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Rationale and design of SCOPE trial: a prospective, multicentre, open-label, randomised controlled trial to evaluate the overall efficacy and safety of a *s*hort-term anticoagulation strategy versus *co*nventional single antiplatelet therapy in patients with severe aortic stenosis without indications for anticoagulation or dual antiplatelet therapy *p*ost-transcatheter aortic valve r*e*placement

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ABSTRACT

Introduction While transcatheter aortic valve replacement (TAVR) has become a well-established standard of care for patients with symptomatic severe aortic stenosis, the optimal antithrombotic strategy post-TAVR remains a subject of debate, particularly in patients without clear indications for anticoagulation or dual antiplatelet therapy. This study aims to investigate the safety and efficacy of rivaroxaban compared with antiplatelet monotherapy in this specific patient population.

Methods and analysis This study is designed as a prospective, multicentre, open-label, randomised controlled trial. A total of 454 patients, who have successfully undergone TAVR and do not have indications for long-term anticoagulation or dual antiplatelet therapy, will be consecutively enrolled from seven centres across China. Participants will be randomly assigned to receive either anticoagulation with rivaroxaban (20/15 mg) or conventional antiplatelet therapy (aspirin or clopidogrel) for 1 month. Follow-up evaluations are scheduled at 1, 3, 6 and 12 months post-procedure. After the initial 1-month antithrombotic therapy, the regimen may be adjusted by the investigator based on the patient's clinical and imaging follow-up results. The primary endpoint is a hierarchical composite of cardiovascular death, first occurrence of myocardial infarction or stroke, first occurrence of life-threatening, disabling or major bleeding, and grade 3 or higher hypo-attenuated leaflet thickening and reduced leaflet motion at 12 months post-TAVR. The win ratio method will be employed to analyse the primary endpoint.

Ethics and dissemination This trial was approved by the Ethics Committee of the Beijing AnZhen Hospital. All relevant results will be disseminated through publications in peer-reviewed journals and presentations at conferences.

Trial registration number ChiCTR2400087453.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The SCOPE trial is the first multicentre, randomised study to assess the safety and efficacy of rivaroxaban monotherapy compared with antiplatelet monotherapy in patients with aortic stenosis who have undergone successful transcatheter aortic valve replacement (TAVR) and have no indications for anticoagulation or dual antiplatelet therapy.
⇒ The SCOPE trial innovatively proposes a short-term anticoagulation strategy using rivaroxaban monotherapy for 1 month after TAVR.
⇒ The use of four-dimensional CT enables the detection of subclinical leaflet thrombosis, characterised by reduced leaflet motion and hypo-attenuated leaflet thickening.
⇒ Open-label design inherently carries the risk of introducing bias. Thus, all endpoints will be adjudicated by independent, blinded Clinical Endpoint Committee and imaging core laboratory, which reduces the potential impact of bias.

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has become the standard of care for symptomatic patients with severe aortic stenosis (AS).[1 2] Despite significant improvements in procedural safety and outcomes, subclinical leaflet thrombosis (SLT) has emerged as a complication of increasing concern. SLT has been associated with a heightened risk of ischaemic cerebrovascular events[3 4] and may accelerate valve degeneration.[5] The advent of four-dimensional CT has led to the detection of SLT in 10–30% of patients.[3 6–9] Studies have demonstrated that anticoagulation reduces the incidence of SLT more effectively than antiplatelet therapy.[4 10–12] However, in patients without a formal indication for oral anticoagulation, current clinical guidelines recommend aspirin as the preferred strategy due to its more favourable bleeding profile.[1 2]

While clinical guidelines are based on evidence from several randomised trials, antiplatelet therapy alone has proven insufficient in preventing SLT.[4 10–12] In the GALILEO trial,[13] a regimen of rivaroxaban plus aspirin was compared with clopidogrel plus aspirin during the first 3 months, followed by rivaroxaban monotherapy versus aspirin monotherapy. The trial, however, revealed an increased risk of bleeding with the anticoagulation-based strategy. Similarly, the POPular TAVI trial demonstrated that combining anticoagulation with clopidogrel led to a higher incidence of bleeding complications.[14] These findings raise the possibility that the inferior outcomes seen with anticoagulation in the GALILEO study may be attributable to the combination of agents and the specific treatment duration. Moreover, emerging evidence suggests that thromboembolic events are most frequent within the first month following TAVR.[15] This leads us to hypothesise that short-term rivaroxaban monotherapy could reduce the risk of SLT without substantially increasing the risk of bleeding, thereby improving clinical outcomes. To date, no study has specifically investigated this strategy.

