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Title page

Title: A Standardized Heart Team Protocol versus Guideline-based Protocol on Revascularization Decisions Stability in Complex Coronary Artery Disease: Rationale and Design of a Randomized Trial

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ABSTRACT

Introduction

Multidisciplinary heart team approach has been recommended by revascularization guidelines, but how to organize and implement heart team standardly has not been validated. Inter- and intra-team decision instability existed in guideline-based heart team protocol, and our standardized heart team protocol based on a mixed-method study may improve the decision stability. The objective of this study is to evaluate the effect of a standardized heart team protocol versus guideline-based protocol on decision-making stability in complex coronary artery disease (CAD).

Methods and analysis

Eighty-four eligible interventional cardiologists, cardiac surgeons, or non-interventional cardiologists were enrolled and randomized to a standardized heart team protocol group or a guideline-based protocol group to make revascularization decisions for 480 complex CAD patients. In standardized group, heart team was implemented based on an evidence-based protocol including specialist selection, specialist training, team composition, team training, and standardized meeting process. In guideline-based group, heart team was implemented according to the key principles mentioned in clinical guidelines, including team composition and standardized meeting process. Twelve heart teams were allocated randomly in each of the group. The primary outcome is the overall percent agreement (OPA) in revascularization decisions between heart teams within a group. To demonstrate the clinical implication of decision-making stability, we will further analyze the association between decision stability and 1-year all-cause death, myocardial infarction, stroke, repeated revascularization, and rehospitalization due to ischemic symptom.

Ethics and dissemination

The study was approved by the Institutional Review Board (IRB) of Fuwai hospital. Results of this trial will be reported to the participating specialists, disseminated through scientific conferences and journals, reported on https://ClinicalTrials.gov, and published in full in peer-reviewed journals.

Trial registrations:

ClinicalTrials.gov, NCT05039567. Registered on 09/08/2021, https://register.clinicaltrials.gov/

Strengths and limitations of this study

1. The standardized heart team protocol was derived from guidelines but more specific than guidelines. Knowledge gained from this trial will facilitate the heart team implementation quality assessment and improvement for complex CAD.
2. Trial procedures are carried out remotely and all heart team meetings are held via video conference using online system, enabling full involvement and eliminating the risk of viral spreading in COVID-19.
3. Up-to-date risk scores were provided for comprehensive assessment in structured information to adjudicate the optimal treatment strategy.
4. Cases were not enrolled prospectively and feasibility of heart team in routine clinical care remains to be known.

KEYWORDS

Heart team; standardized protocol; decision-making stability

INTRODUCTION

Heart Team approach has received a Class 1C/1B recommendation in European and American guidelines on myocardial revascularization in patients with complex coronary artery disease (CAD) to optimize the treatment strategies and may lead to better outcomes.[1-5] Clinical guidelines recommend a heart team, consisting of clinical/non-interventional cardiologists, interventional cardiologists and cardiac surgeons, should take sufficient time to assess all available information of complex cases. However, there are relatively limited data on the heart team implementation in detail, such as the ideal composition, meeting frequency, timing of decision making, and outcomes, potentially leading to suboptimal decision-making quality.

Prior efforts have noted insufficient inter-specialist consistency, intra-team reproducibility and inter-team agreement in heart team decision-making. Denvir et al. found poor agreement existed between cardiac clinical specialist (kappa 0.26)[6]. Several studies reported that on re-discussion of the same patient data 9-12 months later, nearly 20% to 24% decisions differed from the original heart team recommendations.[7 8] In our previous work, the agreement between heart teams for revascularization decision-making was just moderate (kappa 0.58)[9].

Clinical guideline and previous practice experience from different centers have summarized several key principles in heart team implementation.[10-12] Clinical guidelines only recommended the composition of heart team and factors for consideration.[1 5] Sanchez et al. summed up the experience of heart team implementation from their single center, including team composition, data collection, and meeting process. The British cardiovascular Society and Society for Cardiothoracic Surgery in Great Britain and Ireland and British Cardiovascular Intervention Society set out the principles for

the functioning of the heart team across United Kingdom, including composition, frequency and the type of cases discussed.[12] Although these works provide important experiences for heart team implementation, these protocols were not evidence-based and data regarding how these protocols impact decision-making stability were scarce.[12]

To determine the potential factors influencing heart team decision-making comprehensively and explore an evidence-based heart team protocol, we conducted a sequential explanatory mixed method study and summarized 3 themes (specialist quality, team composition, and meeting process) and 10 subthemes of potential factors. In addition, 9 recommendations of heart team implementation were derived based on qualitative and quantitative data and a standardized heart team protocol was developed based on the previous experience, recommendations and guidelines, covering the whole procedure of heart team implementation.

However, the practical effect of the standardized protocol versus guideline-based protocol on decision-making stability and clinical outcomes remains unknown and randomized trial for validation is warranted. Therefore, we designed and conducted the pivotal randomized trial.

METHODS AND ANALYSIS

Study design overview

The current study is a randomized, controlled, 2-arm trial involving 84 cardiac specialists in 26 hospitals from China. Eligible specialists were randomized either to standardized implementation protocol group or guideline-based group and established 12 heart teams in each group to make revascularization decisions for 480 retrospectively enrolled patients with complex CAD. Decision-making stability will be evaluated. (**Figure 1**) SPIRIT[13], CONSORT[14], and TIDieR[15] checklists are

in **Supplemental File 1**. All procedures were approved by the Institutional Review Board (IRB) of Fuwai hospital (2 August 2021). The study start date was 4 January 2022 and the anticipated end date is 30 November 2022.

Objective and hypothesis

The primary objective of this study was to evaluate the effect of the standardized heart team protocol versus guideline-based protocol on the stability of decision-making in patients with complex CAD. The main study hypothesis is that heart teams organized following the standardized protocol will result in a better decision-making consistency compared with heart teams based on guideline principles. The secondary objectives of this study are to (1) evaluate the association between decision-making stability and 1-year composite of death, myocardial infarction (MI), stroke, repeated revascularization, and rehospitalization due to ischemic symptoms; (2) assess the appropriateness of heart team decision-making.

Participants and recruitment

To have access to enough experienced specialists, we enrolled eligible specialists from hospitals that (1) annual volume of percutaneous coronary intervention (PCI) ≥ 500; (2) annual volume of coronary artery bypass grafting (CABG) ≥ 200[1]; (3) have at least 2 interventional cardiologists, 2 cardiac surgeons and 1 non-interventional cardiologists meeting the inclusion criteria and agreeing to participate in the study. The inclusion criteria for the heart team specialists differs from specialties and is required for specified operator volumes and experience **(Table 1)**. Interventional cardiologist is required to have annual PCI volume ≥ 200[16], annual left main (LM)-PCI volume ≥ 25[1], and is capable of chronic total occlusion (CTO)-PCI. Cardiac surgeon is required to have total CABG

volume ≥ 200[17], and is proficient in both on-pump and off-pump CABG. We contacted with all the potential participants via e-mails or telephones to get their information confirmed and obtained their content during December 1,2021 to January 10, 2022. All participants have provided written informed consent for enrollment.

Table 1. Inclusion criteria for heart team specialists

Disciplines	Inclusion Criteria
Interventional Cardiologist	1) Annual PCI volume ≥200[16] 2) Annual LM PCI volume ≥25[1] 3) Capable of CTO PCI 4) Clinical researcher experience in coronary revascularization 5) Proficient in clinical guidelines
Cardiac Surgeon	1) CABG total volume ≥200[17] 2) Proficient in both on-pump and off-pump CABG 3) Clinical researcher experience in coronary revascularization 4) Proficient in clinical guidelines
Non-interventional Cardiologist	1) Proficient in clinical guidelines

CABG indicates coronary artery bypass grafting; CTO, chronic total occlusion; LM, left main; PCI, percutaneous coronary intervention.

Randomization

Randomization was stratified by specialties and was conducted by data manager using random number generation in SAS. Thirty-six cardiac surgeons and 36 interventional cardiologists were randomly allocated in a 2:1 ratio to the standardized protocol group (24 surgeons and 24 interventional cardiologists) or guideline-based group (12 surgeons and 12 interventional

cardiologists). Twelve non-interventional cardiologists were randomly selected and allocated to guideline-based group. After the randomization, each group of specialists were randomly assigned to 12 heart teams and will perform heart team meetings according to standardized protocol or guideline-based protocol. Research staff was informed of the randomization and organized the allocated specialists to establish heart teams. Participating specialists were unaware of the implementation conditions. **(Online Figure 1)**

Case selection and preparation

Selection of cases to be discussed

Adult patients with stable CAD according to the National Cardiovascular Data Registry (NCDR) CathPCI criteria[18] (stable angina, no or silent myocardial ischemia) and angiographically confirmed 3-vessel disease or left main (3VD/LM) disease were eligible for inclusion in the study. Eligible cases were randomly selected from a prospective registry of consecutive patients who underwent coronary angiography between August 2016 and August 2017.[19] Definitions and inclusion/exclusion criteria of cases can be seen in **Supplemental methods.** All patients have provided written informed consent for the study (**Online Figure 2**).

Structured patient information

Patient data were presented in a structured information form onto an electronic meeting support system by a non-clinical coordinator **(Online Table 1).** The structured information included (a) demographics; (b)medical histories and clinical risk factors; (c) medical treatment histories and CVD symptoms of the index hospitalization; (d) laboratory results; (e) noninvasive testing results (e.g.

electrocardiogram, echocardiogram, stress testing results); (f) diagnostic angiogram images and quantitative flow ratio (QFR)[20]; (g) clinical risk scores (i.e. SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score[21], SYNTAX II score[22], SYNTAX II 2020 score[23], Society of Thoracic Surgeons (STS) score[24 25], the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II[26], and sinoSCORE II[27]). All the clinical information were obtained from medical records according to the NCDR CathPCI data definitions[18]. All angiogram images were screened and risk scores were evaluated by an independent angiographic core laboratory using a computer-based automatic calculator.

Case assignment

Four hundred and eighty cases were randomized into 6 sets of 80 cases each using a stratified randomization procedure for discussion to ensure relatively equal heart team exposure to case complexity and a similar ratio of actual treatment strategies (CABG, PCI, or medication therapy).

Intervention

Standardized Heart team protocol

Eligible specialists randomized to this group established 12 heart teams and will conduct heart team meetings based on the standardized heart team protocol.[9] **(Figure 2)**

i. **Specialist selection.** All the cardiac surgeons were required personality test by Ten-Item Personality Inventory in China (TIPI-C)[28] and 24 surgeons with moderate scores were randomly selected. **(Online Table 2)** Twenty-four interventional cardiologists were randomly selected without personality selection.

ii. **Specialist training.** Unified training is required for all heart team members to achieve consensus view on the potential factors influencing revascularization decision. The training will be conducted and recorded by well-prepared coordinators. Consensus view should include clinical considerations on the key characteristics (e.g. age, left ventricular ejection fraction (LVEF), and body mass index (BMI)) and their weightage, interpretation of evidence (e.g. SYNTAX trial, Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial and the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) results). Additionally, the latest technical advancements in PCI and CABG will be discussed, especially for PCI, to narrow cognitive gaps among specialists of different expertise. The consensus view document will be recorded and put onto the electronic meeting support system for specialists' reference at any time. To maintain the fidelity to the consensus view, each bullet point of the consensus view will be presented as a footnote under the corresponding variable.

iii. **Team composition.** All specialists selected were randomly assigned to 12 heart teams consisting of 2 cardiac surgeons and 2 interventional cardiologists in each. Non-interventional cardiologist or other disciplinary specialist is not required in the routine heart team unless necessary. Moreover, technical level and administration position was balanced in each team.

iv. **Team training.** Prior to the formal heart team meeting, a pilot discussion (25-50 retrospective cases) will be performed following the standard meeting procedure to reinforce the practice of former consensus view for a more solid team consensus.

v. **Standardized meeting process.** Heart team meetings will be conducted similarly and standardly in both group according to the procedure widely used in previous studies.[10-12]Each heart team

independently evaluates a set of cases (80 cases) through the heart team assistance system using structured online case presentations, with the members blinded to the other heart teams and the decisions of other heart teams. All specialists are required to make decisions independently among five treatment categories (PCI, CABG, PCI/CABG equipoise, medical therapy, or further testing) before (round I) and after (round II) the heart team discussion. The heart team member only has access to the responses of the other heart team members after all members have submitted their independent decisions. The final treatment strategy is determined by majority decision.[29] **(Online Figure 3)**

Guideline-based protocol

Eligible specialists randomized to this group were randomly assigned to 12 heart teams based on the basic principles of guidelines **(Figure 2)**. Each heart team consists of 1 interventional cardiologist, 1 cardiac surgeon, and 1 non-interventional cardiologist. Pre-meeting training on consensus view and pilot discussion is not required in this group. Formal meeting procedures follow the standardized meeting process as the other group.

All heart team meetings will be held through video conferencing and a quiet environment will be required. For each heart team, the frequency of meeting is one or two times per week and lasting 1.5-2h at a time. Heart teams in each group were divided into six pairs randomly, and each pair of heart teams will evaluate the same randomly assigned 80 cases independently to make optimal revascularization decisions.

Outcomes

The primary outcome is the overall percent agreement, defined as the proportion of patients who

received coincident decision recommendations from paired heart teams. The secondary outcomes include:

(1) 1-year major adverse cardiovascular and cerebrovascular events (MACCEs): a composite of all-cause death, MI, stroke, repeated revascularization, and rehospitalization due to ischemic symptom;

(2) Kappa value of heart team decision-making: Fleiss's (more than 2 raters) and Cohen's (2 raters) kappa coefficients to evaluate inter-team, intra-team, inter-specialist, intra-specialist, and inter-round agreement for treatment decisions; At 1 month after the completion of initial discussion, all assigned cases will be re-presented and re-discussed with the same clinical data but not in the same order, with the heart team blinded to the outcome of the initial meeting, in order to evaluate the intra-team stability.

(3) Inappropriate decision rate: the final heart team recommendations will be adjudicated for appropriateness using the American College of Cardiology/American Association for Thoracic Surgery/American Heart Association 2017 Appropriate Use Criteria for coronary revascularization for each case.[30]

Data management and monitoring

Our IRB-approved protocol specifies plans for data entry, coding, security, and storage of data on a secure server. For retrospective data, all data was double checked or assessed by two independent coordinators. For prospective data on heart team meetings, the online meeting supporting system included several mechanisms to protect data integrity and promote data quality (e.g., warning of missing values, preventing duplicate team participation), and the data manager will maintain detailed

data management procedures. Coordinators will report to and discuss with the principal investigator about the study progress, including participant recruitment, data collection and analysis, and heart team meeting conductions. Any protocol modifications will be discussed with and approved by the IRB, and any significant changes in methods will be reported to the project's program officer and described in an update to the registered protocol on https://ClinicalTrials.gov. Data monitoring committee is not needed in this study, because all the cases discussed were retrospectively selected and their revascularization strategies would not be influenced by heart team recommendations and will be no risk for patients. As for participating specialists, heart team discussion will not interfere their routine clinical work. The Principal Investigator and approved study team members will have access to the final trial datasets.

Statistics

The pairwise comparison between the heart teams' decisions on each case provides data on the agreement (**Online Table 3**). The inter-team, intra-team, inter-specialist, intra-specialist, and inter-round agreement will be assessed using OPA and Cohen's κ coefficient, whenever applicable. Mean decision time will be also calculated. Cox proportional hazards models were used to analyze whether the patients adhering to heart team was associated with better outcomes when the two corresponding teams made the same decision. This analysis was used to demonstrate the association between decision stability and clinical outcomes. Categorical variables will be expressed as frequency and percentage. Continuous variables will be expressed as mean ± standard deviation (SD), or median and interquartile range. Categorical variables will be analyzed with the likelihood ratio χ^2 test or Fisher exact test if more than 25% of the cells have an expected frequency smaller than 5.

Continuous variables will be computed with the 2-sample t-test when data follow a normal distribution and will be compared with the Wilcoxon rank sum test for a non-normal distribution. 95% confidence intervals will be computed for all measurements. All the analyses will be performed at a significance level of 2-sided 0.05. All tests will be performed using SAS software, version 9.4 (SAS Institute, Cary, NC).

Sample Size

Number of assessments necessary to evaluate decision-making agreement

The primary endpoint of this study is to compare the overall percent agreement (OPA) between the standardized protocol group and guideline-based group. In previous study, heart teams were established and held meetings based on guidelines, and it was estimated that the OPA of the control group was 66.3% (unpublished data). We assumed that inter-team agreement is similar to or no better than intra-team reproducibility rate, according to relevant literature,[7 8] it is estimated that the OPA of the standardized protocol group is 76% (the minimum estimate of previous literature). Under this circumstance, the standardized protocol group has the smallest effect on improving the decision consistency rate compared with the guideline-based group. Using a 5% level of 2-side significance and a confidence level with 90%, it was estimated that a total number of 454 pairwise comparisons for each group would be necessary to meet the study acceptance criterion. Considering the feasibility of the study, 480 cases should be reviewed after the sample size was adjusted appropriately.

Number of heart teams needed

Considering the feasibility of implementation and good representation of both samples and heart teams, it was decided that 24 heart teams are needed with 12 in each group. Teams in each group will

be divided into 6 pairs randomly, and each pair of heart teams will evaluate the same randomly assigned 80 cases independently to provide inter-team agreement data, generating 480 pairwise comparison in each group.

Number of heart team specialists

The heart team in standardized group consists of 2 interventional cardiologists and 2 cardiac surgeons, and that in guideline based group consists of 1 interventional cardiologist, 1 cardiac surgeon, and 1 non-interventional cardiologist. In total, with 12 heart teams in each group, a minimum of 36 cardiac surgeons, 36 interventional cardiologists and 12 non-interventional cardiologists is needed in the final study.

Subgroup analysis

The primary and secondary outcomes will be analyzed in pre-specified subgroups, including specialties and professional status. Analysis will also be conducted according to different cases stratified by age, left ventricular ejection fraction (LVEF), body mass index (BMI), degree of the stenosis, calcified lesion, stenosis severity, tandem and bending/tortuous lesion, LM, SYNTAX stratification, SYNTAX Ⅱ recommendations, and SinoSCORE stratification. The comparisons in these analyses are not powered for hypothesis testing and are descriptive in nature.

Patient and Public Involvement statement

No patients were actively involved in setting the research question, outcome measures nor involved in the design of the study. Patients were not involved in interpretation or write up of the results, nor are there plans for the results to be disseminated to the patient community affected by this research.

Current status

Thirty-six cardiac surgeons, 36 interventional cardiologists and 12 non-interventional cardiologists from 26 eligible hospitals agreed to participate in this study. Four hundred and eighty patients with complex CAD were randomly selected for discussion. Specialist and patient baselines are shown in **Table 2** and **Table 3**.

