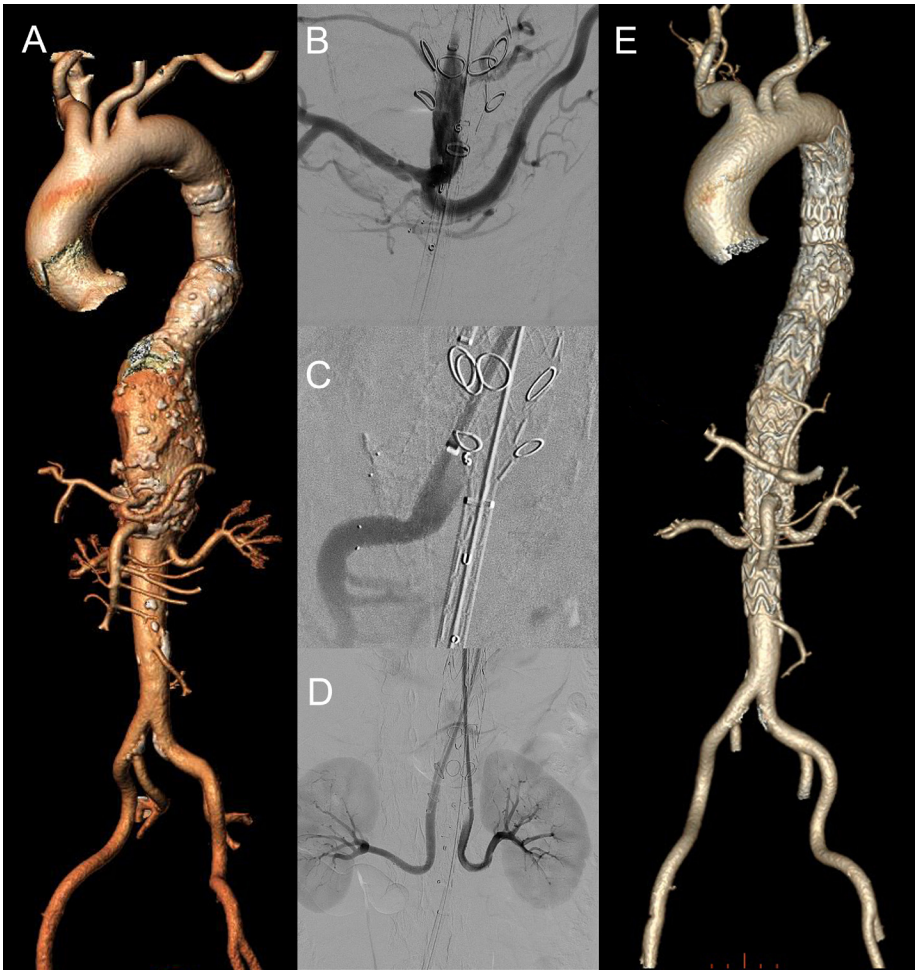

Figure 2 Clinical case of a man aged 58 years with extent type V thoracoabdominal aortic aneurysm. (A) Preoperative CT angiography (CTA) three-dimensional reconstruction showing that the aneurysm involves the splanchnic vessels and extends down to renal arteries. (B, C and D) Intraoperative selective angiography demonstrating patent renovisceral arteries. (E) Postoperative CTA indicating a successful exclusion of the aneurysm, with no evidence of endoleaks, stenosis or occlusion of bridging stent grafts.

Medications

Depending on the individual patient's comorbidities, antiplatelet, anticoagulation, antihypertensive, lipid-lowering, glucose-lowering or antibiotic therapy will be administered at the discretion of vascular surgeons. Single antiplatelet therapy (aspirin or clopidogrel) is recommended as long-term treatment.

CT angiography

CTA scans in the arterial and venous phases from the supra-aortic arch to the common femoral arteries will be performed at admission (preoperatively), postoperatively before discharge to home, and at 6 and 12 months postoperatively. For patients with substantially impaired renal function, postoperative CTA will be replaced by plain CT and Doppler ultrasonography.