In light of these considerations, we designed a multicentre, randomised controlled trial to determine whether a short-term anticoagulation post-TAVR followed by subsequent antithrombotic management based on follow-up results can reduce the overall systemic risk of ischaemic events, bleeding events and SLT.

METHODS AND ANALYSIS

Study design and objectives

This study is an investigator-initiated, multicentre, open-label, randomised controlled trial. A total of 454 patients, who have successfully undergone TAVR without indications for anticoagulation or dual antiplatelet therapy (DAPT), will be consecutively enrolled from multiple centres across China. Participants will be randomly assigned in a 1:1 ratio via central randomisation to either the short-term anticoagulation group or the conventional antiplatelet therapy group (figure 1).

In the short-term anticoagulation group, patients will receive rivaroxaban for anticoagulation, with the dosage determined by the investigator based on the patient's stratified ischaemic and bleeding risk. In the conventional antiplatelet therapy group, patients will be treated with aspirin 100 mg/day or clopidogrel 75 mg/day. The treatment duration for both groups is 1 month. After the first month, the subsequent antithrombotic regimen will be determined by the investigator based on the patient's clinical status, follow-up findings, aortic multidetector CT (MDCT) and echocardiography results.

Patients will be followed up at 1, 3, 6 and 12 months after treatment initiation. Follow-up assessments will include medical history, physical examination, laboratory tests (including complete blood count, liver and renal function tests, coagulation function, cardiac biomarkers and B-type natriuretic peptide/N-terminal pro-B-type natriuretic peptide) and additional tests such as ECG, echocardiography and aortic MDCT.

The primary endpoint is a hierarchical composite of cardiovascular death, first occurrence of myocardial infarction or stroke, first occurrence of life-threatening/disabling/major bleeding, grade 3 or higher reduced leaflet motion (RLM) and grade 3 or higher hypoattenuated leaflet thickening (HALT) at 12 months post-TAVR.

The primary objective of this study is to determine whether a comprehensive antithrombotic strategy, involving short-term (1 month) anticoagulation post-TAVR followed by subsequent antithrombotic management based on follow-up results, can reduce the overall systemic risk of clinical events—including mortality, ischaemic events, bleeding complications and SLT. Additionally, this study aims to explore whether 1 month of anticoagulation post-TAVR can prevent SLT without increasing the risk of bleeding and whether this protective effect can be sustained up to 1 year after the procedure. The findings from this study will provide evidence-based guidance for optimising antithrombotic strategies following TAVR.

Study population

This study aims to enrol 454 patients across seven tertiary hospitals in China. Eligible participants will be those hospitalised with severe symptomatic AS who have successfully undergone TAVR and do not have indications for long-term anticoagulation or DAPT. The specific inclusion and exclusion criteria are as follows.

Inclusion criteria

- Age≥18 years.
- Diagnosed with severe symptomatic AS and having successfully undergone TAVR.
- Capable of understanding the study objectives, willing to participate and able to provide written informed consent approved by the Ethics Committee (online supplemental files 1 and 2).