TABLE 2. Specialist baseline characteristics

Characteristics	Overall (n=84)	Cardiac Surgeon (n=36)	Interventional Cardiologist (n=36)	Non-interventional Cardiologist (n=12)
Male	71 (84.5)	35 (97.2)	34 (94.4)	2 (16.7)
Status				
Chief specialist	46 (54.8)	21 (58.3)	19 (52.8)	6 (50.0)
Associate specialist	34 (40.5)	15 (41.7)	13 (36.1)	6 (50.0)
Attending specialist	4 (4.8)	0 (0.0)	4 (11.1)	0 (0.0)
Personality (TIPI)*	5.20 (4.80-5.70)	5.20 (4.90-5.50)	5.20 (4.60-5.80)	5.45 (4.80-5.60)
Extraversion	4.50 (4.00-5.00)	4.50 (4.00-5.50)	4.50 (4.00-5.00)	4.50 (4.00-5.00)
Agreeableness	5.50 (4.50-6.00)	5.00 (4.50-5.50)	5.75 (4.50-6.50)	5.75 (5.00-6.00)
Conscientiousness	5.50 (5.00-6.50)	6.00 (5.00-6.50)	5.50 (5.00-6.50)	5.75 (5.00-6.00)
Emotional Stability	5.00 (5.00-6.00)	5.00 (5.00-5.50)	5.00 (4.50-6.00)	6.00 (5.00-6.00)
Openness to Experiences	5.00 (4.50-5.50)	5.00 (4.50-5.50)	5.00 (5.00-5.50)	4.75 (4.50-5.50)

TIPI indicates ten-item personality inventory.[28]Data presented as n (%) and median (interquartile range).*Personality was evaluated by TIPI scale in Chinese.

TABLE 3. Demographic and clinical characteristics of retrospective patients

Characteristics	Patients for discussion (n=480)	Characteristics	Patients for discussion (n=480)
Demographics		Stable angina	370 (77.1)
Age, y	62.0 (55.0-67.5)	CCS I-II	325 (87.8)
Male (%)	363 (75.6)	CCS III-IV	45 (12.2)
Risk Factors		Number of anti-anginal medications	
Hypertension	334 (69.6)	0	118 (24.6)
Hyperlipidemia	429 (89.4)	1	154 (32.1)
Diabetes	185 (38.5)	2	149 (31.0)
Cerebrovascular disease	102 (21.3)	3	59 (12.3)
COPD	7 (1.5)	Extent of coronary disease	
Chronic renal disease	14 (2.9)	3-vessel disease	451 (94.0)
Smoker	226 (47.1)	Left main disease	129 (26.9)
Body mass index, kg/m^2	25.6 (23.7-27.5)	**Risk Classification**	
Ccr <60 mL/min/1.73m^2	7 (1.5)	SYNTAX score	22.5 (16.5-29.5)
Cardiovascular Characteristics		SYNTAX score tertiles	
Previous MI	49 (10.2)	Low risk (0-22)	237 (49.4)
Previous heart failure	10 (2.1)	Intermediate risk (23-32)	157 (32.7)
Peripheral vascular disease	46 (9.6)	High risk (≥33)	86 (17.9)
Ejection fraction, %	63.0 (59.0-65.0)	SYNTAX score II recommendation	
Ejection fraction ≤40%	23 (4.8)	PCI	11 (2.3)
CAD symptoms		CABG	153 (31.9)
Silent ischemia (after medical therapy)	90 (18.8)	Equipoise	316 (65.8)
Non-ischemia symptom	20 (4.2)	SYNTAX score II 2020 10-year mortality (%)	

Characteristics	Patients for discussion (n=480)	Characteristics	Patients for discussion (n=480)
CABG	14.8 (9.1-24.7)	Prolonged ventilation (%)	3.20 (2.62-3.98)
PCI	19.4 (11.6-32.2)	DSWI (%)	0.10 (0.08-0.14)
Euroscore II mortality (%)	0.80 (0.58-1.06)	Prolonged hospitalization (%)	1.79 (1.33-2.53)
SinoSCORE II mortality (%)	0.82 (0.47-1.18)	**Treatment Strategy in Real World**	
STS score (incidence of postoperative events)		PCI	287 (59.8)
Mortality (%)	0.49 (0.36-0.70)	CABG	116 (24.2)
Mortality or major complications (%)	5.30 (4.43-6.56)	Medical therapy	77 (16.0)
Reoperation (%)	1.72 (1.46-2.07)		
Renal failure (%)	0.43 (0.32-0.61)		
Stroke (%)	0.96 (0.73-1.36)		

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; Ccr, creatinine clearance rate; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; DSWI, deep sternal wound infection; MI, myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; STS, Society of Thoracic Surgeons; and SYNTAX, Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

Data presented as median (interquartile range, IQR) and n (%).

DISCUSSION

The optimization of heart team implementation including team composition, operation, distribution of responsibilities, and other issues still lack of verification by evidence-based trials. The present study is the first trial focusing on the heart team implementation quality assessment and improvement by evaluating the effect of the standardized heart team protocol compared to guideline-based protocol on decision-making stability for complex CAD.

Stability is a potential metric of decision-making quality. As for the expertise of individual specialists is specific to their professional training and experience, cardiologists and surgeons prefer PCI or CABG, respectively.[10] Prior data showed that 18.1% of the overall decision making for stable angina patients was classified as inappropriate, especially among patients undergoing PCI [31], and heart team recommendations differed from those of the original treating interventional cardiologist in approximately one-third of cases.[32] Therefore, heart team, a medium communication to integrate the input of numerous specialists, can help to minimize fragmented communication between specialists and eliminate specialist-bias in decision-making process. Sanchez et al convened 301 heart team meetings for complex CAD from 2012 to 2015, and reported the concordance of the heart team to appropriate use criteria was up to a 99.3% appropriate primary indication for coronary revascularization.[33] Thus, it is believed that qualified heart teams may perform more evidence-based and neutral in revascularization decision making.

Noteworthily, a dedicated and structured heart team has potential benefit for patient survival. Peyman et al reported patients treated for mitral valve disease based on a dedicated heart team decision have significantly higher survival than a general heart team, which illustrated the

establishment of dedicated heart team consisting of experienced specialists with adequate procedure volume benefit patient survival[34]. Thus, we hypothesize that revascularization recommendations of dedicated heart teams organized by the standardized heart team protocol might be more consistent and more appropriate compared with those of general heart teams based on guideline principles.

Making heart team approach well-structured and efficient contributes for a better quality of cardiovascular care. The current study is essential to answer the following questions: (1) Is it feasible to establish and organize heart team meetings with the guidance of the standardized heart team protocol in real-world clinical practice. (2) Will the standardized heart team protocol improve the decision-making stability in patients with complex CAD compared with the fundamental principles of heart team organizing in guidelines. Moreover, it will enhance educational opportunities for all team members involved and provide experience on the practice of heart team meeting in prospective clinical scenario.

Several novel design underlies the strength of this study. Firstly, all heart team trainings and meetings are held as video conference using an online decision making support system, which make it possible to involve specialists from multiple hospitals, reduce the negative implications from a few influential individuals on decision-making, and eliminate the risk of viral spreading in COVID-19.[35] Secondly, we prepared sufficient cases for discussion based on the premise of sample calculation, which provide good representation of the real-world patients and cover as many multiple types of complex cases as possible, reducing selection bias from case selection. Thirdly, we provide the most up-to-date risk scores (such as SYNTAX Ⅱ 2020 score[23], sinoSCORE Ⅱ[27]) and QFR[20], a novel angiography-derived physiological assessment approach, in structured information for specialist to adjudicate the optimal treatment strategy.

SUMMARY

The present randomized trial compares the effect of the standardized heart team protocol versus guideline-based protocol on decision-making stability. Knowledge gained from this trial may further improve heart team implementation quality for complex CAD.

ETHICS AND DISSEMINATION

Ethics

The study was reviewed and approved by the Ethics Review Committees of Fuwai hospital (2019-1303) on 2 August 2021; subsequent amendments have been approved. Informed consent was provided by all the participating specialists.

Safety

All the eligible cases were selected retrospectively and underwent coronary angiography between August 2016 and August 2017. Heart team decisions have no effect on patients' actual treatments. There will be no adverse event or serious adverse event relating to this study.

Dissemination

Results of this trial will be reported to the participating specialists, disseminated through scientific conferences and journals, reported on https://ClinicalTrials.gov, and published in full in the Health Technology Assessment (HTA) Journal series.

DECLARATIONS

Consent for publication

Not applicable.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Competing interests

The authors declare that they have no competing interests.

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Contributors

Study conception: ZZ; Study design: HPM, SL, XL, BX, ZZ; Drafting the manuscript: HPM, SL; Statistical consultation: XL, YW; Data collection and interpretation: HPM, SL, BX; Revising the manuscript for important intellectual content: HPM, SL, XL, YW, BX, ZZ; Obtaining funding: ZZ; Administrative, technical material support: ZZ.

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information and assessment of clinical scores.

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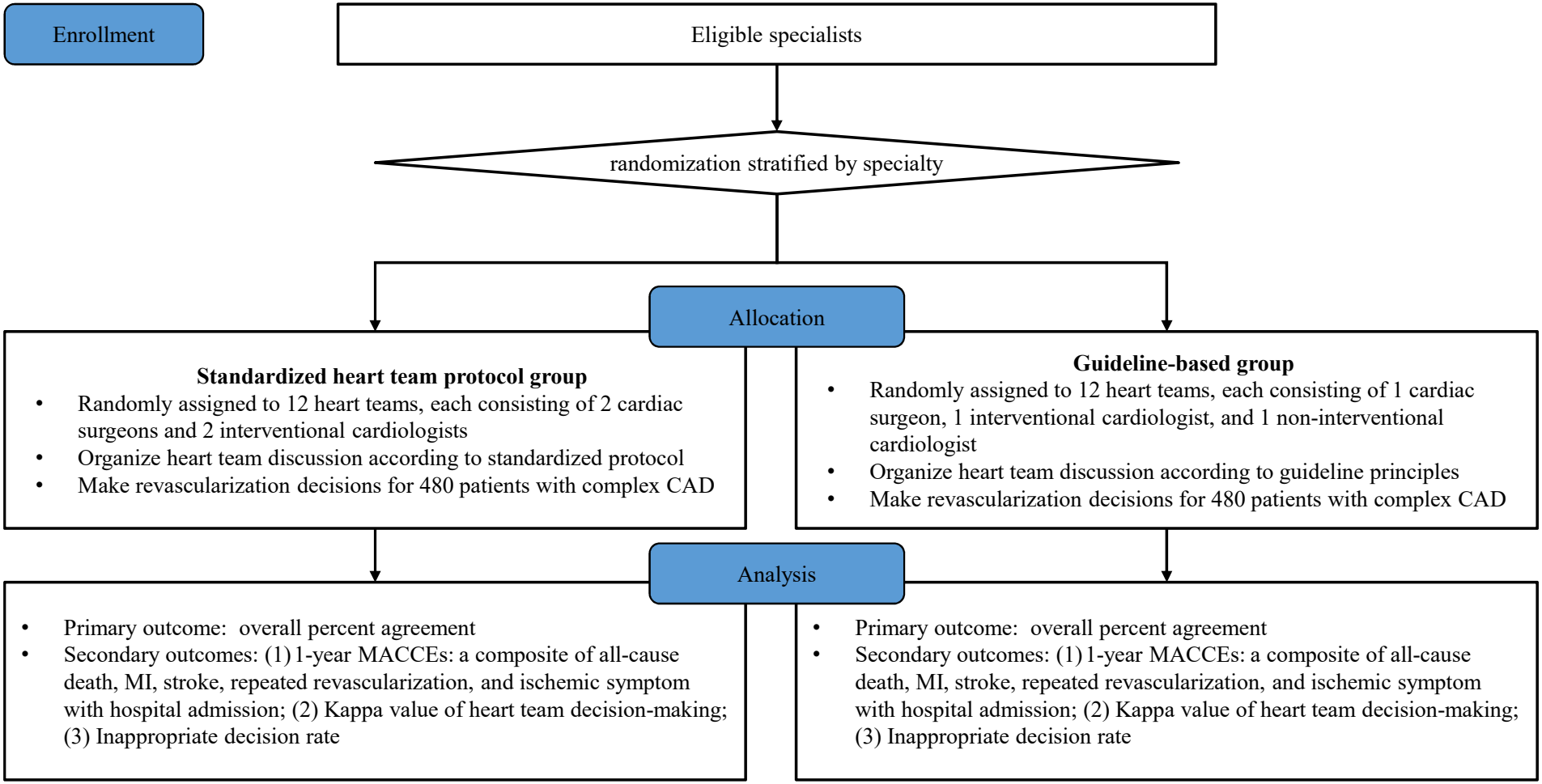
FIGURE LEGENDS

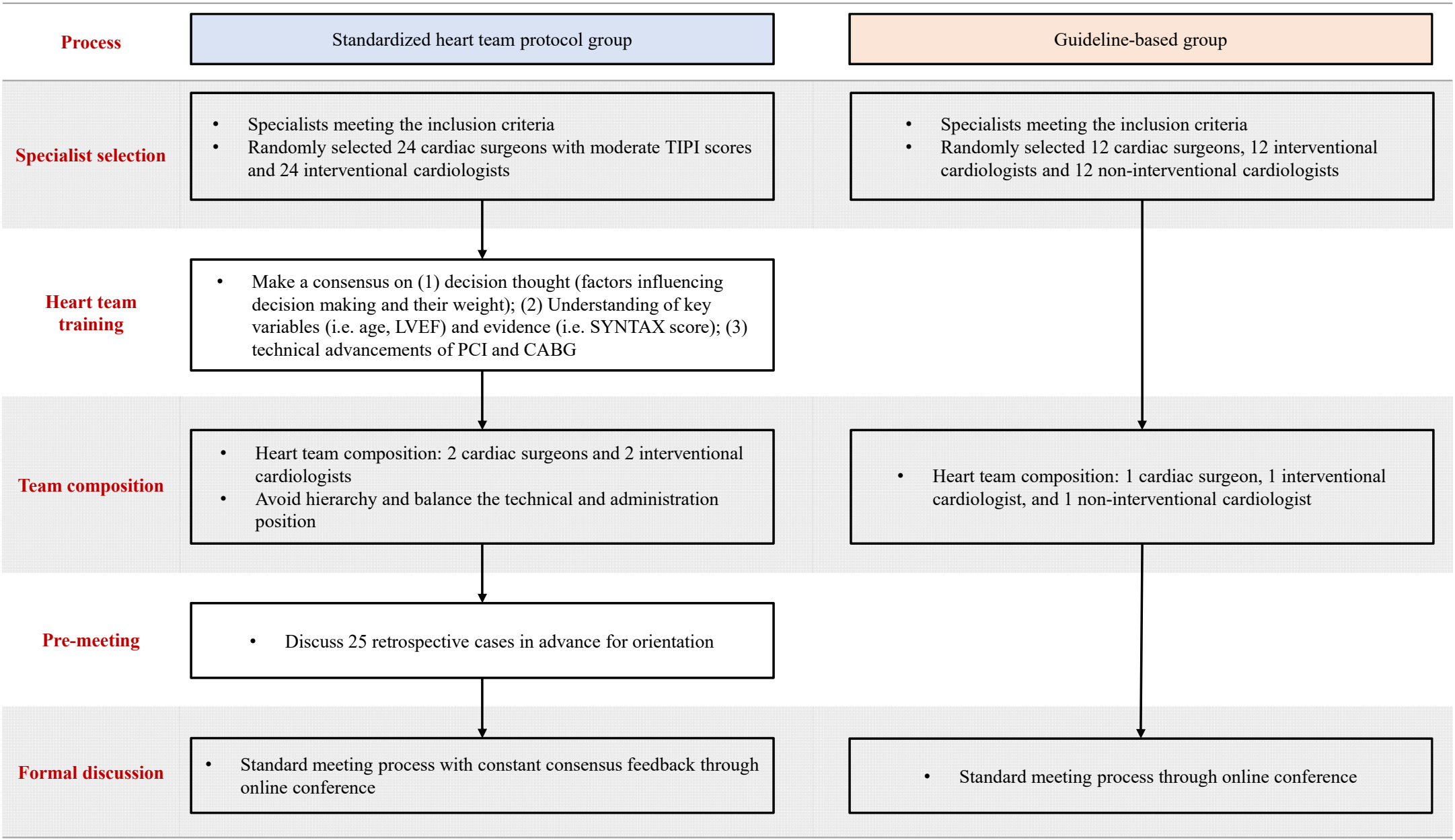
Figure 1. Flow chart

Eligible specialists were randomized either to standardized heart team protocol group or guideline-based group and established 12 heart teams in each group to make revascularization decisions for 480 retrospectively enrolled patients with complex CAD. CAD indicates coronary artery disease; MACCE, major adverse cardiovascular and cerebrovascular event.

Figure 2. Implementation strategies for protocol based group and guideline based group

In standardized protocol group, heart team was implemented based on an evidence-based protocol including specialist selection, specialist training, team composition, team training, and standardized meeting process. In guideline-based group, heart team was implemented according to the key principles mentioned in clinical guidelines, including team composition and standardized meeting process. TIPI indicates ten-item personality inventory; LVEF, left ventricular ejection fraction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; SYNTAX, Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.