Patient timeline

Each patient will attend a total of 10 visits, including 1 preoperative visit and 9 postoperative visits for eligibility screening, baseline data extraction and safety and efficacy evaluation of the stent graft system (table 3). Considering the potential adverse effects of X-ray radiation and contrast agent in patients with multiple morbidities, CTA is not planned after 12 months postoperatively unless there are compelling reasons for persistent surveillance. Adverse events and defects of stent-graft devices will be strictly monitored throughout follow-up.

Data extraction, entry and monitoring

The clinical database contains the patients' electronic record data, CTA image data and follow-up data. Preoperative data will be extracted from the electronic records and entered in the database before the operation, while postoperative in-hospital data will be collected within 2 weeks after discharge. The DICOM image header of all patients at each timepoint will be modified before data extraction, with the identifying information (patient ID, name, date of birth) replaced by a random 6-digit number. Preoperative CTA image data will be extracted before the operation, while postoperative CTA image data will be extracted within 2 weeks after the image acquisition date. Postoperative CTA images obtained at each follow-up timepoint will be independently analysed by two experienced vascular surgeons who are blinded to the CTA findings at the preoperative or other postoperative timepoints, patients' electronic records and follow-up information. After the completion of data extraction, the discrete data from CTA scans will be integrated into one database according to the predesigned 6-digit number. All CTA images will be measured and assessed by the 3Mensio workstation (V.8.1; 3Mensio Medical Imaging). At least 10% of the total CTA scans (including preoperative and postoperative scans) will be randomly selected and re-analysed by the two vascular surgeons to assess interobserver and intraobserver agreement.

Data will be registered via an electronic data capture system and centrally stored a secure password-protected server. Double data entry, range checks and logical consistency checking methods will be used to ensure the quality of data. Clinical research associates who are independent of the investigators will review the study documentation and records held at each site to ensure that the study is conducted in compliance with the regulatory requirements.

Sample size calculation

As the end point of the GUARANTEE study differs from that of the t-Branch studies, the expected end point incidences were obtained based on data extracted from previous studies.[6 11 12] We hypothesised that the performance of this multibranched stent graft system will not be inferior to that of the t-Branch stent graft; in this setting, the expected 30-day major adverse event rate and 12-month successful TAAA treatment rate were determined to be 6.3% and 85.7%, respectively. Currently, no guiding principle exists regarding objective performance criteria (OPC) for a multibranched stent graft system in China. After thorough deliberation by a panel composed of clinical and statistical experts, the OPC of the 30-day adverse event rate and 12-month successful TAAA treatment rate were set as 20% and 70%, respectively.

The minimum study sample size required to obtain at least 80% power with a one-sided significance level of 0.25% (alpha), thereby detecting a difference between the expected technical success rate of 85.7% and the OPC of 70% is 58 patients; assuming a dropout rate of 20%, the required enrolled sample size is 73 patients. To detect a difference between the expected adverse event rate of 6.3% and the OPC of 20% with a power of 80% and one-sided significant level of 0.25%, a sample size of 53 patients is required; assuming a dropout rate of 20%, the required enrolled sample size is 67 patients. Therefore, the aim is to enrol a total of 73 patients in the clinical trial.

Statistical analysis

Normally and non-normally distributed continuous variables will be presented as mean±SD and median (IQR). Categorical variables will be presented as number and percentage. The Kaplan-Meier method will be used to estimate the cumulative rate of each end point. Statistical calculations will be performed using SAS software V.9.4 (SAS Institute).

Patient and public involvement

There was no patient or public involvement in the research design and conception of this study.

DISCUSSION

The aim of the GUARANTEE study is to evaluate the safety and efficacy of a novel multibranched thoracoabdominal stent graft system for TAAA. The first-in-man study was initiated in June 2019 and is being conducted in a single centre (data unpublished). This first-in-man

Table 3 Schedule of patient visits and data collection

	Baseline (−30 days~0 day)	Operation day	Discharge day	Post-30 days (±7 days)	Post-6 months (±30 days)	Post-12 months (±30 days)	Post-24 months (±60 days)	Post-36 months (±60 days)	Post-48 months (±60 days)	Post-60 months (±60 days)
Informed consent	×									
Eligibility screen	×									
Medical/Clinical history	×									
Vital signs	×	×	×							
Blood routine	×		×							
Urine routine	×		×							
Liver/Renal function	×		×	×	×	×				
Coagulation function	×									
Enzymology test	×		×	×						
Pregnancy test	×									
ECG	×		×	×						
CTA images	×		×		×	×				
DSA		×								
Operation note		×								
Adverse events	×	×	×	×	×	×	×	×	×	×
Medications	×	×	×	×	×	×				
Defects of stent graft devices	×	×	×	×	×	×	×	×	×	×