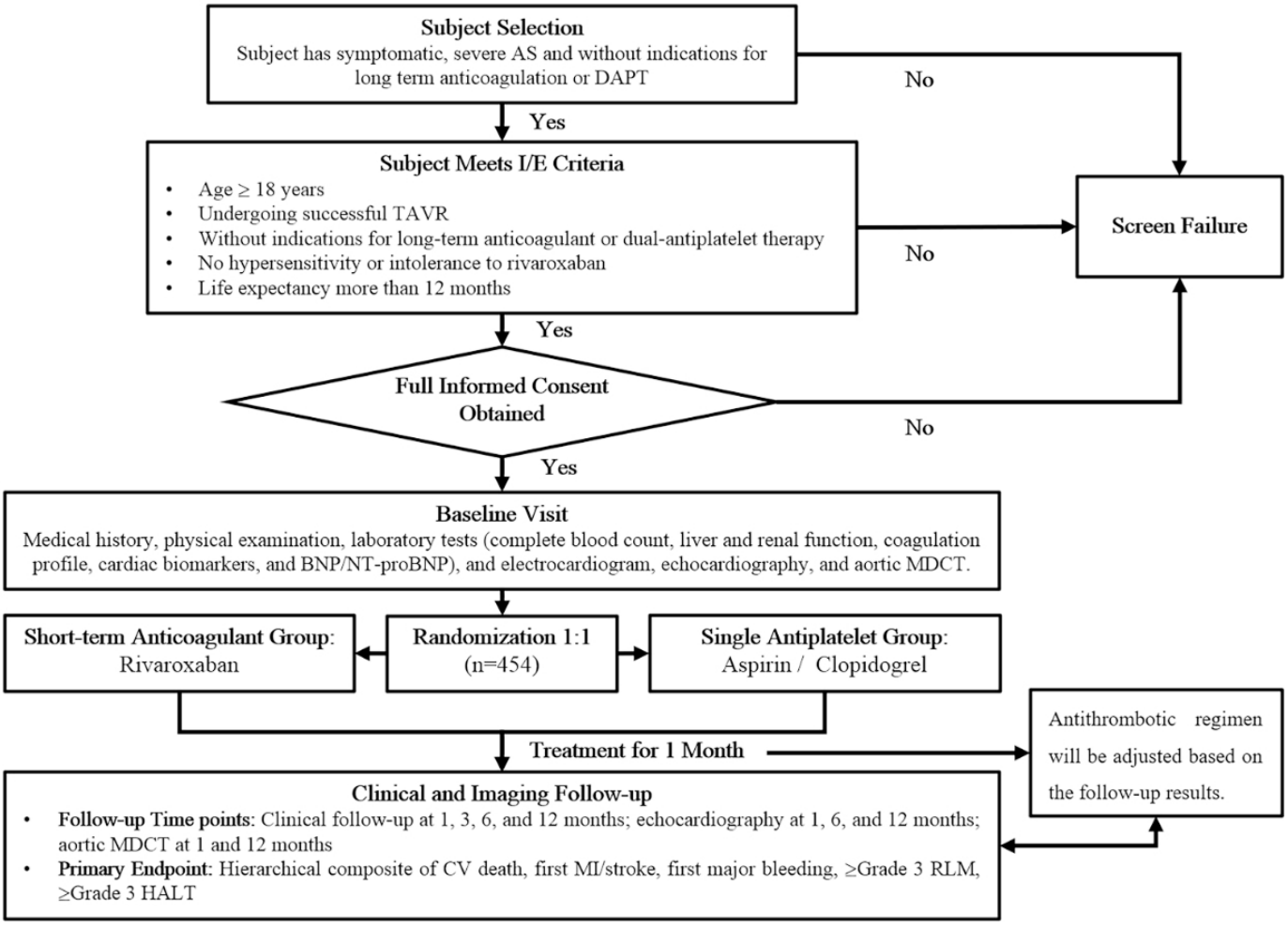

Figure 1 Patient flow for screening, randomisation and follow-up in the SCOPE trial. AS, aortic stenosis; BNP, B-type natriuretic peptide; DAPT, dual antiplatelet therapy; HALT, hypo-attenuated leaflet thickening; I/E criteria, inclusion/exclusion criteria; MDCT, multidetector NT-proBNP, N-terminal pro-B-type natriuretic peptide; RLM, reduced leaflet motion; TAVR, transcatheter aortic valve replacement; CV, cardiovascular; MI, myocardial infarction.

Exclusion criteria

- Indications for long-term oral anticoagulant therapy.
- Indications for oral DAPT.
- History of stroke.
- Known intolerance or hypersensitivity to rivaroxaban.
- Presence of comorbidities at enrolment with a life expectancy of less than 12 months.
- Inability to complete or adhere to the study protocol.

Randomisation, interventions and follow-up

Randomisation methods

Participants will be randomised in a 1:1 ratio to either the short-term anticoagulation group or the conventional antiplatelet group using a centralised, stratified block randomisation method. Stratification will be based on the study centre to ensure equal distribution of participants across the various research sites, which will help minimise potential centre-specific biases. A fixed block size of four will be used to maintain balance within each centre, ensuring that each group receives an equal number of participants in a controlled and predictable manner.