Enrollment
Eligible specialists
randomization stratified by specialty
Allocation
Standardized heart team protocol group
Randomly assigned to 12 heart teams, each consisting of 2 cardiac surgeons and 2 interventional cardiologists
Organize heart team discussion according to standardized protocol
Make revascularization decisions for 480 patients with complex CAD
Guideline-based group
Randomly assigned to 12 heart teams, each consisting of 1 cardiac surgeon, 1 interventional cardiologist, and 1 non-interventional cardiologist
Organize heart team discussion according to guideline principles
Make revascularization decisions for 480 patients with complex CAD
Analysis
Primary outcome: overall percent agreement
Secondary outcomes: (1) 1-year MACCEs: a composite of all-cause death, MI, stroke, repeated revascularization, and ischemic symptom with hospital admission; (2) Kappa value of heart team decision-making; (3) Inappropriate decision rate
Primary outcome: overall percent agreement
Secondary outcomes: (1) 1-year MACCEs: a composite of all-cause death, MI, stroke, repeated revascularization, and ischemic symptom with hospital admission; (2) Kappa value of heart team decision-making; (3) Inappropriate decision rate


Process
Standardized heart team protocol group
Guideline-based group
Specialist selection
• Specialists meeting the inclusion criteria
• Randomly selected 24 cardiac surgeons with moderate TIPI scores and 24 interventional cardiologists
• Specialists meeting the inclusion criteria
• Randomly selected 12 cardiac surgeons, 12 interventional cardiologists and 12 non-interventional cardiologists
Heart team training
• Make a consensus on (1) decision thought (factors influencing decision making and their weight); (2) Understanding of key variables (i.e. age, LVEF) and evidence (i.e. SYNTAX score); (3) technical advancements of PCI and CABG
Team composition
• Heart team composition: 2 cardiac surgeons and 2 interventional cardiologists
• Avoid hierarchy and balance the technical and administration position
• Heart team composition: 1 cardiac surgeon, 1 interventional cardiologist, and 1 non-interventional cardiologist
Pre-meeting
• Discuss 25 retrospective cases in advance for orientation
Formal discussion
• Standard meeting process with constant consensus feedback through online conference
• Standard meeting process through online conference

SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	see clinicaltrials.gov
Protocol version	3	Date and version identifier	7
Funding	4	Sources and types of financial, material, and other support	24
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1-2, 24
	5b	Name and contact information for the trial sponsor	see clinicaltrials.gov
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	24
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	13-14

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-6
	6b	Explanation for choice of comparators	4-6
Objectives	7	Specific objectives or hypotheses	7
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	6-7
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	6-7
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	10-12
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	11
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12-13
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	see clinicaltrials.gov

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	15-16
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	8
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8-9
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	NA
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	7-12
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	9
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9-10,13-14
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13-14
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	14-15
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	16
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	NA
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	13-14
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	NA
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	13-14
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	21
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	21

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	8, 24
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	13-14
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	24
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	24
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	21
	31b	Authorship eligibility guidelines and any intended use of professional writers	21
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	24
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	available from authors
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	3-4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	4-6
	2b	Specific objectives or hypotheses	7
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6-7
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	7-8
	4b	Settings and locations where the data were collected	7-8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	10-12
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	12-13
	6b	Any changes to trial outcomes after the trial commenced, with reasons	NA
Sample size	7a	How sample size was determined	15-16
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	8-9
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	9-10
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	NA
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	7-12
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	9

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	13-14
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	13-14
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	16
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	8-9
	13b	For each group, losses and exclusions after randomisation, together with reasons	NA
Recruitment	14a	Dates defining the periods of recruitment and follow-up	7
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	18-20
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	NA
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	NA
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	NA
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	NA
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	NA
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	NA
Other information			
Registration	23	Registration number and name of trial registry	4
Protocol	24	Where the full trial protocol can be accessed, if available	See ClinicalTrial.gov
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	24

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

TIDieR Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	10-12	
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	10	Ma H, Lin S, Li X, et al. Exploring optimal heart team protocol to improve decision-making stability for complex coronary artery disease: a sequential explanatory mixed method study. Eur Heart J Qual Care Clin Outcomes 2021 doi: 10.1093/ehjqcco/qcab074 [published Online First: 2021/10/12]
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	10-12	Online table 1
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	9-12	

	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	9-12	
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	11	
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	11	
	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	12	
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	N/A	
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	N/A	
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	11	
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	N/A	

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

ǂ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).

SUPPLEMENTAL MATERIALS

A Standardized Heart Team Protocol versus Guideline-based Protocol on Revascularization Decisions Stability in Complex Coronary Artery Disease: Rationale and Design of a Randomized Trial

Contents

Supplemental Methods

Full Definitions of key variables and clinical endpoints

1. **Three-vessel disease:** three lesions with a percent diameter stenosis (DS%) between 50%-99% or total occlusion in a coronary artery with a ≥ 2.5 mm reference vessel diameter by visual assessment.
2. **Left main desease:** left main coronary artery is visually assessed DS% ≥ 50%.
3. **Major adverse cardiovascular and cerebrovascular events (MACCEs):** a composite of death, myocardial infarction, stroke, repeated revascularization, and rehospitalization due to ischemic symptoms.
4. **Death:** death from any cause. The cause of death will be adjudicated as being due to cardiac death or non-cardiac death.
5. **Myocardial infarction (MI)**

   (1) In-hospital MI: Defined as the occurrence during hospitalization after PCI, CABG or coronary angiography meeting at least 1 of the following criteria:

   1) The rise in cardiac troponin I (cTnI) is ⩾ 70 times the 99th percentile URL (where the baseline is lower than the URL, elevated and stable, or falling).
   2) If cTnI was not available, MI was defined with at least one of the following:
      i. New ischaemic ECG changes;
      ii. Development of new pathological Q waves;
      iii. Imaging evidence of loss of viable myocardium that is presumed to be new and in a pattern consistent with an ischaemic etiology;

iv. Angiographic findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or graft, side-branch occlusion-thrombus, disruption of collateral flow or distal embolization.

(2) Spontaneous MI: Defined as detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL after discharge and with at least one of the following:

1) Symptoms of acute myocardial ischemia;
2) New ischaemic ECG changes;
3) Development of pathological Q waves;
4) Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic etiology;
5) Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy.

6. Stroke was confirmed by a neurologist on the basis of imaging studies and was defined as follows:

1) A focal neurologic deficit of central origin lasting >72 hours, or
2) A focal neurologic deficit of central origin lasting >24 hours, with imaging evidence of cerebral infarction or intracerebral hemorrhage, or
3) A non-focal encephalopathy lasting >24 hours with imaging evidence of cerebral infarction or hemorrhage adequate to account for the clinical state.

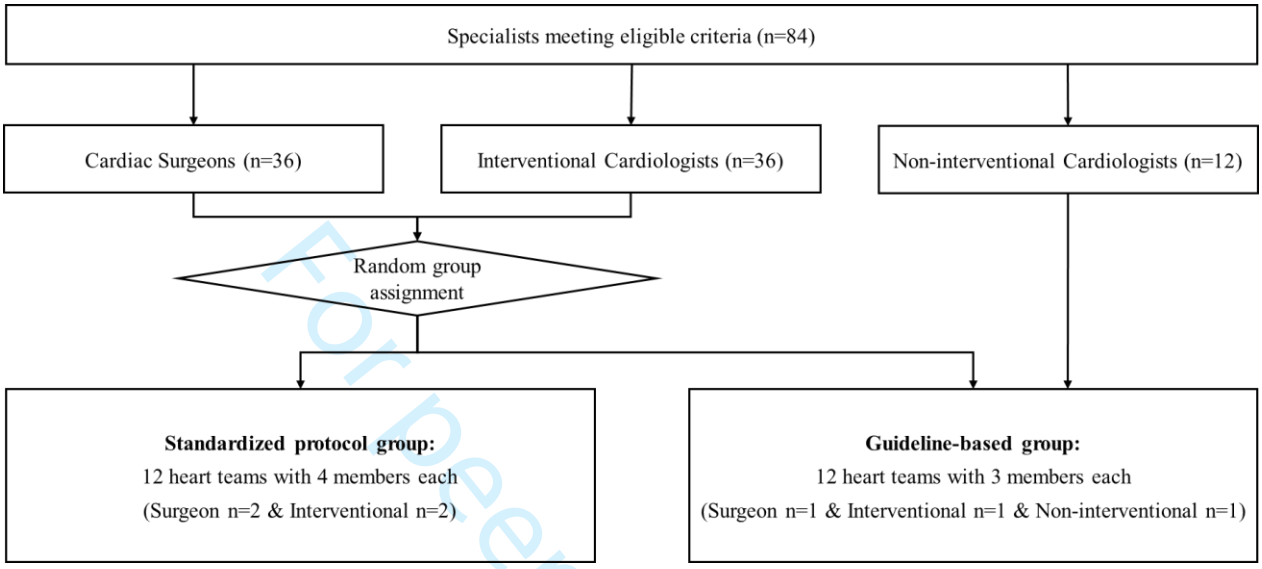
7. **Repeat revascularization** was defined as any repeat coronary artery bypass graft (CABG) or PCI.
    1) Target Lesion: Lesions were revascularized in the index procedure (or during a planned or provisional staged procedure).
    2) Non-Target Vessel: Lesions were not treated by either PCI or CABG at the index procedure.
8. **Rehospitalization due to ischmic symptoms:** rehospitalization because of ischemic discomfort (angina or symptoms thought to be equivalent).

Inclusion and exclusion criteria of cases to be discussed

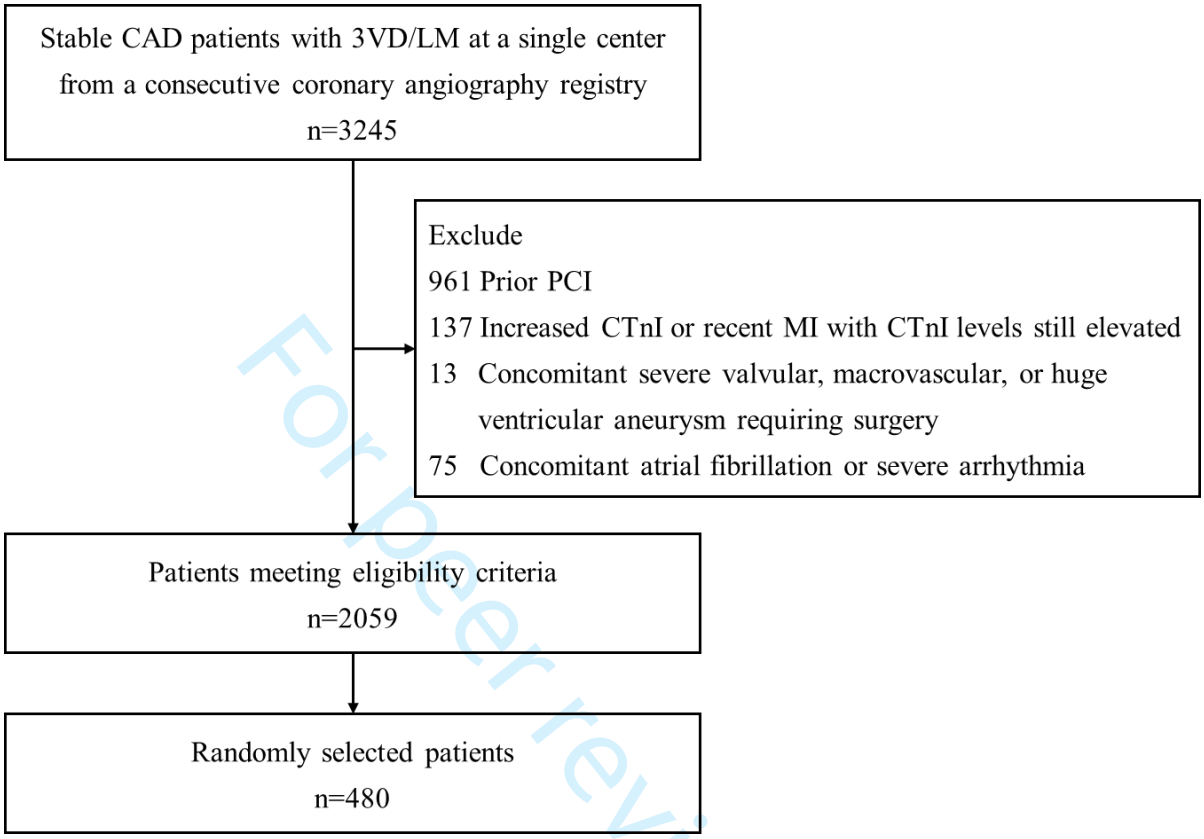
Adult patients with stable CAD according to the National Cardiovascular Data Registry (NCDR) CathPCI criteria (stable angina, no or silent myocardial ischemia) and angiographically confirmed 3-vessel disease or left main (3VD/LM) disease will be eligible for inclusion in the study. The exclusion criteria included: (1) prior coronary artery bypass grafting (CABG); (2) cardiac troponin I (CTnI) greater than the local laboratory upper limit of normal or recent myocardial infarction with CTnI levels still elevated; (3) concomitant severe valvular disease, macrovascular disease, or huge ventricular aneurysm requiring surgery; (4) concomitant atrial fibrillation or severe arrhythmia; or (5) unavailable de novo angiography images of the current hospitalization. Eligible cases will be randomly selected from a prospective registry of consecutive patients who underwent coronary angiography between August 2016 and August 2017.

Supplementary Figures

Online Figure 1. Specialist Enrollment Flowchart

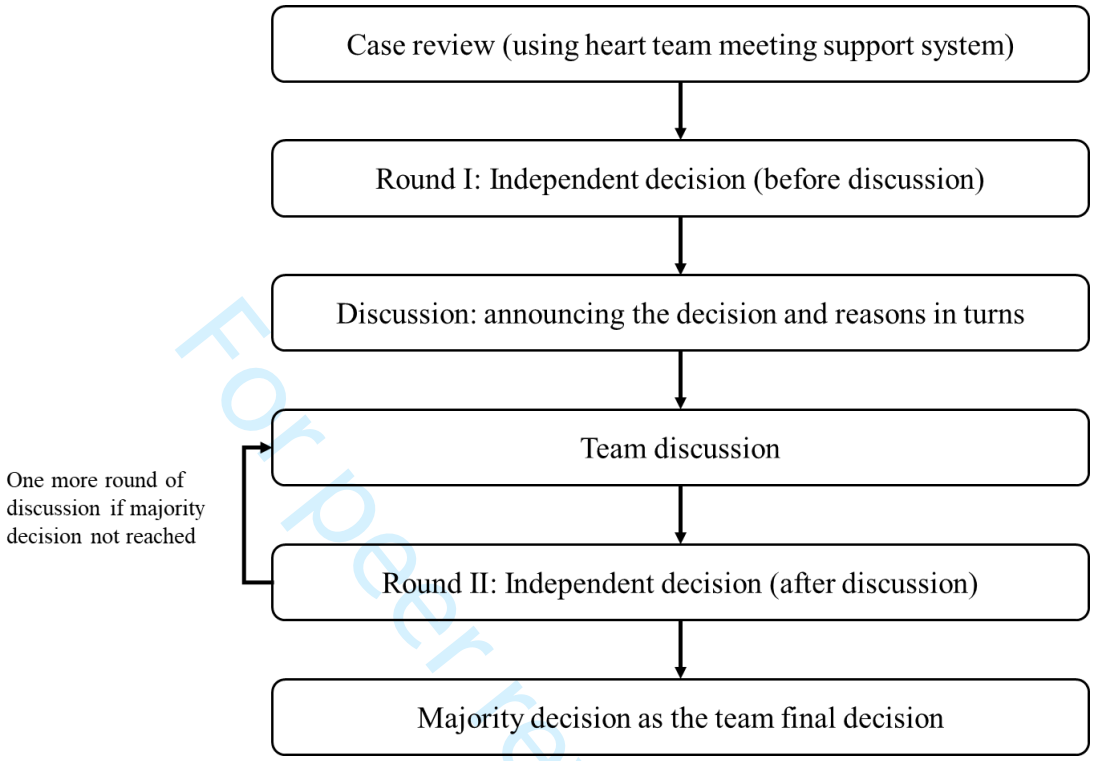


Online Figure 2. Patient Enrollment Flowchart



3VD indicates 3-vessel disease; CTnI, cardiac troponin I, LM, left main; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Online Figure 3. Standard heart team meeting procedure



Supplementary Tables

Online Table 1. Structured patient information

Heart Team Patient Information Sheet

A. Demograpgics

Patient ID:_____ Gender: ☐Male ☐female Age:_____y BMI :_____kg/m ^{2}

B. Medical history and risk factors

Diabetes	☐ Yes ☐No	
History of myocardial infarction	☐ Yes ☐No	Time: _____
History of heart failure	☐ Yes ☐No	EF value: _____%
History of stroke	☐ Yes ☐No	
renal insufficiency	☐ Yes ☐No	Creatinine: _____umol/L (44-133) Creatinine clearance: _____ml/min
Chronic obstructive pulmonary disease	☐ Yes ☐No	
Other comorbidities: *congenital mitral valve prolapse, hypertension, post-operative hypothyroidism, kidney stones*		

C. Coronary heart disease symptoms

Coronary heart disease symptoms	☐Unstable Angina ☐stable angina ☐Asymptomatic
Home antianginal medication	☐ Long-acting nitrates ☐ β -blockers ☐ Ca2+ channel blockers
CCS classification (stable angina)	☐I ☐II ☐III ☐IV ☐Asymptomatic
NYHA classification	☐I ☐II ☐III ☐IV

D. Laboratory test

Hemoglobin: _____g/L	White blood cells:_____ *10^9/L	Platelets:_____*10^9/L
PT: _____s (11.5-14.5)	APTT: _____s (28.5-43.5)	INR: _____(0.8-1.2)
Troponin I: _____ng/ml (ll_____:ul_____)		

E. Preoperative non-invasive examination

	Result
Admission ECG	*Sinus bradycardia 58 beats/min*
Echocardiography	*Mitral valve posterior leaflet prolapse, mitral valve regurgitation*
Stress Testing and Nuclear Medicine	
Coronary CTA	
Cardiac MRI	

F. Invasive coronary examination

Anigiography	FFR:	IVUS:	OCT:
QFR	LM (left main artery): _____		LAD (left anterior descending artery:_
	LCX (left circumflex artery):_____		RCA (right coronary artery):_____
	Obtusemarginal:_____		Diagonal:_____
	Posterior descending artery:_____		Left posterior artery:_____
	Ramus medianus:_____		

G. Clinical risk scores

SYNTAX	Score:_____

S YNTAX II	PCI Score: 30.0(9.8%)	CABG Score: 32.5(10.2%)	Recommended:/
SYNTAX II 2020	PCI score: 9.8%	CABG Score: 10.2%	
EuroScore II	Mortality: 0.7%		
SinoScore II	Mortality: 0.7%		
STS Score	Mortality: 0.49%	Mortality and complication rate: 9.95%	
	Renal failure rate: 0.39%	Stroke rate: 1.27%	
	Prolonged ventilation rate: 5.8%	Deep sternum infection rate: 0.36%	
	Reoperation rate: 2.37%	Extended hospital stay rate: 4.34%	

* Guidelines recommend STSscore mortality >2% with higher surgical risk

H. Decision result (single choice)

Independent decision before discussion	☐PCI ☐CABG ☐PCI /CABG ☐Drugs ☐Further inspection
Independent decision after discussion	☐PCI ☐CABG ☐PCI /CABG ☐Drugs ☐Further inspection

Online Table 2. Ten-Item Personality Inventory in China (TIPI-C)

Question No.*	Original items (Gosling et al., 2003)	Rating Scale						
		Absolutely disagree	Quite disagree	Almost disagree	Uncertain	Almost agree	Quite agree	Absolutely agree
		1	2	3	4	5	6	7
1	Extraverted, enthusiastic							
2	Critical, quarrelsome							
3	Dependable, self-disciplined							
4	Anxious, easily upset							
5	Open to new experience, complex							
6	Reserved, quiet							
7	Sympathetic, warm							
8	Disorganized, careless							

9	Calm, emotionally stable							
10	Conventional, uncreative							

*Scale scoring ("R" denotes reverse-scored items): Extraversion: 1, 6R; Agreeableness: 2R, 7; Conscientiousness: 3, 8R; Emotional Stability: 4R, 9; Openness to Experiences: 5, 10R.