CTA, CT angiography; DSA, digital substraction angiography.

study involved a total of 15 patients with complex aortic aneurysm, and 14 patients have currently completed at least 6 months of follow-up imaging. The purpose of this multicentre clinical trial is to enrol more patients and investigators to evaluate the clinical safety, technical feasibility, device functionality and anatomical features of TAAA in the Chinese population to help guide future device modifications.

The G-Branch endograft has a mixed multibranched configuration, with two inner branches for the CT and SMA, and two outer branches for the bilateral renal arteries. Only the two inner branches are integrated with preloaded guidewires to facilitate visceral artery cannulation. The preloaded guidewire design substantially differs between stent grafts produced by different manufacturers. The market-available t-Branch stent graft and the investigational TAMBE stent graft both have an outer branch design; however, the former has no preloaded guidewire, while the latter has four preloaded guidewire tubes for renovisceral artery cannulations.[3 4] The off-the-shelf E-nside stent graft is a unique endovascular device with four inner branches and four preloaded guidewires.[5]

In clinical practice, direct inner branch cannulation without the assistance of a preloaded guidewire may lead to technical difficulties owing to the relatively larger space surrounding the inlet of the inner branch. For the G-Branch endograft specifically, cannulation is affected by another factor. Because the two inner branches are closely parallel inside the G-Branch endograft, direct cannulation of a certain inner branch without the assistance of preloading guidewire may be unintentionally inserted into the other inner branch even with repeated adjustments and attempts, especially under specific anatomical conditions. Therefore, to simplify the procedure, the G-Branch endograft is designed with two preloaded guidewires for the inner branches. In contrast to the inner branches, the inlets of the outer branches in the t-Branch, TAMBE and G-Branch devices are usually located at the waist part, where the surrounding space is relatively limited; in addition, the two outer branches are respectively sewn at the right and left lateral walls of the multibranched stent graft so that the existence of one inner branch does not influence the cannulation of the other one. Therefore, outer branch cannulation does not seem to require preloaded guidewires, which would substantially increase the delivery system profile.

Compared with the G-Branch endograft, a multibranched stent graft with four outer branches theoretically needs a larger visceral aortic lumen to allow enough room for branch expansion, target vessel cannulation and bridging stent implantation.[8 13] The G-Branch endograft with proximal inner branch configuration may reduce the required aortic diameter, broadening its applicability for TAAA with a limited visceral aortic lumen. Another advantage of the G-Branch endograft is that the portion where the proximal inner branch is longitudinally attached can be used as the proximal landing zone, especially for the treatment of extent IV TAAA, pararenal or even infrarenal aortic aneurysm. A shorter proximal landing zone is associated with limited coverage of healthy aorta, which may reduce the risk of spinal cord ischaemia.[14–16]

In contrast to the t-Branch, TAMBE and E-nside endografts, the G-Branch endograft has a large size range for the proximal diameter, stent graft length, branch size and distal diameter. Different stent graft sizes can cover a variety of anatomical conditions[17 18]; however, a wide stent graft size range also causes issues with stent graft stock, limiting the device applicability in the emergency setting. In the GUARANTEE study, experience in device use and anatomical features of TAAA in the Chinese population will be analysed for future size simplification and design modifications. Furthermore, stock allocation of an off-the-shelf stent graft is less time-consuming than a custom-made device that needs a manufacturing time of 8–10 weeks.

There are two limitations in this study. First, as this is a single-arm study without a control group, it is susceptible to confounding factors. However, the single-arm design is being used because it is ethically inappropriate to treat TAAA using conventional open surgery or hybrid surgery due to the high perioperative mortality, and the t-Branch is not yet available in China. Second, all patients will be recruited only in tertiary referral centres with high-volume aortic disease cases, which may introduce selection bias. Patients referred to high-volume centres may have different comorbidities at presentation, anatomical features of aortic aneurysm and economic and healthcare conditions. Future studies involving a diverse group of patients will help provide more generalisable results.

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