Randomisation will be conducted through a secure, web-based Interactive Web Response System. After participant enrolment and the completion of baseline data collection, the system will generate and send the randomisation code to a designated researcher who is not involved in evaluating the clinical endpoints. This procedure ensures that allocation concealment is maintained throughout the trial.

Once the randomisation code is received, the investigator will assign the appropriate treatment according to the group allocation and inform the participant of the corresponding treatment and follow-up procedures.

To ensure that the study meets its recruitment targets in a timely manner, competitive enrolment will be allowed during the final phase of recruitment. The entire randomisation process will be overseen by the project coordination centre at Beijing Anzhen Hospital affiliated with Capital Medical University, ensuring that data managers and statisticians remain blinded to group assignments throughout the study. The randomisation list will be securely stored at the project coordination centre for the duration of the study.

Interventions

In the short-term anticoagulation group, patients will receive rivaroxaban therapy. Those who are low in body weight (60 kg) and older than 75 years will be treated with rivaroxaban at 15 mg/day, while all other patients will receive 20 mg/day. In the conventional antiplatelet therapy group, patients will be administered aspirin 100 mg/day or clopidogrel 75 mg/day. The study protocol does not impose restrictions on the use of other non-antiplatelet or non-anticoagulant medications; these may be adjusted at the investigator's discretion in accordance with the patient's clinical condition and current guideline recommendations for valvular heart disease and heart failure management.[1 2 16 17] The treatment duration for both groups will be 1 month. After this period, the subsequent antithrombotic regimen will be determined by the investigator based on the patient's clinical status, follow-up imaging (including MDCT and echocardiography) and other relevant factors. Although the protocol allows flexibility regarding post-1-month antithrombotic management, it is recommended that patients who develop indications for anticoagulation (eg, atrial fibrillation, pulmonary embolism or deep vein thrombosis) or DAPT (eg, following myocardial infarction or coronary revascularisation) be treated according to established guidelines. For patients presenting with HALT and/or RLM at the 1-month MDCT follow-up, along with haemodynamic changes—such as an increase in the mean transvalvular gradient by ≥10 mm Hg resulting in a mean gradient ≥20 mm Hg, a reduction in effective orifice area by ≥0.3 cm^2 or ≥25%, a decrease in Doppler velocity index by ≥0.1 or ≥20% or the new onset or worsening of intraprosthetic aortic regurgitation (AR) by ≥1 grade resulting in moderate or greater AR—warfarin anticoagulation therapy is advised, in accordance with the recommendations from the Review Topic of the Week on the Treatment of Transcatheter Aortic Valve Thrombosis published in the *Journal of American College of Cardiology*.[18] For patients who were previously on single antiplatelet therapy (SAPT), the international normalised ratio (INR) should be maintained between 2.0 and 3.0. For those previously on rivaroxaban, the target INR should be between 2.5 and 3.5. In cases of SLT without accompanying haemodynamic changes, the use of warfarin anticoagulation may be considered at the investigator's discretion. Furthermore, investigators may schedule additional follow-up visits beyond the planned study schedule to ensure timely adjustments to the antithrombotic strategy in response to emerging clinical needs.

Patient follow-up

Patients who have signed the informed consent form and have been confirmed by the investigator to meet the inclusion and exclusion criteria will be enrolled in the study. Participants will be randomised via a central randomisation system in a 1:1 ratio to either the short-term anticoagulation group or the conventional antiplatelet group. After randomisation, the assigned treatment will be administered, and participants will undergo follow-up visits at 1, 3, 6 and 12 months post-treatment. Follow-up assessments will include medical history review, physical examination, laboratory tests (complete blood count, liver and renal function, coagulation profile, cardiac biomarkers and heart failure biomarkers), as well as ancillary tests (ECG, echocardiography and aortic MDCT).

The scheduled visits are as follows: immediately post-TAVR (V1), 1 month post-procedure (V2), 3 months post-procedure (V3), 6 months post-procedure (V4) and 12 months post-procedure (V5). Clinical endpoint events will be evaluated at each follow-up visit, with aortic MDCT performed at V2 and V5 to assess for the presence of HALT and RLM (table 1).