Online Table 3. Tabular analysis of inter-team agreement

Case ID	Interventional group			Guideline group		
	Hear team 1 decision	Hear team 2 decision	agreement	Hear team 1' decision	Hear team 2' decision	agreement
001	CABG	CABG	Yes	PCI	CABG	No
002	CABG	PCI	No	PCI	PCI	Yes
003	Medication	PCI	No	Further testing	PCI	No
…	…	…	…	…	…	…
…	…	…	…	…	…	…
480	PCI	PCI	Yes	PCI	Medication	No

Online Table 3. Tabular analysis of inter-team agreement. Each case will be discussed by two assigned heart teams. The pairwise comparison between the heart team's decision on each case provides data on the agreement. CABG indicates coronary artery bypass grafting; PCI, percutaneous coronary intervention.

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Effect of a Standardized Heart Team Protocol versus Guideline-based Protocol on Revascularization Decisions Stability in Stable Complex Coronary Artery Disease: Rationale and Design of a Randomized Trial

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Secondary Subject Heading:	Evidence based practice
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Title page

Title: Effect of a Standardized Heart Team Protocol versus Guideline-based Protocol on Revascularization Decisions Stability in Stable Complex Coronary Artery Disease: Rationale and Design of a Randomized Trial

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ABSTRACT

Introduction

The multidisciplinary heart team approach has been recommended by revascularization guidelines, but how to organize and implement the heart team standardly has not been validated. Inter- and intra-team decision instability existed in guideline-based heart team protocol, and our standardized heart team protocol based on a mixed-method study may improve the decision stability. The objective of this study is to evaluate the effect of a standardized heart team protocol versus the guideline-based protocol on decision-making stability in stable complex coronary artery disease (CAD).

Methods and analysis

Eighty-four eligible interventional cardiologists, cardiac surgeons, or non-interventional cardiologists from 26 hospitals in China have been enrolled. They will be randomized to a standardized heart team protocol group or a guideline-based protocol group to make revascularization decisions for 480 historic cases with stable complex CAD. In the standardized group, we will establish 12 heart teams based on an evidence-based protocol, including specialist selection, specialist training, team composition, team training, and a standardized meeting process. In the guideline-based group, we will organize 12 heart teams according to the guideline principles, including team composition and standardized meeting process. The primary outcome is the overall percent agreement (OPA) in revascularization decisions between heart teams within a group. To demonstrate the clinical implication of decision-making stability, we will further analyze the association between decision stability and 1-year all-cause death, myocardial infarction, stroke, repeated revascularization, and re-hospitalization due to ischemic symptoms.

Ethics and dissemination

The study was approved by the Institutional Review Board (IRB) of Fuwai hospital (No. 2019-1303). All participants have provided informed consent for enrollment. The results of this trial will be reported to the participating specialists, disseminated through scientific conferences and journals, reported on https://ClinicalTrials.gov, and published in full in peer-reviewed journals.

Trial registrations:

ClinicalTrials.gov, NCT05039567. Registered on 09/08/2021, https://register.clinicaltrials.gov/

Strengths and limitations of this study

1. The study is a randomized controlled trial testing an evidence-based standardized heart team protocol covering the whole heart team organization process with up-to-date information provision against an approach following guideline basic recommendations.
2. Randomization is used in three aspects: stratified randomization in group allocation, randomization in heart team membership, and randomization in case allocation, which controls the social factors that may have negative implications for true group decision-making and ensures relatively heart team exposure to case complexity.
3. Trial procedures will be carried out remotely, and all heart team meetings will be held via video conference using an online system, enabling full involvement and eliminating the risk of viral spreading in COVID-19.

4. The cases discussed are retrospectively instead of prospectively selected, and the study does not investigate the impact of the standardized heart team protocol on true treatment decisions and clinical outcomes in routine clinical care, which is the next step to be tested.
5. The intervention in the standardized protocol group is an integrated approach, and the potential differential outcomes associated with its use cannot be attributed to a single point of the process.

KEYWORDS

Heart team; standardized protocol; decision-making stability

INTRODUCTION

The heart team approach has received a Class 1C/1B recommendation in European and American guidelines on myocardial revascularization in patients with complex coronary artery disease (CAD) to optimize the treatment strategies and may lead to better outcomes.[1-5] Clinical guidelines recommend that a heart team, consisting of clinical/non-interventional cardiologists, interventional cardiologists, and cardiac surgeons, should take sufficient time to assess all available information on complex cases. However, there are relatively limited data on the heart team implementation in detail, such as the ideal composition, meeting frequency, the timing of decision-making, and outcomes, potentially leading to suboptimal decision-making quality.

Prior efforts have noted insufficient inter-specialist consistency, intra-team reproducibility, and inter-team agreement in heart team decision-making. Denvir et al. found poor agreement existed between cardiac clinical specialists (kappa 0.26)[6]. Several studies reported that on re-discussion of the same patient data 9-12 months later, nearly 20% to 24% of decisions differed from the original heart team recommendations.[7 8] In our previous work, the agreement between heart teams for revascularization decision-making was just moderate (kappa 0.58)[9].

Clinical guidelines and previous practice experience from different centers have summarized several critical principles in heart team implementation.[10-12]Guidelines recommend the composition should be at least a cardiac surgeon, a interventional cardiologist, and a non-interventional cardiologist.[1 5] Sanchez et al. summed up the experience of the heart team implementation from their single center, including team composition, data collection, and meeting process. The British Cardiovascular Society (BCS), Society for Cardiothoracic Surgery in Great Britain and Ireland

(SCTS), and British Cardiovascular Intervention Society (BCIS) set out the principles for the functioning of the heart team across United Kingdom, including composition, frequency, and the type of cases discussed.[12] Although these works provided essential experiences for heart team implementation, the protocols were not evidence-based, and data regarding how these protocols impact decision-making stability were scarce.[12]

To determine the potential factors influencing heart team decision-making comprehensively and explore an evidence-based heart team protocol, we conducted a sequential explanatory mixed method study and summarized three themes (specialist quality, team composition, and meeting process) and ten subthemes of potential factors. In addition, nine recommendations for heart team implementation were derived based on qualitative and quantitative data, and a standardized heart team protocol was developed based on the previous experience, recommendations, and guidelines, covering the whole procedure of heart team implementation.

However, the practical effect of the standardized protocol versus the guideline-based protocol on decision-making stability and clinical outcomes remains unknown, and a randomized trial for validation is warranted. Therefore, we designed this pivotal randomized trial.

METHODS AND ANALYSIS

Study design overview

The current study is a randomized, controlled, 2-arm trial involving 84 cardiac specialists from 26 hospitals in China. Eligible specialists have been randomized to a standardized implementation protocol group or a guideline-based group to establish 24 heart teams and make revascularization decisions for 480 stable complex CAD cases retrospectively enrolled. We will evaluate the decision-

making stability. (**Figure 1**) SPIRIT[13], CONSORT[14], and TIDieR[15] checklists are in **Supplemental File 1**. All procedures have been approved by the Institutional Review Board (IRB) of Fuwai hospital (2 August 2021). The study start date is 4 January 2022, and the anticipated end date is 31 January 2023.

Objective and hypothesis

The primary objective of this study is to evaluate the effect of the standardized heart team protocol versus the guideline-based protocol on the stability of decision-making in stable complex CAD. The primary hypothesis is that heart teams organized on the standardized protocol will result in better decision-making consistency compared with those based on guideline principles. The secondary objectives of this study are to (1) evaluate the association between decision-making stability and 1-year composite of death, myocardial infarction (MI), stroke, repeated revascularization, and re-hospitalization due to ischemic symptoms; (2) assess the appropriateness of heart team decision-making.

Participants and recruitment

To have access to enough experienced specialists, we will enroll eligible specialists from hospitals with (1) annual volume of percutaneous coronary intervention (PCI) ≥ 500; (2) annual volume of coronary artery bypass grafting (CABG) ≥ 200[1]; (3) have at least two interventional cardiologists, two cardiac surgeons and one non-interventional cardiologist meeting the inclusion criteria and agreeing to participate in the study. The inclusion criteria for the heart team specialists differ from specialties and require specified operator volumes and experience **(Table 1)**. The interventional cardiologist is required to have an annual PCI volume ≥ 200[16], an annual left main (LM)-PCI volume

≥ 25[1], and is capable of chronic total occlusion (CTO)-PCI. The cardiac surgeon must have a total CABG volume ≥ 200[17] and be proficient in both on-pump and off-pump CABG. We have contacted all the potential participants via e-mails or telephones to get their information confirmed and obtained their content from 1 December 2021 to 10 January 2022. All participating specialists have provided written informed consent for enrollment (**Supplemental File 2)**.

Table 1. Inclusion criteria for heart team specialists

Disciplines	Inclusion Criteria
Interventional Cardiologist	1) Annual PCI volume ≥200[16] 2) Annual LM PCI volume ≥25[1] 3) CTO PCI total volume ≥10 4) Clinical researcher experience in coronary revascularization 5) Proficient in clinical guidelines
Cardiac Surgeon	1) CABG total volume ≥200[17] 2) Proficient in both on-pump and off-pump CABG 3) Clinical researcher experience in coronary revascularization 4) Proficient in clinical guidelines
Non-interventional Cardiologist	1) Proficient in clinical guidelines

CABG indicates coronary artery bypass grafting; CTO, chronic total occlusion; LM, left main; PCI, percutaneous coronary intervention.

Randomization

Randomization is stratified by specialties and conducted by a data manager using random number generation in SAS. We have randomized 36 cardiac surgeons and 36 interventional cardiologists in a 2:1 ratio to the standardized protocol group (24 surgeons and 24 interventional cardiologists) or the

guideline-based group (12 surgeons and 12 interventional cardiologists). Twelve non-interventional cardiologists have been randomly selected and allocated to the guideline-based group. After the randomization, each group of specialists will be randomly assigned to 12 heart teams and perform heart team meetings according to corresponding protocols. Research staff will be informed of the randomization and organize the allocated specialists to establish heart teams. Participating specialists are unaware of the implementation conditions. **(Online Figure 1)**

Case selection and preparation

Selection of cases to be discussed

Adult cases with stable CAD according to the National Cardiovascular Data Registry (NCDR) CathPCI criteria[18] (stable angina, no or silent myocardial ischemia) and angiographically confirmed 3-vessel disease or left main (3VD/LM) disease are eligible for inclusion in the study. We have randomly selected eligible cases from a prospective registry of consecutive patients who underwent coronary angiography between August 2016 and August 2017 (**Online Figure 2**).[19] All cases provided written informed consent at the time of registration and agreed to use their data for subsequent approved cardiovascular-related medical research. Definitions and inclusion/exclusion criteria of cases can be seen in **Supplemental methods.**

Structured patient information

Patient data will be presented in a structured information form on an electronic meeting support system by non-clinical coordinators **(Online Table 1).** The structured information includes (a) demographics; (b)medical histories and clinical risk factors; (c) medical treatment histories and CVD

symptoms of the index hospitalization; (d) laboratory results; (e) noninvasive testing results (e.g., electrocardiogram, echocardiogram, stress testing results); (f) diagnostic angiogram images and quantitative flow ratio (QFR)[20]; (g) clinical risk scores (i.e., SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score[21], SYNTAX II score[22], SYNTAX II 2020 score[23], Society of Thoracic Surgeons (STS) score[24 25], the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II[26], and sinoSCORE II[27]). All the clinical information have been obtained from medical records according to the NCDR CathPCI data definitions[18]. An independent angiographic core laboratory takes responsibility for all angiogram images screening and risk scores evaluation by using a computer-based automatic calculator.

Case assignment

Four hundred and eighty cases will be randomized into 6 sets of 80 cases each, using a stratified randomization procedure to ensure relatively equal heart team exposure to case complexity and a similar ratio of actual treatment strategies (CABG, PCI, or medication therapy).

Intervention

Standardized Heart team protocol

Eligible specialists randomized to this group will establish 12 heart teams and conduct heart team meetings based on the standardized heart team protocol.[9] **(Figure 2)**

i. **Specialist selection.** All the cardiac surgeons are required personality tests by Ten-Item Personality Inventory in China (TIPI-C)[28] and 24 surgeons with moderate scores will be randomly selected. **(Online Table 2)** Twenty-four interventional cardiologists will be randomly

selected without personality selection.

ii. **Specialist training.** All heart team members must undergo unified training to achieve a consensus on the potential factors influencing revascularization decisions. The training will be conducted and recorded by well-prepared coordinators. Consensus view should include clinical considerations on the essential characteristics (e.g., age, left ventricular ejection fraction (LVEF), and body mass index (BMI)) and their weightage, interpretation of evidence (e.g., SYNTAX trial, Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial and the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) results). Additionally, the latest technical advancements in PCI and CABG will be discussed, especially for PCI, to narrow cognitive gaps among specialists of different expertise. The consensus view document will be recorded and put onto the electronic meeting support system for reference at any time. To maintain fidelity to the consensus view, we will present each bullet point of the consensus view as a footnote under the corresponding variable.

iii. **Team composition.** All specialists selected will be randomly assigned to 12 heart teams consisting of 2 cardiac surgeons and 2 interventional cardiologists. Non-interventional cardiologist or other disciplinary specialist is not required in the routine heart team unless necessary. Moreover, the technical level and administration position will be balanced in each team.

iv. **Team training.** Before the formal heart team meeting, a pilot discussion (25-50 retrospective cases) will be performed following the standard meeting procedure to reinforce the practice of the former consensus view for a more solid team consensus.

v. **Standardized meeting process.** Heart team meetings will be conducted standardly in both groups according to the procedure widely used in the previous studies.[10-12]Each heart team independently evaluates a set of cases (80 cases) through the heart team assistance system using structured online case presentations, with the members blinded to the other heart teams and the decisions of other heart teams. All specialists are required to make decisions independently among five treatment categories (PCI, CABG, PCI/CABG equipoise, medical therapy, or further testing) before (round I) and after (round II) the heart team discussion. The heart team member only has access to the responses of the other heart team members after all members have submitted their independent decisions. The final treatment strategy is determined by a majority decision.[29] **(Online Figure 3)**

Guideline-based protocol

We will randomly assigned eligible specialists randomized to this group to 12 heart teams based on the principles of guidelines **(Figure 2)**. Each heart team consists of 1 interventional cardiologist, 1 cardiac surgeon, and 1 non-interventional cardiologist. This group does not require pre-meeting training on consensus view and pilot discussion. Formal meeting procedures follow the standardized meeting process as the other group.

All heart team meetings will be held through video conferencing, and a quiet environment will be required. For each heart team, the frequency of meetings is one or two times per week and lasts 1.5-2h at a time.

Outcomes

The primary outcome is the overall percent agreement (OPA), defined as the proportion of patients

who received coincident decision recommendations from paired heart teams. The secondary outcomes include:

(1) 1-year major adverse cardiovascular and cerebrovascular events (MACCEs): a composite of all-cause death, MI, stroke, repeated revascularization, and re-hospitalization due to ischemic symptoms;

(2) Kappa value of heart team decision-making: Fleiss's (more than 2 raters) and Cohen's (2 raters) kappa coefficients to evaluate inter-team, intra-team, inter-specialist, intra-specialist, and inter-round agreement for treatment decisions. To evaluate the reproducibility, all assigned cases will be re-discussed with the same clinical data but not in the same order at 1 month after the completion of initial discussion, with the heart team blinded to the outcome of the initial meeting.

(3) Inappropriate decision rate: the final heart team recommendations will be adjudicated for appropriateness using the American College of Cardiology (ACC) /American Association for Thoracic Surgery (AATS) /American Heart Association (AHA) 2017 Appropriate Use Criteria (AUC) and the Chinese AUC for coronary revascularization for each case.[30 31]Two investigators who do not participate in data collection will take responsibility for reviewing the team decisions and adjudicating the decision appropriateness independently. Any disputes will be settled via review by a third investigator, with decision by consensus.

Data management and monitoring

Our IRB-approved protocol specifies plans for data entry, coding, security, and data storage on a secure server. For retrospective data, all data will b double-checked or assessed by two independent coordinators. For prospective data on heart team meetings, the online meeting supporting system

included several mechanisms to protect data integrity and promote data quality (e.g., warning of missing values and preventing duplicate team participation). The data manager will maintain detailed data management procedures. Coordinators will report to and discuss with the principal investigator about the study progress, including participant recruitment, data collection and analysis, and heart team meeting conductions. Any protocol modifications will be discussed with and approved by the IRB. Any significant changes in methods will be reported to the project's program officer and updated on the registeration site https://ClinicalTrials.gov. This study does not need a data monitoring committee because all the cases discussed are retrospectively selected. Their revascularization strategies would not be influenced by heart team recommendations and will be no risk for cases. As for participating specialists, heart team discussion will not interfere with their routine clinical work. The Principal Investigator and approved study team members will have access to the final trial datasets.

Statistics

The pairwise comparison between the heart team decisions in each case provides data on the agreement (**Online Table 3**). The inter-team, intra-team, inter-specialist, intra-specialist, and inter-round agreements will be assessed using OPA and Cohen's κ coefficient, whenever applicable. Mean decision time will also be calculated. Cox proportional hazards models will be used to analyze whether the treatment decision adhering to the heart team recommendations is associated with better outcomes. Categorical variables will be expressed as frequency and percentage. Continuous variables will be expressed as mean ± standard deviation (SD), or median and interquartile range. Categorical variables will be analyzed with the likelihood ratio χ^2 test or Fisher exact test if more than 25% of the

cells have an expected frequency smaller than 5. Continuous variables will be computed with the 2-sample t-test when data follow a normal distribution and will be compared with the Wilcoxon rank sum test for non-normal distribution. 95% confidence intervals will be computed for all measurements. All the analyses will be performed at a significance level of 2-sided 0.05. All tests will be performed using SAS software, version 9.4 (SAS Institute, Cary, NC).