Study endpoints

Primary efficacy endpoint

The primary endpoint of the study is a hierarchical composite endpoint, evaluated at 12 months post-TAVR. The components of the composite endpoint are as follows:

- Cardiovascular death.
- Myocardial infarction and/or stroke.
- Life-threatening and/or disabling and/or major bleeding events.
- Grade 3 or higher RLM.
- Grade 3 or higher HALT.

Leaflet thrombosis events will be assessed at 1 month and 12 months post-TAVR using aortic MDCT. The occurrence of grade 3 or higher RLM and/or HALT at either of these time points will be considered an RLM and/or HALT event within the 12-month period.

Secondary efficacy endpoints

- Grade 3 or higher HALT at 1 and 12 months post-TAVR.
- Grade 3 or higher RLM at 1 and 12 months post-TAVR.

Safety endpoints

- All-cause mortality at 1, 3, 6 and 12 months post-TAVR.
- Cardiovascular mortality at 1, 3, 6 and 12 months post-TAVR.
- Myocardial infarction at 1, 3, 6 and 12 months post-TAVR.
- Stroke at 1, 3, 6 and 12 months post-TAVR.
- Life-threatening or disabling bleeding at 1, 3, 6 and 12 months post-TAVR.
- Major bleeding at 1, 3, 6 and 12 months post-TAVR.
- Minor bleeding at 1, 3, 6 and 12 months post-TAVR.
- Total bleeding at 1, 3, 6 and 12 months post-TAVR.

Endpoint definition and assessment

The definition of bleeding-related events will follow the second version of the Valve Academic Research Consortium (VARC-2) standardised endpoint definitions for TAVR clinical studies.[19] All other endpoints will be defined in accordance with the VARC-3 standardised definitions.[20]

Table 1 Schedule of assessments

Visit number	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Visit timing	Day 0 post-TAVR	Day 30±3 days post-TAVR	Day 90±30 days post-TAVR	Day 180±30 days post-TAVR	Day 360±30 days post-TAVR
Informed consent signing	x				
Verification of inclusion/exclusion criteria	x	x			
Demographic information	x				
Medical, personal, medication, treatment and allergy history*	x				
Vital signs and physical examination	x	x		x	x
Complete blood count	x	x		x	x
Liver and renal function†	x	x		x	x
Coagulation profile	x	x		x	x
BNP/NT-proBNP	x	x		x	x
Cardiac biomarkers‡	x	x		x	x
ECG	x	x		x	x
Echocardiography	x	x		x	x
Aortic MDCT scan		x			x
Randomisation	x				
Treatment		x	x	x	x
Concomitant medications and adverse events		x	x	x	x
Clinical endpoints		x	x	x	x

*Medical history includes cardiovascular and cerebrovascular history, other medical or surgical history.
†Liver and renal function tests include liver enzymes (ALT, AST), renal function (serum creatinine, blood urea nitrogen, eGFR).
‡Cardiac biomarkers include troponin (cTnT/cTnI) or creatine kinase and its isoenzymes (CK/CK-MB). Cardiac biomarkers should be measured at 12–24 hours post-TAVR, and then monitored every 24–72 hours or until levels decline (only one measurement is required).
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BNP, B-type natriuretic peptide; CK/CK-MB, creatine kinase / creatine kinase - myocardial band; cTnT/cTnI, cardiac troponin T / cardiac troponin I; eGFR, estimated glomerular filtration rate; MDCT, multidetector CT; NT-proBNP, N-terminal pro-B-type natriuretic peptide; TAVR, transcatheter aortic valve replacement.

The adjudication of clinical endpoint events will be conducted by an independent Clinical Endpoint Committee (CEC). The CEC will review the original source documents and adjudicate events according to the predefined endpoint definitions. The CEC will be composed of independent experts in clinical medicine, internal medicine and imaging, and will be aware of participant group assignments. Their role is to adjudicate endpoint events consistently across centres, thereby minimising bias and ensuring a more accurate evaluation of trial outcomes.

HALT and RLM will be assessed by an independent imaging core laboratory (ICL) based on raw aortic MDCT images. Both the MDCT scans and their analysis will be conducted according to predefined standard operating procedures. Upon completion of the MDCT scan, the imaging data will be transmitted to the ICL, where blinded ICL personnel will perform comprehensive measurements and provide an official ICL imaging report.