Sample Size

Number of assessments necessary to evaluate decision-making agreement

The primary endpoint of this study is to compare the OPA between the standardized protocol group and the guideline-based group. In our previous study, heart teams were established totally based on guidelines, and it was estimated that the OPA was 66.3% (unpublished data), serving as the reference rate of the controlled group in this study. We assumed that inter-team agreement is similar to or no better than intra-team reproducibility rate. According to relevant literature,[7 8] it is estimated that the OPA of the standardized protocol group is 76% (the minimum estimate of previous literature). Under this circumstance, the standardized protocol group has the minor effect on improving the decision consistency compared with the guideline-based group. Using a 5% level of 2-side significance and a confidence level of 90%, it was estimated that a total number of 454 pairwise comparisons for each group would be necessary to meet the study acceptance criterion. Considering the feasibility of the study, we adjusted the sample size to 480 cases.

Number of heart teams needed

Considering the feasibility of implementation and a good representation of both samples and heart teams, it was decided that 24 heart teams are needed with 12 in each arm. Teams in each group will

be divided into 6 pairs randomly, and each pair of heart teams will evaluate the same randomly assigned 80 cases independently to provide inter-team agreement data, generating 480 pairwise comparisons in each group.

Number of heart team specialists

The heart team in the standardized group consists of 2 interventional cardiologists and 2 cardiac surgeons, and that in the guideline-based group consists of 1 interventional cardiologist, 1 cardiac surgeon, and 1 non-interventional cardiologist. With 12 heart teams in each group, a minimum of 36 cardiac surgeons, 36 interventional cardiologists, and 12 non-interventional cardiologists are needed in the final study in total.

Subgroup analysis

The primary and secondary outcomes will be analyzed in pre-specified subgroups, including specialties and professional status. The analysis will also be conducted according to different cases stratified by age, left ventricular ejection fraction (LVEF), body mass index (BMI), degree of the stenosis, calcified lesion, stenosis severity, tandem and bending/tortuous lesion, LM, SYNTAX stratification, SYNTAX Ⅱ recommendations, and SinoSCORE stratification. The comparisons in these analyses may be not powered for hypothesis testing but are descriptive in nature.

Patient and Public Involvement statement

None.

Current status

Thirty-six cardiac surgeons, 36 interventional cardiologists, and 12 non-interventional cardiologists

from 26 eligible hospitals have agreed to participate in this study and provided informed consent. Four hundred and eighty cases with stable complex CAD have been randomly selected for discussion. Specialist and patient baselines are shown in **Table 2** and **Table 3**.

TABLE 2. Specialist baseline characteristics

Characteristics	Overall (n=84)	Cardiac Surgeon (n=36)	Interventional Cardiologist (n=36)	Non-interventional Cardiologist (n=12)
Male	71 (84.5)	35 (97.2)	34 (94.4)	2 (16.7)
Status				
Chief specialist	46 (54.8)	21 (58.3)	19 (52.8)	6 (50.0)
Associate specialist	34 (40.5)	15 (41.7)	13 (36.1)	6 (50.0)
Attending specialist	4 (4.8)	0 (0.0)	4 (11.1)	0 (0.0)
Personality (TIPI)*	5.20 (4.80-5.70)	5.20 (4.90-5.50)	5.20 (4.60-5.80)	5.45 (4.80-5.60)
Extraversion	4.50 (4.00-5.00)	4.50 (4.00-5.50)	4.50 (4.00-5.00)	4.50 (4.00-5.00)
Agreeableness	5.50 (4.50-6.00)	5.00 (4.50-5.50)	5.75 (4.50-6.50)	5.75 (5.00-6.00)
Conscientiousness	5.50 (5.00-6.50)	6.00 (5.00-6.50)	5.50 (5.00-6.50)	5.75 (5.00-6.00)
Emotional Stability	5.00 (5.00-6.00)	5.00 (5.00-5.50)	5.00 (4.50-6.00)	6.00 (5.00-6.00)
Openness to Experiences	5.00 (4.50-5.50)	5.00 (4.50-5.50)	5.00 (5.00-5.50)	4.75 (4.50-5.50)

TIPI indicates the ten-item personality inventory.[28]Data presented as n (%) and median (interquartile range).*Personality was evaluated by the TIPI scale in Chinese.

TABLE 3. Demographic and clinical characteristics of retrospective patients

Characteristics	Patients for discussion (n=480)	Characteristics	Patients for discussion (n=480)
Demographics		Silent ischemia (after medical therapy)	90 (18.8)
Age, y	62.0 (55.0-67.5)	Non-ischemia symptom	20 (4.2)
Male (%)	363 (75.6)	Stable angina	370 (77.1)
Risk Factors		CCS I-II	325 (87.8)
Hypertension	334 (69.6)	CCS III-IV	45 (12.2)
Hyperlipidemia	429 (89.4)	Number of anti-anginal medications	
Diabetes	185 (38.5)	0	118 (24.6)
Cerebrovascular disease	102 (21.3)	1	154 (32.1)
COPD	7 (1.5)	2	149 (31.0)
Chronic renal disease	14 (2.9)	3	59 (12.3)
Smoker	226 (47.1)	Extent of coronary disease	
Body mass index, kg/m^2	25.6 (23.7-27.5)	3-vessel disease	451 (94.0)
Ccr <60 mL/min/1.73m^2	7 (1.5)	Left main disease	129 (26.9)
Cardiovascular Characteristics		**Risk Classification**	
Previous MI	49 (10.2)	SYNTAX score	22.5 (16.5-29.5)
Previous heart failure	10 (2.1)	SYNTAX score tertiles	
Peripheral vascular disease	46 (9.6)	Low risk (0-22)	237 (49.4)
Ejection fraction, %	63.0 (59.0-65.0)	Intermediate risk (23-32)	157 (32.7)
Ejection fraction ≤40%	23 (4.8)	High risk (≥33)	86 (17.9)
CAD symptoms		SYNTAX score II recommendation	

Characteristics	Patients for discussion (n=480)	Characteristics	Patients for discussion (n=480)
PCI	11 (2.3)	Reoperation (%)	1.72 (1.46-2.07)
CABG	153 (31.9)	Renal failure (%)	0.43 (0.32-0.61)
Equipoise	316 (65.8)	Stroke (%)	0.96 (0.73-1.36)
SYNTAX score II 2020 10-year mortality (%)		Prolonged ventilation (%)	3.20 (2.62-3.98)
CABG	14.8 (9.1-24.7)	DSWI (%)	0.10 (0.08-0.14)
PCI	19.4 (11.6-32.2)	Prolonged hospitalization (%)	1.79 (1.33-2.53)
Euroscore II mortality (%)	0.80 (0.58-1.06)	**Treatment Strategy in Real World**	
SinoSCORE II mortality (%)	0.82 (0.47-1.18)	PCI	287 (59.8)
STS score (incidence of postoperative events)		CABG	116 (24.2)
Mortality (%)	0.49 (0.36-0.70)	Medical therapy	77 (16.0)
Mortality or major complications (%)	5.30 (4.43-6.56)		

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; Ccr, creatinine clearance rate; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; DSWI, deep sternal wound infection; MI, myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; STS, Society of Thoracic Surgeons; and SYNTAX, Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

Data presented as median (interquartile range, IQR) and n (%).

ETHICS AND DISSEMINATION

Ethics

The study was reviewed and approved by the Ethics Review Committees of Fuwai hospital (2019-1303) on 2 August 2021; subsequent amendments have been approved. All the participants have provided informed consents.

Safety

All the eligible cases were retrospectively selected and underwent coronary angiography between August 2016 and August 2017. Heart team decisions do not effect on patients' actual treatments. There will be no adverse event or serious adverse event relating to this study.

Dissemination

Results of this trial will be reported to the participating specialists, disseminated through scientific conferences and journals, reported on https://ClinicalTrials.gov, and published in full in peer-reviewed journals.

DISCUSSION

The optimization of heart team implementation including team composition, operation, distribution of responsibilities, and other issues still lacks verification by evidence-based trials. The present study is the first trial focusing on the heart team implementation quality assessment and improvement by evaluating the effect of the standardized heart team protocol compared to

the guideline-based protocol on decision-making stability for stable complex CAD.

Stability is a potential metric of decision-making quality. As the expertise of individual specialists is specific to their professional training and experience, cardiologists and surgeons prefer PCI or CABG, respectively.[10] Prior data showed that 18.1% of the overall decision-making for stable angina patients was classified as inappropriate based on a single disciplinary decision, especially among patients undergoing PCI [32]. The heart team, a medium of communication to integrate the input of numerous specialists, can help to minimize fragmented communication between specialists and eliminate specialist bias in the decision-making process. It was reported that heart team recommendations differed from those of the original treating interventional cardiologist in approximately one-third of cases.[33] Sanchez et al convened 301 heart team meetings for complex CAD from 2012 to 2015 and reported the concordance of the heart team to appropriate use criteria was up to a 99.3% appropriate primary indication for coronary revascularization.[34] Therefore, qualified heart teams perform more evidence-based and neutral in revascularization decision-making. The success of the heart team approach is apparent in a growing number of optimal revascularization decisions made according to professional guidelines.

Notably, a dedicated and structured heart team has a potential benefit for patient survival. Peyman et al reported patients treated for mitral valve disease based on a dedicated heart team decision have significantly higher survival than a general heart team, which illustrated the establishment of a dedicated heart team consisting of experienced specialists with adequate procedure volume benefits patient survival[35]. In addition, appropriate revascularization is

associated with improved 1-year outcomes in patients with appropriate indications and has no benefit in those with uncertain or inappropriate indications.[19] Thus, we assume that revascularization recommendations of dedicated heart teams organized by the standardized heart team protocol would be more stable and appropriate compared with those of general heart teams based on guideline principles, which leads to better clinical outcomes.

Making the heart team approach well-structured and efficient contributes to a better quality of cardiovascular care. The current study is essential to answer the following questions: (1) Is it feasible to establish and organize heart team meetings with the guidance of the standardized heart team protocol? (2) Will the standardized heart team protocol improve the decision-making stability in patients with stable complex CAD compared with the fundamental principles of heart team organizing in guidelines? Moreover, it will enhance educational opportunities for all team members involved and provide experience in the practice of heart team meetings in prospective clinical scenarios.

Several novel designs underlie the strength of this study. Firstly, we use a randomized controlled design to demonstrate the structure and effect of an evidence-based standardized heart team protocol on decision-making stability against the controlled approach based on guideline principles, which fills the gap with no randomized data currently available in optimal heart team implementation[12 33]. Secondly, the study applies randomization three times. Eligible specialists are first randomly selected and assigned to different arms by stratification randomization. Then we establish heart teams with randomized membership to reduce social factors that may have negative implications on individual decision-making[36]. Cases are also randomized into 6 sets of

80 cases each to ensure relatively equal heart team exposure to case complexity. Thirdly, all heart team training and meetings are held via video conference using an online decision-making support system, which makes it possible to involve specialists from multiple hospitals, reduce the negative influence of a few influential individuals on face-to-face decision-making, and eliminate the risk of viral spreading in COVID-19.[37] Fourthly, we provide the most up-to-date risk scores (such as SYNTAX Ⅱ 2020 score[23], sinoSCORE Ⅱ[27]) and QFR[20], a novel angiography-derived physiological assessment approach, in structured information for the specialists to adjudicate the optimal treatment strategy.

The study has several limitations. First, cases discussed are retrospectively selected rather than prospectively enrolled. All cases have already been treated from August 2016 to August 2017 in the original hospitalization, thus it is unable to reveal the true impact and benefits of heart team meetings on real-world decision-making and outcomes in routine clinical practice. Prospective design is needed for the next step. Second, the intervention in the standardized protocol group is an integrated approach and the potential differential outcomes associated with its use cannot be attributed to a single point of the process. Additional quantitative and qualitative analysis is needed to find out which steps work on the decision-making stability. Third, heart team decisions will be made independently of patient preferences, while in real-world clinical practice, patient preference is an important factor for the final treatment decision. Patient involvement in shared decision-making should be considered in future trials.

DECLARATIONS

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Contributors

ZZ contributed to study conception, funding obtaining, administration, and technical material support. HPM, SL, XL, BX, and ZZ contributed to the study design. HPM and SL drafted the manuscript. XL and YW contributed to statistical consultation. HPM, SL, and BX contributed to data collection and interpretation. All authors revised the manuscript for important intellectual content and approved the final version.

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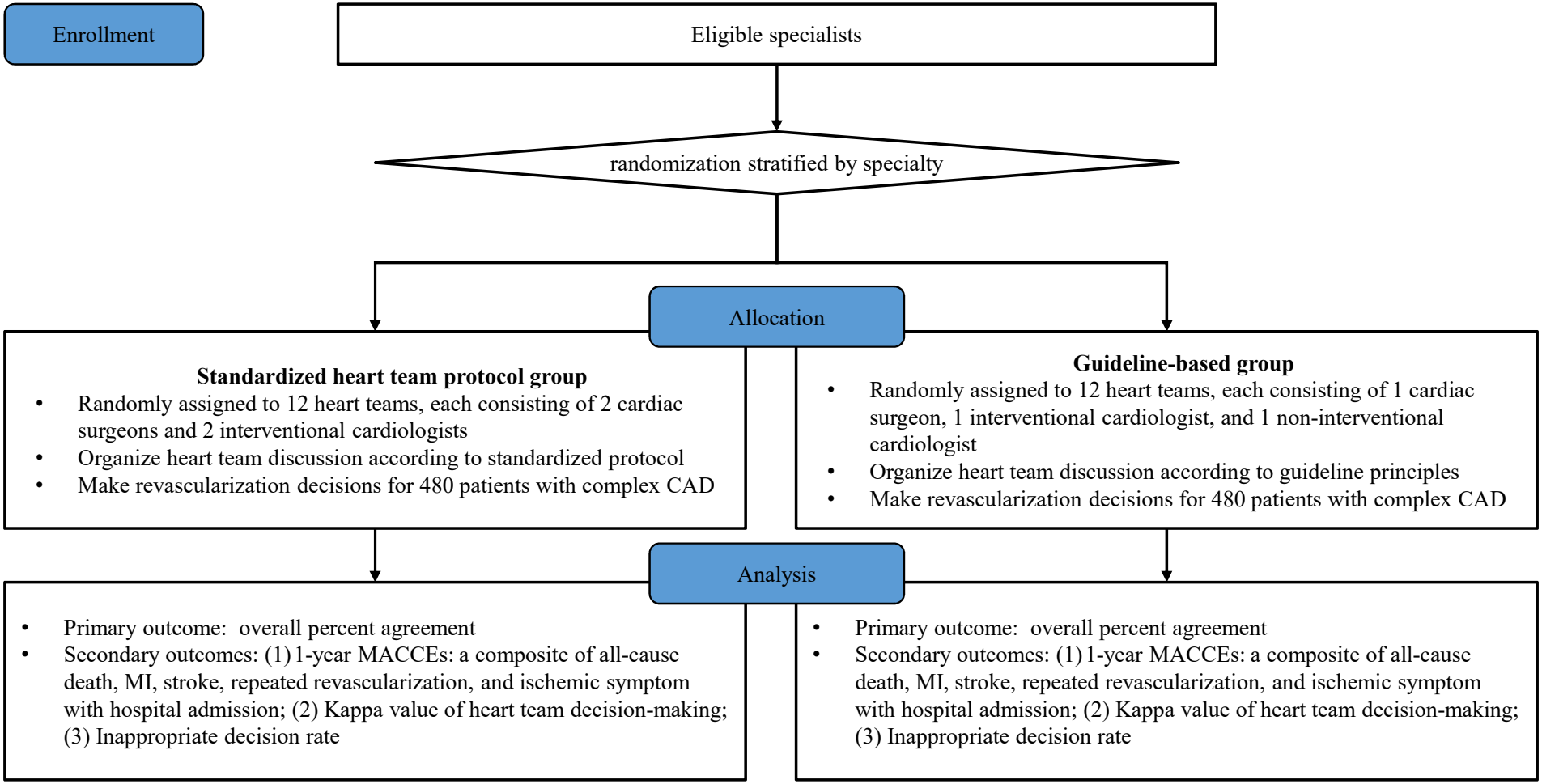
FIGURE LEGENDS

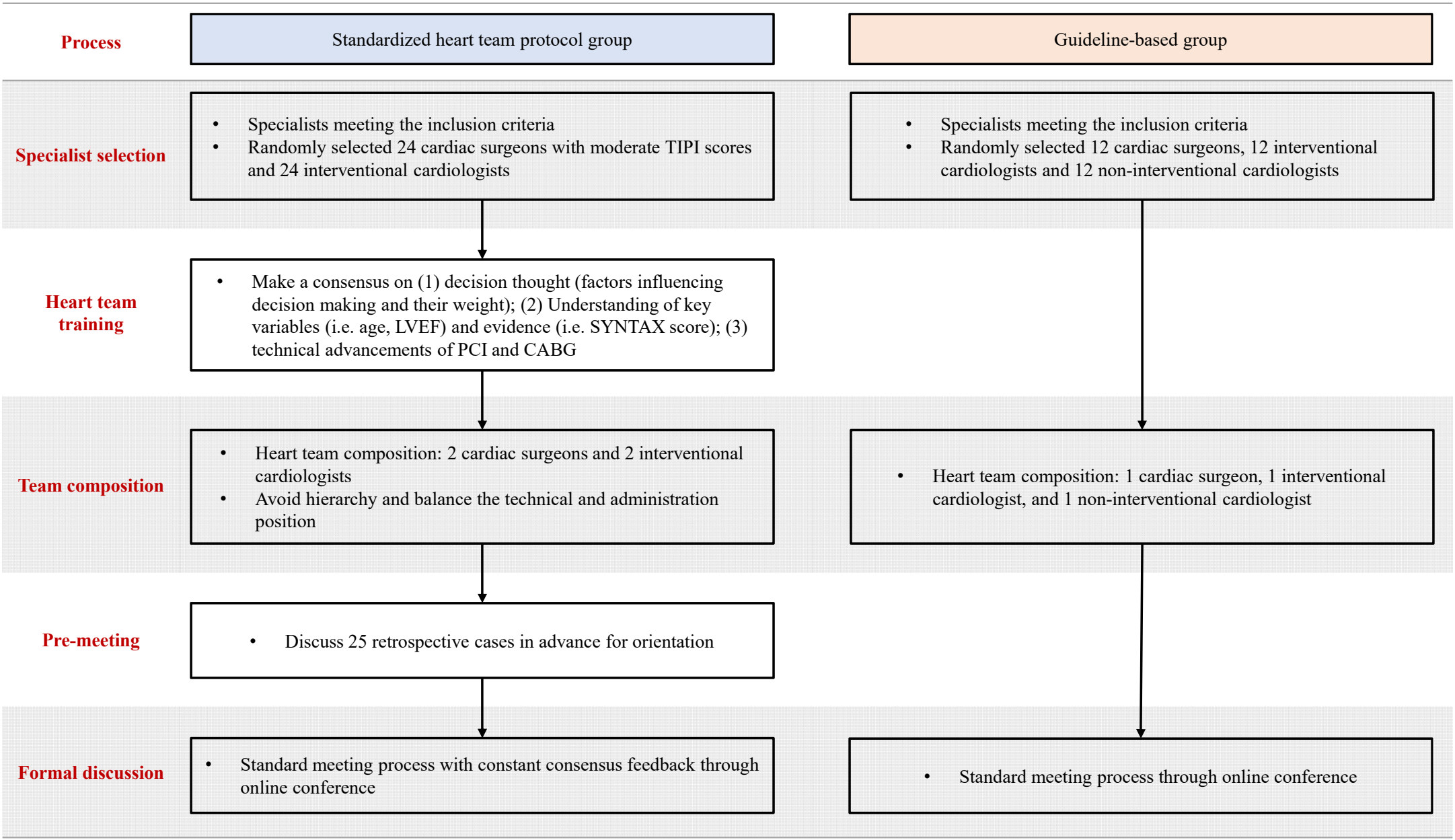
Figure 1. Flow chart

Eligible specialists will be randomized to a standardized heart team protocol group or guideline-based group and established 12 heart teams in each group to make revascularization decisions for 480 historic cases with stable complex CAD. CAD indicates coronary artery disease; MACCE, major adverse cardiovascular and cerebrovascular event.