Power, sample size and statistical considerations

Sample size calculation

Based on previous studies[10 14 21 22] and considering the heterogeneity of these results, along with retrospective data from the Interventional Center of Valvular Heart Diseases at Beijing Anzhen Hospital, and expert clinical opinions, the following hypotheses are formulated to assess the superiority of the treatment group over the control group:

1. Cardiovascular mortality at 1 year: the expected cardiovascular mortality rate at 1 year is 2.6% in the treatment group and 2.5% in the control group.
2. Myocardial infarction or stroke at 1 year: the anticipated incidence of myocardial infarction or stroke at 1 year is 2.6% in the treatment group and 2.9% in the control group.
3. Life-threatening, disabling or major bleeding events at 1 year: the projected incidence of life-threatening, disabling or major bleeding events at 1 year is 7.0% in the treatment group and 6.5% in the control group.

Table 2 The correlation matrix for the primary endpoint

	Cardiovascular mortality	Myocardial infarction or stroke	Life-threatening, disabling or major bleeding	Grade 3 or higher RLM	Grade 3 or higher HALT
Cardiovascular mortality	1				
Myocardial infarction or stroke	0.375	1			
Life-threatening, disabling or major bleeding	0.225	0.225	1		
Grade 3 or higher RLM	0.1	0.1	0	1	
Grade 3 or higher HALT	0.1	0.1	0	0.375	1

HALT, hypo-attenuated leaflet thickening; RLM, reduced leaflet motion.

4. Grade 3 or higher RLM at 1 year: the expected incidence of grade 3 or higher RLM at 1 year is 1.0% in the treatment group and 7.5% in the control group.
5. Grade 3 or higher HALT at 1 year: the projected incidence of grade 3 or higher HALT at 1 year is 3.5% in the treatment group and 13.8% in the control group.

Considering the correlations between the outcome events, the joint distribution of these outcomes will be characterised using a Copula function. Based on prior clinical experience, the correlation matrix for the outcome measures is defined in table 2.

The hypotheses will be tested using the Finkelstein–Schoenfeld method.[23 24] To calculate the sample size and power for the primary endpoints, 10 000 simulations with three iterations will be conducted. A total sample size of 408 participants (204 per group) is expected to provide approximately 80% power, assuming a one-sided significance level of 0.025. To account for an anticipated dropout rate of up to 10%, the final sample size will be adjusted to 454 participants (227 per group).

Analysis populations

In this study, the population will be divided into two analysis sets as follows:

1. Full analysis set (FAS): based on the intention-to-treat (ITT) principle, this set includes all randomised participants, analysed according to the treatment group to which they were originally assigned, irrespective of their adherence to the trial protocol or whether they completed the study.
2. Per-protocol set (PPS): this set consists of participants who strictly adhered to the trial protocol, excluding those who deviated from the protocol or withdrew prematurely. The PPS is a subset of the FAS.

Statistical analysis

1. Descriptive analysis: Categorical data will be summarised using frequencies and percentages, while continuous data will be described as mean±SD ($\bar{x} \pm$ SD) or median (IQR), depending on the normality of their distribution.
2. Baseline characteristics comparison: Baseline characteristics between groups will be compared as follows: categorical variables will be analysed using the continuity-corrected χ^2 test, with Fisher's exact test employed when >25% of cells have expected frequencies <5. For continuous variables following a normal distribution, comparisons will be made using the t-test. For non-normally distributed continuous variables, the Wilcoxon rank-sum test will be applied.
3. Efficacy analysis: The primary endpoint will be analysed according to the ITT principle, where all randomised participants will be included based on their assigned intervention, regardless of protocol adherence. Primary endpoints will be analysed using the win ratio method and tested using the Finkelstein–Schoenfeld approach. The win ratio is determined by pairing subjects from the experimental and control groups and calculating the ratio of 'wins' (ie, when the experimental group outcome is superior to the control group) to 'losses'. The 95% CI for the win ratio will be calculated using the bootstrap method. As for other secondary endpoints, categorical data will be compared using the continuity-corrected χ^2 test, and Fisher's exact test will be used when >25% of cells have expected frequencies <5. For normally distributed continuous data, the t-test will be employed, while the Wilcoxon rank-sum test will be applied for non-normally distributed data.
4. Safety analysis: Safety endpoints and adverse events (AEs) will be reported by frequency and incidence in both the experimental and control groups. Proportions will be analysed using the likelihood ratio χ^2 test or Fisher's exact test, as appropriate. Furthermore, all observed AEs will be comprehensively described in terms of their nature, severity and potential relationship to the investigational product.
5. Subgroup analysis: Subgroup analyses in this study will be stratified by key baseline factors, including age (≥70 years or <70 years), gender, New York heart association (NYHA) functional classification, society of thoracic surgeons score (STS) risk category (low, intermediate, high), high bleeding risk as defined by valve academic research consortium - high bleeding risk (VARC-HBR),[25] type of transcatheter aortic valve implantation (TAVI) valve (balloon-expandable or self-expanding) and valve size.