Figure 2. Implementation strategies for the standardized protocol group and guideline-based group

In the standardized protocol group, the heart team will be implemented based on an evidence-based protocol including specialist selection, specialist training, team composition, team training, and a standardized meeting process. In the guideline-based group, the heart team will be implemented according to the key principles mentioned in clinical guidelines, including team composition and standardized meeting process. TIPI indicates a ten-item personality inventory; LVEF, left ventricular ejection fraction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; SYNTAX, Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.


Enrollment
Eligible specialists
randomization stratified by specialty
Allocation
Standardized heart team protocol group
Randomly assigned to 12 heart teams, each consisting of 2 cardiac surgeons and 2 interventional cardiologists
Organize heart team discussion according to standardized protocol
Make revascularization decisions for 480 patients with complex CAD
Guideline-based group
Randomly assigned to 12 heart teams, each consisting of 1 cardiac surgeon, 1 interventional cardiologist, and 1 non-interventional cardiologist
Organize heart team discussion according to guideline principles
Make revascularization decisions for 480 patients with complex CAD
Analysis
Primary outcome: overall percent agreement
Secondary outcomes: (1) 1-year MACCEs: a composite of all-cause death, MI, stroke, repeated revascularization, and ischemic symptom with hospital admission; (2) Kappa value of heart team decision-making; (3) Inappropriate decision rate
Primary outcome: overall percent agreement
Secondary outcomes: (1) 1-year MACCEs: a composite of all-cause death, MI, stroke, repeated revascularization, and ischemic symptom with hospital admission; (2) Kappa value of heart team decision-making; (3) Inappropriate decision rate


Process
Standardized heart team protocol group
Guideline-based group
Specialist selection
• Specialists meeting the inclusion criteria
• Randomly selected 24 cardiac surgeons with moderate TIPI scores and 24 interventional cardiologists
• Specialists meeting the inclusion criteria
• Randomly selected 12 cardiac surgeons, 12 interventional cardiologists and 12 non-interventional cardiologists
Heart team training
• Make a consensus on (1) decision thought (factors influencing decision making and their weight); (2) Understanding of key variables (i.e. age, LVEF) and evidence (i.e. SYNTAX score); (3) technical advancements of PCI and CABG
Team composition
• Heart team composition: 2 cardiac surgeons and 2 interventional cardiologists
• Avoid hierarchy and balance the technical and administration position
• Heart team composition: 1 cardiac surgeon, 1 interventional cardiologist, and 1 non-interventional cardiologist
Pre-meeting
• Discuss 25 retrospective cases in advance for orientation
Formal discussion
• Standard meeting process with constant consensus feedback through online conference
• Standard meeting process through online conference

SUPPLEMENTAL MATERIALS

Effect of a Standardized Heart Team Protocol versus Guideline-based Protocol on Revascularization Decisions Stability in Stable Complex Coronary Artery Disease: Rationale and Design of a Randomized Trial

Contents

Supplemental Methods

Full Definitions of key variables and clinical endpoints

1. **Three-vessel disease:** three lesions with a percent diameter stenosis (DS%) between 50%-99% or total occlusion in a coronary artery with a ≥ 2.5 mm reference vessel diameter by visual assessment.
2. **Left main desease:** left main coronary artery is visually assessed DS% ≥ 50%.
3. **Major adverse cardiovascular and cerebrovascular events (MACCEs):** a composite of death, myocardial infarction, stroke, repeated revascularization, and rehospitalization due to ischemic symptoms.
4. **Death:** death from any cause. The cause of death will be adjudicated as being due to cardiac death or non-cardiac death.
5. **Myocardial infarction (MI)**

   (1) In-hospital MI: Defined as the occurrence during hospitalization after PCI, CABG or coronary angiography meeting at least 1 of the following criteria:

   1) The rise in cardiac troponin I (cTnI) is ⩾ 70 times the 99th percentile URL (where the baseline is lower than the URL, elevated and stable, or falling).
   2) If cTnI was not available, MI was defined with at least one of the following:
      i. New ischaemic ECG changes;
      ii. Development of new pathological Q waves;
      iii. Imaging evidence of loss of viable myocardium that is presumed to be new and in a pattern consistent with an ischaemic etiology;

iv. Angiographic findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or graft, side-branch occlusion-thrombus, disruption of collateral flow or distal embolization.

(2) Spontaneous MI: Defined as detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL after discharge and with at least one of the following:

1) Symptoms of acute myocardial ischemia;
2) New ischaemic ECG changes;
3) Development of pathological Q waves;
4) Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic etiology;
5) Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy.

6. Stroke was confirmed by a neurologist on the basis of imaging studies and was defined as follows:

1) A focal neurologic deficit of central origin lasting >72 hours, or
2) A focal neurologic deficit of central origin lasting >24 hours, with imaging evidence of cerebral infarction or intracerebral hemorrhage, or
3) A non-focal encephalopathy lasting >24 hours with imaging evidence of cerebral infarction or hemorrhage adequate to account for the clinical state.

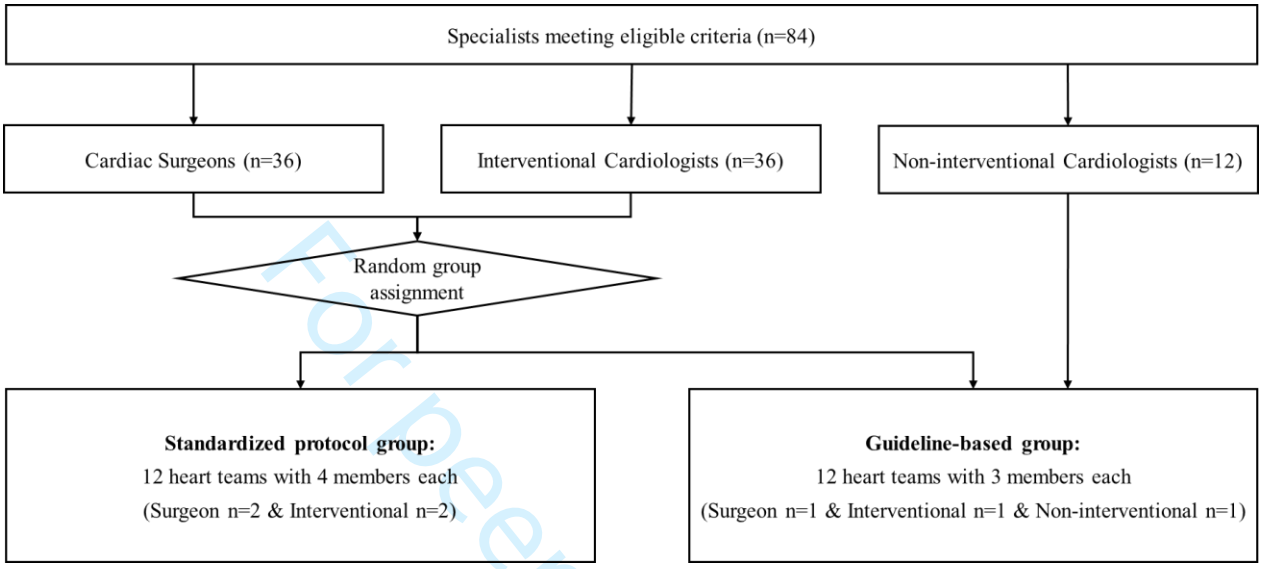
7. **Repeat revascularization** was defined as any repeat coronary artery bypass graft (CABG) or PCI.
    1) Target Lesion: Lesions were revascularized in the index procedure (or during a planned or provisional staged procedure).
    2) Non-Target Vessel: Lesions were not treated by either PCI or CABG at the index procedure.
8. **Rehospitalization due to ischmic symptoms:** rehospitalization because of ischemic discomfort (angina or symptoms thought to be equivalent).

Inclusion and exclusion criteria of cases to be discussed

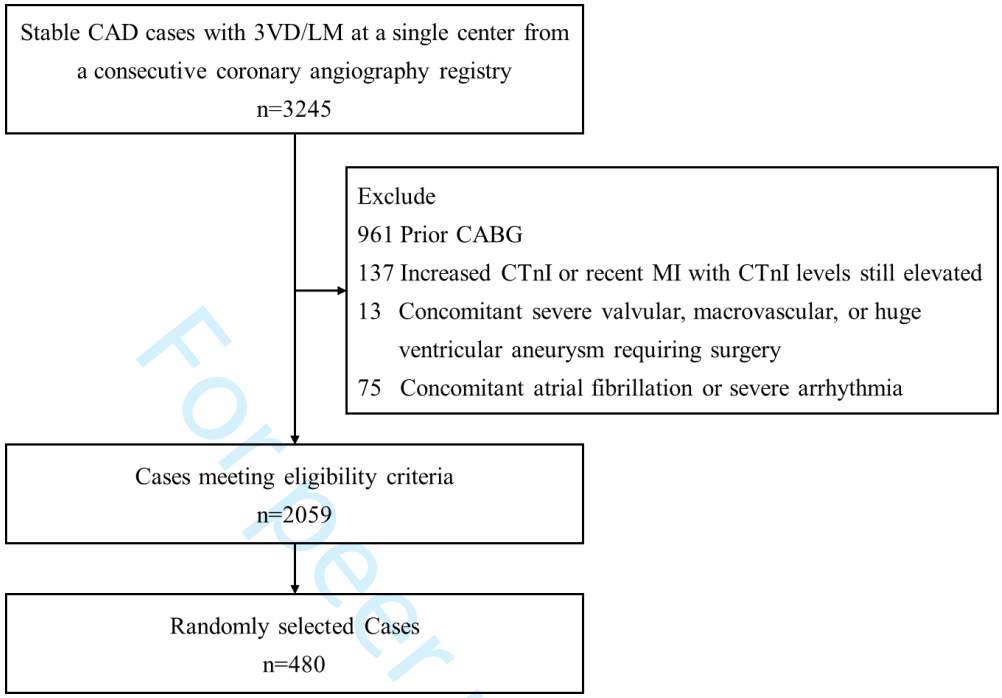
Adult patients with stable CAD according to the National Cardiovascular Data Registry (NCDR) CathPCI criteria (stable angina, no or silent myocardial ischemia) and angiographically confirmed 3-vessel disease or left main (3VD/LM) disease will be eligible for inclusion in the study. The exclusion criteria included: (1) prior coronary artery bypass grafting (CABG); (2) cardiac troponin I (CTnI) greater than the local laboratory upper limit of normal or recent myocardial infarction with CTnI levels still elevated; (3) concomitant severe valvular disease, macrovascular disease, or huge ventricular aneurysm requiring surgery; (4) concomitant atrial fibrillation or severe arrhythmia; or (5) unavailable de novo angiography images of the current hospitalization. Eligible cases will be randomly selected from a prospective registry of consecutive patients who underwent coronary angiography between August 2016 and August 2017.

Supplementary Figures

Online Figure 1. Specialist Enrollment Flowchart

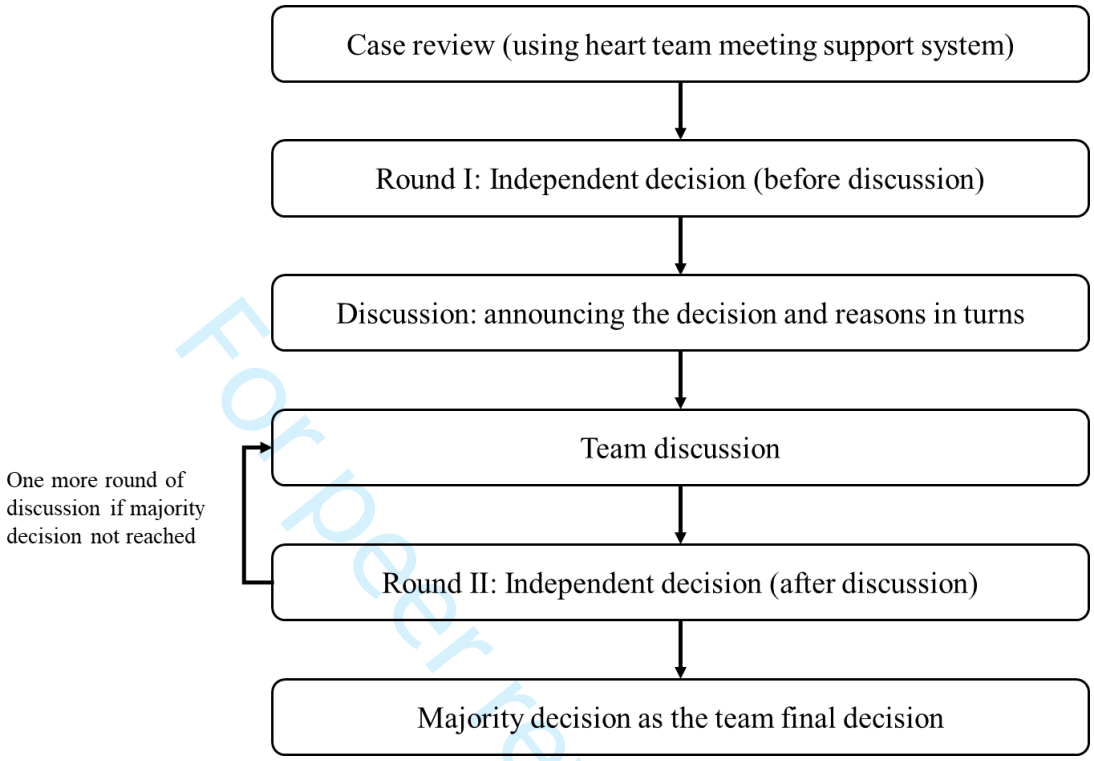


Online Figure 2. Cases Selection Flowchart



3VD indicates 3-vessel disease; CTnI, cardiac troponin I, LM, left main; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Online Figure 3. Standard heart team meeting procedure



Supplementary Tables

Online Table 1. Structured patient information

Heart Team Patient Information Sheet

A. Demograpgics

Patient ID:_____ Gender: ☐Male ☐female Age:_____y BMI :_____kg/m ^{2}

B. Medical history and risk factors

Diabetes	☐ Yes ☐No	
History of myocardial infarction	☐ Yes ☐No	Time: _____
History of heart failure	☐ Yes ☐No	EF value: _____%
History of stroke	☐ Yes ☐No	
renal insufficiency	☐ Yes ☐No	Creatinine: _____umol/L (44-133) Creatinine clearance: _____ml/min
Chronic obstructive pulmonary disease	☐ Yes ☐No	
Other comorbidities: *congenital mitral valve prolapse, hypertension, post-operative hypothyroidism, kidney stones*		

C. Coronary heart disease symptoms

Coronary heart disease symptoms	☐Unstable Angina ☐stable angina ☐Asymptomatic
Home antianginal medication	☐ Long-acting nitrates ☐ β -blockers ☐ Ca2+ channel blockers
CCS classification (stable angina)	☐I ☐II ☐III ☐IV ☐Asymptomatic
NYHA classification	☐I ☐II ☐III ☐IV

D. Laboratory test

Hemoglobin: _____g/L	White blood cells:_____ *10^9/L	Platelets:_____*10^9/L
PT: _____s (11.5-14.5)	APTT: _____s (28.5-43.5)	INR: _____(0.8-1.2)
Troponin I: _____ng/ml (ll_____:ul_____)		

E. Preoperative non-invasive examination

	Result
Admission ECG	*Sinus bradycardia 58 beats/min*
Echocardiography	*Mitral valve posterior leaflet prolapse, mitral valve regurgitation*
Stress Testing and Nuclear Medicine	
Coronary CTA	
Cardiac MRI	

F. Invasive coronary examination

Anigiography	FFR:	IVUS:	OCT:
QFR	LM (left main artery): _____		LAD (left anterior descending artery:_
	LCX (left circumflex artery):_____		RCA (right coronary artery):_____
	Obtusemarginal:_____		Diagonal:_____
	Posterior descending artery:_____		Left posterior artery:_____
	Ramus medianus:_____		

G. Clinical risk scores

SYNTAX	Score:_____

S YNTAX II	PCI Score: 30.0(9.8%)	CABG Score: 32.5(10.2%)	Recommended:/
SYNTAX II 2020	PCI score: 9.8%	CABG Score: 10.2%	
EuroScore II	Mortality: 0.7%		
SinoScore II	Mortality: 0.7%		
STS Score	Mortality: 0.49%	Mortality and complication rate: 9.95%	
	Renal failure rate: 0.39%	Stroke rate: 1.27%	
	Prolonged ventilation rate: 5.8%	Deep sternum infection rate: 0.36%	
	Reoperation rate: 2.37%	Extended hospital stay rate: 4.34%	

* Guidelines recommend STSscore mortality >2% with higher surgical risk

H. Decision result (single choice)

Independent decision before discussion	☐PCI ☐CABG ☐PCI /CABG ☐Drugs ☐Further inspection
Independent decision after discussion	☐PCI ☐CABG ☐PCI /CABG ☐Drugs ☐Further inspection

Online Table 2. Ten-Item Personality Inventory in China (TIPI-C)

Question No.*	Original items (Gosling et al., 2003)	Rating Scale						
		Absolutely disagree	Quite disagree	Almost disagree	Uncertain	Almost agree	Quite agree	Absolutely agree
		1	2	3	4	5	6	7
1	Extraverted, enthusiastic							
2	Critical, quarrelsome							
3	Dependable, self-disciplined							
4	Anxious, easily upset							
5	Open to new experience, complex							
6	Reserved, quiet							
7	Sympathetic, warm							
8	Disorganized, careless							

9	Calm, emotionally stable							
10	Conventional, uncreative							

*Scale scoring ("R" denotes reverse-scored items): Extraversion: 1, 6R; Agreeableness: 2R, 7; Conscientiousness: 3, 8R; Emotional Stability: 4R, 9; Openness to Experiences: 5, 10R.

Online Table 3. Tabular analysis of inter-team agreement

Case ID	Interventional group			Guideline group		
	Hear team 1 decision	Hear team 2 decision	agreement	Hear team 1' decision	Hear team 2' decision	agreement
001	CABG	CABG	Yes	PCI	CABG	No
002	CABG	PCI	No	PCI	PCI	Yes
003	Medication	PCI	No	Further testing	PCI	No
…	…	…	…	…	…	…
…	…	…	…	…	…	…
480	PCI	PCI	Yes	PCI	Medication	No

Online Table 3. Tabular analysis of inter-team agreement. Each case will be discussed by two assigned heart teams. The pairwise comparison between the heart team's decision on each case provides data on the agreement. CABG indicates coronary artery bypass grafting; PCI, percutaneous coronary intervention.

SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	see clinicaltrials.gov
Protocol version	3	Date and version identifier	8
Funding	4	Sources and types of financial, material, and other support	27
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1-2, 27
	5b	Name and contact information for the trial sponsor	see clinicaltrials.gov
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	27
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	15-16

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	6-7
	6b	Explanation for choice of comparators	6-7
Objectives	7	Specific objectives or hypotheses	8
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	7-8
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7-8
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	13
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	14-15
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	see clinicaltrials.gov

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	17-18
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	9
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	NA
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8-14
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10-11,16-17
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15-16
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	16-17
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	18
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	NA
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	15-16
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	NA
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	15-16
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	23
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	23

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	9, 11
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15-16
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	27
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	23
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	23
	31b	Authorship eligibility guidelines and any intended use of professional writers	27
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	27
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplemental file 2
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	3-4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	6-7
	2b	Specific objectives or hypotheses	8
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	7-8
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	7-8
	4b	Settings and locations where the data were collected	7-8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	12-14
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	14-15
	6b	Any changes to trial outcomes after the trial commenced, with reasons	NA
Sample size	7a	How sample size was determined	17-18
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	10
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	10
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	NA
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	10
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	10

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	14
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	16-17
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	18
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	10
	13b	For each group, losses and exclusions after randomisation, together with reasons	NA
Recruitment	14a	Dates defining the periods of recruitment and follow-up	8-9
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	20-22
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	NA
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	NA
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	NA
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	NA
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	NA
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	NA
Other information			
Registration	23	Registration number and name of trial registry	4
Protocol	24	Where the full trial protocol can be accessed, if available	See ClinicalTrial.gov
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	27

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

TIDieR Template for Intervention Description and Replication

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	12-14	
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	12-14	Ma H, Lin S, Li X, et al. Exploring optimal heart team protocol to improve decision-making stability for complex coronary artery disease: a sequential explanatory mixed method study. Eur Heart J Qual Care Clin Outcomes 2021 doi: 10.1093/ehjqcco/qcab074 [published Online First: 2021/10/12]
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	11-12	Online table 1
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	12-14	

	WHO PROVIDED		
5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	12-14	
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	13-14	
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	13-14	
	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	13-14	
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	N/A	
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	N/A	
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	13	
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	N/A	

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

ǂ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.

* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).

复杂冠心病心脏团队决策一致性对比研究（随机对照试验）知情同意书

我们邀请您参加由中国医学科学院阜外医院发起的一项“复杂冠心病心脏团队决策一致性对比研究”，本研究已通过中国医学科学院阜外医院伦理委员会审批（电话 010-88396281）。请仔细阅读说明，了解您在研究中的权利和义务，明确研究性质和风险。参加研究属完全自愿。当研究人员向您说明和讨论知情同意书时，您可以随时提问并让研究人员向您解释您不明白的地方。若您目前正参加其他临床研究，请告知研究人员。本项研究的项目负责人是郑哲（中国医学科学院阜外医院），本项研究的资助方是中国医学科学院阜外医院。

为什么进行这项研究？

当前复杂冠心病心脏团队实践流程存在标准不统一及决策一致性欠佳的问题。前期的一项序贯解释性混合方法研究探索出了一套优化流程的标准化心脏团队实践方案，其对改善心脏团队决策一致性的效果有待验证。本研究拟通过随机对照设计，评价标准化心脏团队实践方案改善复杂冠心病心脏团队决策一致性的效果。

为什么邀您请参加这项研究？

因为您（作为介入医生）具备年介入手术量至少 200 例、左主干病变介入年手术量至少 25 例，且可独立完成慢性完全性闭塞病变的介入手术的能力；或（作为心脏外科医生）具备总搭桥手术量至少 200 例，且可熟练完成体外循环和非体外循环搭桥手术的能力；或（作为非介入手术医生）具备副主任医师及以上的技术资格。此外，您还需具备相关临床研究经验及循证医学素养。因此，我们邀请您参加本项研究。是否最终入选由研究者根据您的实际情况来判断。

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本研究计划在内外科合作良好的医院中最终招募 84 位心血管病医生，其中包含介入医生 36 位、心外科医生 36 位及非介入手术医生 12 位。

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感谢您花时间阅读本知情同意书。如果您通过充分考虑之后同意参加本临床试验，希望您能按照研究人员的要求完成本次临床试验。参加本试验前，请与您的研究人员共同完成并签署此文件最后一页（签署页），一式两份，您和医院各保留一份签署的文件。

签署页

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受试者姓名	签名：
	日期：
研究者	签名：
	日期：

A comparative study on the stability of heart team decision-making in complex coronary artery disease (a randomized controlled trial)

INFORMED CONSENT

We invite you to participate in a " comparative study on the stability of heart team decision-making in complex coronary artery disease (a randomized controlled trial)" initiated by Fuwai Hospital, Chinese Academy of Medical Sciences. This study has been approved by the Ethics Committee of Fuwai Hospital, Chinese Academy of Medical Sciences (Tel: 010-88396281). Please read the instructions carefully to understand your rights and obligations in the research and to clarify the nature and risks of the research. Participation in research is entirely voluntary. When the researcher explains and discusses the informed consent form to you, you can always ask questions and ask the researcher to explain to you what you don't understand. If you are currently participating in other clinical studies, please inform the investigators. The project leader of this research is Zheng Zhe (Fuwai Hospital, Chinese Academy of Medical Sciences), and the sponsor of this research is Fuwai Hospital, Chinese Academy of Medical Sciences.

Why do this research?

The current practice processes of coronary revascularization heart team have problems with inconsistent standards and poor consistency of decision-making. A previous sequential explanatory mixed methods study explored a standardized heart team implementation protocol to optimize the process, and its effect on improving the consistency of heart team decision-making remains to be verified. This randomized controlled trial aims to evaluate the effect of a standardized heart team implementation protocol on improving decision-making consistency in complex coronary artery disease.

Why are you invited to participate in this study?

Because you (as an interventional cardiologist) have the ability to have annual PCI volume ≥ 200, annual left main (LM)-PCI volume ≥ 25, and is capable of chronic total occlusion (CTO)-PCI; or (as a cardiac surgeon) have total CABG volume ≥ 200, and is proficient in both on-pump and off-pump CABG; or (as a non-interventional surgeon) have the technical qualifications of associate chief physician or above. In addition, you need to have relevant clinical research experience and evidence-based medicine literacy. Therefore, we invite you to participate in this study. Whether you are finally selected or not will be judged by the researcher based on the actual situation.

How many people will be involved in this study?

This study plans to eventually recruit 84 specialists from hospitals with good cooperation in internal medicine and surgery, including 36 interventional cardiologists, 36 cardiac surgeons, and 12 non-interventional cardiologists.

What do you need to do to participate in this study?

Under the guidance of the project team, you need to learn to use the heart team meeting system, receive team training, and participate in the heart team meeting discussions to provide optimal treatment decisions for retrospective cases. At the same time, it is necessary to keep confidential of any form of information provided to you, including but not limited to research protocols, basic clinical information of cases, electrocardiogram pictures, echocardiography reports, angiography images, unpublished clinical documents or other confidential information. Any means (photographing, audio recording, video recording, screenshots, etc.) to make any third party aware of the data provided by the project or the results of data analysis by the project team is forbidden.

How long will this study last?

The study will last for 12 months.

Risks and adverse effects of participants in this study?

This study only invites you to participate in the heart team and make decisions for retrospective cases. The study will not interfere with your normal clinical practice, and there will be no risks and adverse effects during the process.

What are the possible benefits of participating in this study?

You will not directly benefit from participating in this study, but your participation will help promote the exchange of disciplines and techniques between cardiologists and cardiac surgeons, and provide valuable information and experience for real-world optimization and improvement of heart team practice.

If not participating in this study, are there other options?

You can choose not to participate in this study, which will not have any impact on your normal clinical work.

Fees and Compensation for Participation in the Study

This study only invites you to participate in the heart team and make decisions for retrospective cases, and there is no related cost and compensation.

What happens to research-related injuries?

This study only invites you to participate in the heart team and make decisions for retrospective cases, which will not interfere with your normal clinical work and will not cause research-related injuries.

Will my information be kept private?

Yes, your information will be kept strictly confidential during the study. When your research data is used in this trial, your personal information is kept confidential, and all your information will be kept securely and used for research purposes only. The information in the research database will be strictly desensitized to eliminate personally identifiable characteristics, and information that may identify you will not be disclosed to anyone other than the researcher without your permission. Without violating the principle of confidentiality and relevant regulations, the reviewers of the ethics committee can consult the original medical records of the subjects to verify the process and data of the clinical trial. If the research results are published publicly, your personal information will not appear in any publications, and we will not disclose this information to anyone or any institution.

Do I have to participate in and complete this study?

Participation in this study is voluntary, and you are free to decide to participate or refuse to participate in this study. Whether you agree to participate in this research or not will not affect your normal clinical work. If you want to participate in this research, you need to read this informed consent form carefully and sign this informed consent form after confirming that you fully understand the relevant issues. You will not lose any legal rights conferred on you by law by signing this document. You may refuse to participate at any time or have the right to withdraw from the research at any time during the research period without any reason, without discrimination or retaliation, and the corresponding rights will not be affected. If you want to withdraw from the research project during the participation, please notify the researcher, complete the relevant procedures before withdrawal as required by the researcher, and complete the relevant withdrawal procedures in writing as required; after withdrawal, the researcher will no longer continue to collect and use your trial data, but data collected anonymized prior to your opt-out cannot be deleted or withdrawn.

Would you like to participate in future research?

With your consent, we wish to retain your data during the study period. Your anonymous research data will continue to be used for subsequent approved cardiovascular-related medical research. If you do not agree, after the completion of this research, your research data will be kept for a specified period of time in accordance with national regulations and will be kept strictly confidential. Participating in future research will not increase your additional risk and financial burden. All future research samples and materials will be properly stored in FuwaiHospital, Chinese Academy of Medical Sciences and will be kept strictly confidential. You may voluntarily choose to participate in future research and to withdraw from research at any time in writing by contacting the researcher.

Who should I contact with questions or difficulties?

Please contact the researchers at 010-88398027 . If you have any questions about your rights, please contact the Ethics Committee of Fuwai Hospital, Tel: 010-88396281.

Thank you for taking time to read this informed consent form. If you agree to participate in this clinical trial after due consideration, I hope you can complete this clinical trial in accordance with the requirements of the researchers. Before participating in this trial, please complete and sign the last page (signature page) of this document together with your investigator in duplicate, with one signed document each for you and the hospital.

SIGN PAGE

I have carefully read, understood and agreed to all the terms of this informed consent form.

I have been informed of the purpose, content, procedures of this research/clinical trial, possible adverse effects of the research/trial, research compensation, and my rights and interests; I have enough time and opportunity to ask questions, and have received satisfactory answers.

I promise that the information I provide is true; if false information is provided, I promise to be responsible for the consequences.

I confirm that the contact information left in the signature office is my valid contact information. If I change the contact information, I should inform your hospital in time. Otherwise, I am willing to bear the corresponding consequences of not being able to contact and not being notified.

I know that I can withdraw from this trial at any time without affecting my normal clinical work.

I will get the original copy of this informed consent form, signed by me and the researcher.

I agree to participate in this study.

I agree to participate in the future study. ☐Agree ☐Disagree

SUBJECT'S NAME	sign:
	date:
RESEARCHER	sign:
	date:

BMJ Open

Effect of a standardized heart team protocol versus a guideline-based protocol on revascularization decision stability in stable complex coronary artery disease: rationale and design of a randomized trial of cardiology specialists using historic cases

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Effect of a standardized heart team protocol versus a guideline-based protocol on revascularization decision stability in stable complex coronary artery disease: rationale and design of a randomized trial of cardiology specialists using historic cases

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ABSTRACT

Introduction

A multidisciplinary heart team approach has been recommended by revascularization guidelines, but how to organize and implement the heart team in a standardized way has not been validated. Inter- and intra-team decision instability existed in the guideline-based heart team protocol, and our standardized heart team protocol based on a mixed-method study may improve decision stability. The objective of this study is to evaluate the effect of the standardized heart team protocol versus the guideline-based protocol on decision-making stability in stable complex coronary artery disease (CAD).

Methods and analysis

Eighty-four eligible interventional cardiologists, cardiac surgeons, or non-interventional cardiologists from 26 hospitals in China have been enrolled. They will be randomized to a standardized heart team protocol group or a guideline-based protocol group to make revascularization decisions for 480 historic cases (from a prospective registry) with stable complex CAD. In the standardized group, we will establish 12 heart teams based on an evidence-based protocol, including specialist selection, specialist training, team composition, team training, and a standardized meeting process. In the guideline-based group, we will organize 12 heart teams according to the guideline principles, including team composition and standardized meeting process. The primary outcome is the overall percent agreement (OPA) in revascularization decisions between heart teams within a group. To demonstrate the clinical implication of decision-making stability, we will further explore the association between decision stability and 1-year clinical outcomes.

Ethics and dissemination

The study was approved by the Institutional Review Board (IRB) of Fuwai hospital (No. 2019-1303). All participants have provided informed consent and all patients included as historic cases provided written informed consent at the time of entry to the prospective registry. The results of this trial will be disseminated through manuscript publication and national/international conferences, and reported in the trial registry entry.

Trial registration number

ClinicalTrials.gov, NCT05039567.

Strengths and limitations of this study

- ⇨ The study is a randomized controlled trial testing an evidence-based standardized heart team protocol covering the whole heart team organization process with up-to-date information provision against an approach following guideline basic recommendations.
- ⇨ Randomization is used in three aspects, stratified randomization in group allocation, randomization in heart team membership, and randomization in case allocation, which controls the social factors that may have negative implications for true group decision-making and ensures relatively heart team exposure to case complexity.
- ⇨ Trial procedures will be carried out remotely, and all heart team meetings will be held via video conference using an online system, enabling full involvement and eliminating the risk of spreading COVID-19.

- ⇨ The cases discussed are retrospectively instead of prospectively selected, and the study does not investigate the impact of the standardized heart team protocol on true treatment decisions and clinical outcomes in routine clinical care, which is the next step to be tested.
- ⇨ The intervention in the standardized protocol group is an integrated approach, and the potential differential outcomes associated with its use cannot be attributed to a single point of the process.

KEYWORDS

Heart team; standardized protocol; decision-making stability

INTRODUCTION

The heart team approach has received a Class 1C/1B recommendation in European and American guidelines on myocardial revascularization in patients with complex coronary artery disease (CAD) to optimize the treatment strategies and may lead to better outcomes.[1-5] Clinical guidelines recommend that a heart team, consisting of clinical/non-interventional cardiologists, interventional cardiologists, and cardiac surgeons, should take sufficient time to assess all available information on complex cases. However, there are relatively limited data on the heart team implementation in detail, such as the ideal composition, meeting frequency, the timing of decision-making, and outcomes, potentially leading to suboptimal decision-making quality.

Prior efforts have noted insufficient inter-specialist consistency, intra-team reproducibility, and inter-team agreement in heart team decision-making. Denvir et al. found poor agreement existed between cardiac clinical specialists (kappa 0.26)[6]. Several studies reported that on re-discussion of the same patient data 9-12 months later, nearly 20% to 24% of decisions differed from the original heart team recommendations.[7 8] In our previous work, the agreement between heart teams for revascularization decision-making was just moderate (kappa 0.58)[9].

Clinical guidelines and previous practice experience from different centers have summarized several critical principles in heart team implementation.[10-12]Guidelines recommend the composition should be at least a cardiac surgeon, an interventional cardiologist, and a non-interventional cardiologist.[1 5] Sanchez et al. summed up the experience of the heart team implementation from their single center, including team composition, data collection, and meeting process. The British Cardiovascular Society (BCS), Society for Cardiothoracic Surgery in Great Britain and Ireland

(SCTS), and British Cardiovascular Intervention Society (BCIS) set out the principles for the functioning of the heart team across the United Kingdom, including composition, frequency, and the type of cases discussed.[12] Although these works provided essential experiences for heart team implementation, the protocols were not evidence-based, and data regarding how these protocols impact decision-making stability were scarce.[12]

To determine the potential factors influencing heart team decision-making comprehensively and explore an evidence-based heart team protocol, we conducted a sequential explanatory mixed method study and summarized three themes (specialist quality, team composition, and meeting process) and ten subthemes of potential factors. In addition, nine recommendations for heart team implementation were derived based on qualitative and quantitative data, and a standardized heart team protocol was developed based on the previous experience, recommendations, and guidelines, covering the whole procedure of heart team implementation.

However, the practical effect of the standardized protocol versus the guideline-based protocol on decision-making stability and clinical outcomes remains unknown, and a randomized trial for validation is warranted. Therefore, we designed this pivotal randomized trial.

METHODS AND ANALYSIS

Study design

The current study is a randomized, controlled, two-arm trial involving 84 cardiac specialists from 26 hospitals in China. Eligible specialists have been randomized to a standardized implementation protocol group or a guideline-based group to establish 24 heart teams and make revascularization decisions for 480 stable complex CAD cases retrospectively enrolled. We will evaluate the decision-

making stability (**Figure 1**). SPIRIT[13], CONSORT[14], and TIDieR[15] checklists are in **Supplemental File 1**. All procedures have been approved by the Institutional Review Board (IRB) of Fuwai hospital (2 August 2021). The study start date is 4 January 2022, and the anticipated end date is 31 January 2023.

Objective and hypothesis

The primary objective of this study is to evaluate the effect of the standardized heart team protocol versus the guideline-based protocol on the stability of decision-making in stable complex CAD. The primary hypothesis is that heart teams organized on the standardized protocol will result in better decision-making consistency compared with those based on guideline principles. The secondary objectives of this study are to (1) evaluate the association between decision-making stability and 1-year composite of death, myocardial infarction (MI), stroke, repeated revascularization, and re-hospitalization due to ischemic symptoms; (2) assess the appropriateness of heart team decision-making.