6. Sensitivity analysis: Sensitivity analyses will be conducted using the PPS to evaluate the robustness of the findings.
7. General analysis: All statistical tests will be performed with a one-sided significance level of 0.025. Statistical analyses will be conducted using SAS software (V.9.4, SAS Institute Inc, Cary, North Carolina, USA), R software (V.4.2.1, R Foundation for Statistical Computing, Vienna, Austria) and SPSS software (V.23.0, IBM Corp, Armonk, New York, USA).

DISCUSSION

The SCOPE study is the first multicentre randomised trial to specifically evaluate the safety and efficacy of rivaroxaban monotherapy versus antiplatelet monotherapy in patients with severe AS who have undergone successful TAVR but have no indications for long-term anticoagulation or DAPT. The optimal antithrombotic strategy in this patient population remains a critical topic of ongoing investigation.

Previous studies, such as the ARTE trial,[26] demonstrated the superiority of aspirin monotherapy over DAPT, primarily due to a significant reduction in bleeding events. This finding was further corroborated by the POPular TAVI trial (Cohort A).[14] The GALILEO trial,[13] which compared rivaroxaban plus aspirin with clopidogrel plus aspirin, reported that rivaroxaban plus aspirin was associated with a higher risk of death and thromboembolic complications, alongside an increased incidence of bleeding. Similarly, the ATLANTIS trial,[21] which included 1049 patients, found no superiority of anticoagulation over DAPT. As a result, current clinical guidelines recommend single antiplatelet therapy as the standard approach for patients without an indication for anticoagulation.[1 2]

However, the potential inadequacy of antiplatelet therapy to prevent leaflet thrombosis has often been overlooked. In the GALILEO-4D study,[11] which focused on SLT, anticoagulation was shown to be superior to antiplatelet therapy in preventing SLT. This conclusion has been supported by the ADAPT-TAVR and ATLANTIS-4D-CT trials.[10 22] SLT is not a rare phenomenon, with reported incidences ranging between 10% and 30%.[3 6–9] The adverse effects of SLT have also been well-documented. Alexander *et al* reported that SLT is associated with accelerated prosthesis degeneration.[5] In their retrospective analysis of 397 explanted bioprosthetic valves, the median longevity of bioprosthetic valves with thrombosis was only 24 months compared with 108 months in valves without thrombosis. This underscores the detrimental effect of valve thrombosis on prosthesis durability. Furthermore, SLT has been linked to an increased risk of transient ischaemic attacks.[3 4] Haemodynamically, Tarun *et al*, in their analysis of 931 patients, demonstrated that those with SLT were more likely to present with aortic valve gradients exceeding 20 mm Hg compared with those without SLT.[4]

Although anticoagulation has been effective in preventing SLT, the clinical benefits of this strategy remain uncertain. Pavel Overtchouk *et al* reported that anticoagulation is associated with a lower rate of bioprosthetic valve dysfunction,[27] while other studies identified the absence of anticoagulation as an independent predictor of valve haemodynamic deterioration.[28] These findings suggest that anticoagulation may reduce valve deterioration by mitigating SLT. However, in the ADAPT-TAVR trial, anticoagulation did not demonstrate a significant clinical benefit in reducing leaflet thrombosis.[22] Similarly, other randomised trials have reported no significant superiority of anticoagulation in preventing major clinical events, such as death, stroke, myocardial infarction and systemic embolism.[13 14 21 26] Two potential explanations for these findings warrant consideration: (1) the relatively short follow-up periods in these trials (median follow-up of 17 months in the GALILEO trial and 12 months in the ATLANTIS trial) may have been insufficient to fully capture the long-term effects of anticoagulation on SLT and clinical outcomes; and (2) these studies analysed each composite endpoint independently using Cox regression models, which may overlook the varying clinical significance of different outcomes. This method treats all endpoints equally, potentially missing the nuanced trade-offs between mortality, ischaemic or haemorrhagic events and SLT. In contrast, the win ratio method allows for prioritising endpoints based on clinical importance, providing a more comprehensive assessment of treatment effects. By ranking outcomes hierarchically, the win ratio offers a clearer evaluation of the overall benefit–risk profile, especially in balancing the risks of ischaemic, haemorrhagic events and SLT. In this study, we employed a hierarchical approach and the win ratio method to evaluate the overall systemic risk, allowing for a more integrated analysis of both safety and efficacy outcomes of short-term anticoagulation compared with SAPT.

Furthermore, in the GALILEO trial, rivaroxaban was used in combination with aspirin, raising the question of whether the increased bleeding risk observed was attributable to the combination therapy rather than rivaroxaban alone.[13] To date, no study has directly compared rivaroxaban monotherapy with antiplatelet monotherapy. This trial is designed to address this gap, providing a head-to-head comparison between rivaroxaban and aspirin/clopidogrel monotherapy to assess whether rivaroxaban offers superior clinical benefits.

In this study, rivaroxaban monotherapy was administered for the first month, followed by adjustment of antithrombotic regime based on clinical and imaging follow-up results. This design was based on evidence suggesting that the incidence of SLT is the highest within the first month after TAVR. At the 2022 TCT Congress, Professor Yu Sato presented a pathological study that found the median time to thrombosis was 16 days (range, 10–66 days). Their findings suggest that acute thrombus formation predominantly occurs within the first month

post-TAVR, indicating that early treatment is most effective in preventing SLT.[15]

Limitations

This study has several limitations. First, the open-label design inherently carries the risk of introducing bias as both the investigators and participants are aware of the treatment allocation. However, to minimise these risks, the study's primary endpoints include both clinical outcomes and objective assessments of leaflet thrombosis using CT imaging. Importantly, these endpoints will be adjudicated by independent, blinded CEC and ICL—which reduces the potential impact of bias. Second, the clinical relevance of SLT remains uncertain, and the inclusion of SLT-related events in the composite primary endpoint may reduce its overall clinical significance. To address this concern, we have implemented a hierarchical structure within the composite endpoint, prioritising the importance of its components. Furthermore, the use of the win ratio methodology allows for a more nuanced comparison of intergroup differences, thereby strengthening the interpretability of the primary endpoint. Third, the study's follow-up period of 1 year may be insufficient to fully assess the durability of short-term anticoagulation in preventing SLT beyond the cessation of therapy or its long-term impact on valve durability and other clinical outcomes. To mitigate this limitation, we plan to conduct extended follow-up in participants who consent to continued monitoring, allowing for a more comprehensive evaluation of these longer-term outcomes. Lastly, the study population is restricted to patients without indications for long-term anticoagulation or DAPT. As a result, the generalisability of the findings may be limited, and the results may not be extrapolated to the broader population of patients undergoing TAVR.

ETHICS AND DISSEMINATION

This study has been approved by the Ethics Committee of Beijing Anzhen Hospital (ethics approval no. 2024KLSD15) and will be conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The trial has been registered at the Chinese Clinical Trial Registry (registration no. ChiCTR2400087453). Informed consent will be obtained from all participants prior to their enrolment. Participants will be fully informed about the study's objectives, procedures, potential risks and benefits, as well as their right to withdraw from the study at any point without affecting their ongoing care. All participant data will be anonymised and securely stored in a password-protected database. Only authorised research personnel will have access to the data, and data handling will comply with relevant data protection regulations, such as the General Data Protection Regulation, where applicable.

The study results will be disseminated through peer-reviewed publications and presentations at national and international conferences. All findings, whether positive or negative, will be reported transparently.

Patient and public involvement

Patients and/or the public were not involved in the design or conduct of this study, but participants will be informed of the results through appropriate communication channels.

TRIAL STATUS

The trial is currently in the recruitment phase. The first patient was enrolled on 7 August 2024, and recruitment is expected to be completed by December 2025. The estimated study completion date is December 2026. This protocol is based on V.1.1, dated 25 June 2024.

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