Participants and recruitment

To have access to enough experienced specialists, we will enroll eligible specialists from hospitals with (1) annual volume of percutaneous coronary intervention (PCI) ≥ 500; (2) annual volume of coronary artery bypass grafting (CABG) ≥ 200[1]; (3) have at least two interventional cardiologists, two cardiac surgeons and one non-interventional cardiologist meeting the inclusion criteria and agreeing to participate in the study. The inclusion criteria for the heart team specialists differ from specialties and require specified operator volumes and experience (**Table 1**). The interventional cardiologist is required to have an annual PCI volume ≥ 200[16], an annual left main (LM)-PCI volume

≥ 25[1], and is capable of chronic total occlusion (CTO)-PCI. The cardiac surgeon must have a total CABG volume ≥ 200[17] and be proficient in both on-pump and off-pump CABG. We have contacted all the potential participants via e-mails or telephones to get their information confirmed and obtained their content from 1 December 2021 to 10 January 2022. All participating specialists have provided written informed consent for enrollment (**Supplemental File 2)**.

Table 1. Inclusion criteria for heart team specialists

Disciplines	Inclusion Criteria
Interventional Cardiologist	1) Annual PCI volume ≥200[16] 2) Annual LM PCI volume ≥25[1] 3) CTO PCI total volume ≥10 4) Clinical researcher experience in coronary revascularization 5) Proficient in clinical guidelines
Cardiac Surgeon	1) CABG total volume ≥200[17] 2) Proficient in both on-pump and off-pump CABG 3) Clinical researcher experience in coronary revascularization 4) Proficient in clinical guidelines
Non-interventional Cardiologist	1) Proficient in clinical guidelines

CABG indicates coronary artery bypass grafting; CTO, chronic total occlusion; LM, left main; PCI, percutaneous coronary intervention.

Randomization

Randomization is stratified by specialties and conducted by a data manager using random number generation in SAS. We have randomized 36 cardiac surgeons and 36 interventional cardiologists in a 2:1 ratio to the standardized protocol group (24 surgeons and 24 interventional cardiologists) or the

guideline-based group (12 surgeons and 12 interventional cardiologists). Twelve non-interventional cardiologists have been randomly selected and allocated to the guideline-based group. After the randomization, each group of specialists will be randomly assigned to 12 heart teams and perform heart team meetings according to corresponding protocols. Research staff will be informed of the randomization and organize the allocated specialists to establish heart teams. Participating specialists are unaware of the implementation conditions (**Supplementary Figure 1**).

Case selection and preparation

Selection of cases to be discussed

Adult cases with stable CAD according to the National Cardiovascular Data Registry (NCDR) CathPCI criteria[18] (stable angina, no or silent myocardial ischemia) and angiographically confirmed 3-vessel disease or left main (3VD/LM) disease are eligible for inclusion in the study. We have randomly selected eligible cases from a prospective registry of consecutive patients who underwent coronary angiography between August 2016 and August 2017 (**Supplementary Figure 2**).[19] All cases provided written informed consent at the time of registration and agreed to use their data for subsequent approved cardiovascular-related medical research. Definitions and inclusion/exclusion criteria of cases can be seen in **Supplemental methods.**

Structured patient information

Patient data will be presented in a structured information form on an electronic meeting support system by non-clinical coordinators (**Supplementary Table 1**)**.** The structured information includes (a) demographics; (b)medical histories and clinical risk factors; (c) medical treatment histories and

CVD symptoms of the index hospitalization; (d) laboratory results; (e) noninvasive testing results (e.g., electrocardiogram, echocardiogram, stress testing results); (f) diagnostic angiogram images and quantitative flow ratio (QFR)[20]; (g) clinical risk scores (i.e., SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score[21], SYNTAX II score[22], SYNTAX II 2020 score[23], Society of Thoracic Surgeons (STS) score[24 25], the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II[26], and sinoSCORE II[27]). All the clinical information has been obtained from medical records according to the NCDR CathPCI data definitions[18]. An independent angiographic core laboratory takes responsibility for all angiogram image screening and risk score evaluation by using a computer-based automatic calculator.

Case assignment

Four hundred and eighty cases will be randomized into 6 sets of 80 cases each, using a stratified randomization procedure to ensure relatively equal heart team exposure to case complexity and a similar ratio of actual treatment strategies (CABG, PCI, or medication therapy).

Intervention

Standardized heart team protocol

Eligible specialists randomized to this group will establish 12 heart teams and conduct heart team meetings based on the standardized heart team protocol[9] (**Figure 2**).

i. **Specialist selection.** All the cardiac surgeons are required personality tests by Ten-Item Personality Inventory in China (TIPI-C)[28] and 24 surgeons with moderate scores will be randomly selected (**Supplementary Table 2**). Twenty-four interventional cardiologists will be

randomly selected without personality selection.

ii. **Specialist training.** All heart team members must undergo unified training to achieve a consensus on the potential factors influencing revascularization decisions. The training will be conducted and recorded by well-prepared coordinators. Consensus view should include clinical considerations on the essential characteristics (e.g., age, left ventricular ejection fraction (LVEF), and body mass index (BMI)) and their weightage, interpretation of evidence (e.g., SYNTAX trial, Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial and the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) results). Additionally, the latest technical advancements in PCI and CABG will be discussed, especially for PCI, to narrow cognitive gaps among specialists of different expertise. The consensus view document will be recorded and put onto the electronic meeting support system for reference at any time. To maintain fidelity to the consensus view, we will present each bullet point of the consensus view as a footnote under the corresponding variable.

iii. **Team composition.** All specialists selected will be randomly assigned to 12 heart teams consisting of 2 cardiac surgeons and 2 interventional cardiologists. Non-interventional cardiologist or other disciplinary specialist is not required in the routine heart team unless necessary. Moreover, the technical level and administration position will be balanced in each team.

iv. **Team training.** Before the formal heart team meeting, a pilot discussion (25-50 retrospective cases) will be performed following the standard meeting procedure to reinforce the practice of the former consensus view for a more solid team consensus.

v. **Standardized meeting process.** Heart team meetings will be conducted standardly in both groups according to the procedure widely used in the previous studies.[10-12]Each heart team independently evaluates a set of cases (80 cases) through the heart team assistance system using structured online case presentations, with the members blinded to the other heart teams and the decisions of other heart teams. All specialists are required to make decisions independently among five treatment categories (PCI, CABG, PCI/CABG equipoise, medical therapy, or further testing) before (round I) and after (round II) the heart team discussion. The heart team member only has access to the responses of the other heart team members after all members have submitted their independent decisions. The final treatment strategy is determined by a majority decision[29] (**Supplementary Figure 3**).

Guideline-based protocol

We will randomly assign eligible specialists randomized to this group to 12 heart teams based on the principles of guidelines (**Figure 2**). Each heart team consists of 1 interventional cardiologist, 1 cardiac surgeon, and 1 non-interventional cardiologist. This group does not require pre-meeting training on consensus view and pilot discussion. Formal meeting procedures follow the standardized meeting process as the other group.

All heart team meetings will be held through video conferencing, and a quiet environment will be required. For each heart team, the frequency of meetings is one or two times per week and lasts 1.5-2h at a time.

Outcomes

The primary outcome is the overall percent agreement (OPA), defined as the proportion of patients

who received coincident decision recommendations from paired heart teams. The secondary outcomes include:

(1) 1-year major adverse cardiovascular and cerebrovascular events (MACCEs): a composite of all-cause death, MI, stroke, repeated revascularization, and re-hospitalization due to ischemic symptoms;

(2) Kappa value of heart team decision-making: Fleiss's (more than 2 raters) and Cohen's (2 raters) kappa coefficients to evaluate inter-team, intra-team, inter-specialist, intra-specialist, and inter-round agreement for treatment decisions. To evaluate the reproducibility, all assigned cases will be re-discussed with the same clinical data but not in the same order 1 month after the completion of the initial discussion, with the heart team blinded to the outcome of the initial meeting.

(3) Inappropriate decision rate: the final heart team recommendations will be adjudicated for appropriateness using the American College of Cardiology (ACC) /American Association for Thoracic Surgery (AATS) /American Heart Association (AHA) 2017 Appropriate Use Criteria (AUC) and the Chinese AUC for coronary revascularization for each case.[30 31]Two investigators who do not participate in data collection will take responsibility for reviewing the team decisions and adjudicating the decision appropriateness independently. Any disputes will be settled via review by a third investigator, with a decision by consensus.

Data management and monitoring

Our IRB-approved protocol specifies plans for data entry, coding, security, and data storage on a secure server. For retrospective data, all data will be double-checked or assessed by two independent coordinators. For prospective data on heart team meetings, the online meeting supporting system

included several mechanisms to protect data integrity and promote data quality (e.g., warning of missing values and preventing duplicate team participation). The data manager will maintain detailed data management procedures. Coordinators will report to and discuss with the principal investigator about the study progress, including participant recruitment, data collection and analysis, and heart team meeting conductions. Any protocol modifications will be discussed with and approved by the IRB. Any significant changes in methods will be reported to the project's program officer and updated on the registration site https://ClinicalTrials.gov. This study does not need a data monitoring committee because all the cases discussed are retrospectively selected. Their revascularization strategies would not be influenced by heart team recommendations and will be no risk for cases. As for participating specialists, heart team discussion will not interfere with their routine clinical work. The Principal Investigator and approved study team members will have access to the final trial datasets.

Statistical analysis

The pairwise comparison between the heart team decisions in each case provides data on the agreement (**Supplementary Table 3**). The inter-team, intra-team, inter-specialist, intra-specialist, and inter-round agreements will be assessed using OPA and Cohen's κ coefficient, whenever applicable. Mean decision time will also be calculated. Cox proportional hazards models will be used to analyze whether the treatment decision adhering to the heart team recommendations is associated with better outcomes. Categorical variables will be expressed as frequency and percentage. Continuous variables will be expressed as mean ± standard deviation (SD), or median and interquartile range. Categorical variables will be analyzed with the likelihood ratio χ^2 test or Fisher

exact test if more than 25% of the cells have an expected frequency smaller than 5. Continuous variables will be computed with the 2-sample t-test when data follow a normal distribution and will be compared with the Wilcoxon rank sum test for non-normal distribution. 95% confidence intervals will be computed for all measurements. All the analyses will be performed at a significance level of 2-sided 0.05. All tests will be performed using SAS software, version 9.4 (SAS Institute, Cary, NC).

Sample size

Number of assessments necessary to evaluate decision-making agreement

The primary endpoint of this study is to compare the OPA between the standardized protocol group and the guideline-based group. In our previous study, heart teams were established based on guidelines, and it was estimated that the OPA was 66.3% (unpublished data), serving as the reference rate of the controlled group in this study. We assumed that inter-team agreement is similar to or no better than intra-team reproducibility rate. According to relevant literature,[7 8] it is estimated that the OPA of the standardized protocol group is 76% (the minimum estimate of previous literature). Under this circumstance, the standardized protocol group has a minor effect on improving decision consistency compared with the guideline-based group. Using a 5% level of 2-side significance and a confidence level of 90%, it was estimated that a total number of 454 pairwise comparisons for each group would be necessary to meet the study acceptance criterion. For the convenience of case assignment, we adjusted the sample size to 480 cases.

Number of heart teams needed

Considering the feasibility of implementation and a good representation of both samples and heart teams, it was decided that 24 heart teams are needed with 12 in each arm. Teams in each group will

be divided into 6 pairs randomly, and each pair of heart teams will evaluate the same randomly assigned 80 cases independently to provide inter-team agreement data, generating 480 pairwise comparisons in each group.

Number of heart team specialists

The heart team in the standardized group consists of 2 interventional cardiologists and 2 cardiac surgeons, and that in the guideline-based group consists of 1 interventional cardiologist, 1 cardiac surgeon, and 1 non-interventional cardiologist. With 12 heart teams in each group, a minimum of 36 cardiac surgeons, 36 interventional cardiologists, and 12 non-interventional cardiologists are needed in the final study in total.

Subgroup analysis

The primary and secondary outcomes will be analyzed in pre-specified subgroups, including specialties and professional status. The analysis will also be conducted according to different cases stratified by age, left ventricular ejection fraction (LVEF), body mass index (BMI), degree of the stenosis, calcified lesion, stenosis severity, tandem and bending/tortuous lesion, LM, SYNTAX stratification, SYNTAX Ⅱ recommendations, and SinoSCORE stratification. The comparisons in these analyses may be not powered for hypothesis testing but are descriptive in nature.

Current status

Thirty-six cardiac surgeons, 36 interventional cardiologists, and 12 non-interventional cardiologists from 26 eligible hospitals agreed to participate in this study and have provided informed consent. Four hundred and eighty cases with stable complex CAD have been randomly selected for discussion. Specialist and patient baseline data are shown in **Table 2** and **Table 3**. The study start

date is 4 January 2022, and the anticipated end date is 31 January 2023.

Patient and public involvement

None.

Table 2. Specialist baseline characteristics

Characteristics	Overall (n=84)	Cardiac Surgeon (n=36)	Interventional Cardiologist (n=36)	Non-interventional Cardiologist (n=12)
Male	71 (84.5)	35 (97.2)	34 (94.4)	2 (16.7)
Status				
Chief specialist	46 (54.8)	21 (58.3)	19 (52.8)	6 (50.0)
Associate specialist	34 (40.5)	15 (41.7)	13 (36.1)	6 (50.0)
Attending specialist	4 (4.8)	0 (0.0)	4 (11.1)	0 (0.0)
Personality (TIPI)*	5.20 (4.80-5.70)	5.20 (4.90-5.50)	5.20 (4.60-5.80)	5.45 (4.80-5.60)
Extraversion	4.50 (4.00-5.00)	4.50 (4.00-5.50)	4.50 (4.00-5.00)	4.50 (4.00-5.00)
Agreeableness	5.50 (4.50-6.00)	5.00 (4.50-5.50)	5.75 (4.50-6.50)	5.75 (5.00-6.00)
Conscientiousness	5.50 (5.00-6.50)	6.00 (5.00-6.50)	5.50 (5.00-6.50)	5.75 (5.00-6.00)
Emotional Stability	5.00 (5.00-6.00)	5.00 (5.00-5.50)	5.00 (4.50-6.00)	6.00 (5.00-6.00)
Openness to Experiences	5.00 (4.50-5.50)	5.00 (4.50-5.50)	5.00 (5.00-5.50)	4.75 (4.50-5.50)

TIPI indicates the ten-item personality inventory.[28]Data presented as n (%) and median (interquartile range).*Personality was evaluated by the TIPI scale in Chinese.

Table 3. Demographic and clinical characteristics of retrospective patients

Characteristics	Patients for discussion (n=480)	Characteristics	Patients for discussion (n=480)
Demographics		Silent ischemia (after medical therapy)	90 (18.8)
Age, y	62.0 (55.0-67.5)	Non-ischemia symptom	20 (4.2)
Male (%)	363 (75.6)	Stable angina	370 (77.1)
Risk Factors		CCS I-II	325 (87.8)
Hypertension	334 (69.6)	CCS III-IV	45 (12.2)
Hyperlipidemia	429 (89.4)	Number of anti-anginal medications	
Diabetes	185 (38.5)	0	118 (24.6)
Cerebrovascular disease	102 (21.3)	1	154 (32.1)
COPD	7 (1.5)	2	149 (31.0)
Chronic renal disease	14 (2.9)	3	59 (12.3)
Smoker	226 (47.1)	Extent of coronary disease	
Body mass index, kg/m^2	25.6 (23.7-27.5)	3-vessel disease	451 (94.0)
Ccr <60 mL/min/1.73m^2	7 (1.5)	Left main disease	129 (26.9)
Cardiovascular Characteristics		**Risk Classification**	
Previous MI	49 (10.2)	SYNTAX score	22.5 (16.5-29.5)
Previous heart failure	10 (2.1)	SYNTAX score tertiles	
Peripheral vascular disease	46 (9.6)	Low risk (0-22)	237 (49.4)
Ejection fraction, %	63.0 (59.0-65.0)	Intermediate risk (23-32)	157 (32.7)
Ejection fraction ≤40%	23 (4.8)	High risk (≥33)	86 (17.9)
CAD symptoms		SYNTAX score II recommendation	

Characteristics	Patients for discussion (n=480)	Characteristics	Patients for discussion (n=480)
PCI	11 (2.3)	Reoperation (%)	1.72 (1.46-2.07)
CABG	153 (31.9)	Renal failure (%)	0.43 (0.32-0.61)
Equipoise	316 (65.8)	Stroke (%)	0.96 (0.73-1.36)
SYNTAX score II 2020 10-year mortality (%)		Prolonged ventilation (%)	3.20 (2.62-3.98)
CABG	14.8 (9.1-24.7)	DSWI (%)	0.10 (0.08-0.14)
PCI	19.4 (11.6-32.2)	Prolonged hospitalization (%)	1.79 (1.33-2.53)
Euroscore II mortality (%)	0.80 (0.58-1.06)	**Treatment Strategy in Real World**	
SinoSCORE II mortality (%)	0.82 (0.47-1.18)	PCI	287 (59.8)
STS score (incidence of postoperative events)		CABG	116 (24.2)
Mortality (%)	0.49 (0.36-0.70)	Medical therapy	77 (16.0)
Mortality or major complications (%)	5.30 (4.43-6.56)		

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; Ccr, creatinine clearance rate; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; DSWI, deep sternal wound infection; MI, myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; STS, Society of Thoracic Surgeons; and SYNTAX, Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.

Data presented as median (interquartile range, IQR) and n (%).

ETHICS AND DISSEMINATION

Ethics

The study was reviewed and approved by the Ethics Review Committees of Fuwai hospital (2019-1303) on 2 August 2021; subsequent amendments have been approved. All participants have provided informed consent and all patients included as historic cases provided written informed consent at the time of entry to the prospective registry.

Safety

All the eligible cases were retrospectively selected and underwent coronary angiography between August 2016 and August 2017. Heart team decisions do not affect patients' actual treatments. There will be no adverse event or serious adverse event relating to this study.

Dissemination

The results of this trial will be reported to the participating specialists, disseminated through manuscript publication and national/international conferences, and reported in the trial registry entry.

DISCUSSION

The optimization of heart team implementation including team composition, operation, distribution of responsibilities, and other issues still lacks verification by evidence-based trials. The present study is the first trial focusing on the heart team implementation quality assessment

and improvement by evaluating the effect of the standardized heart team protocol compared to the guideline-based protocol on decision-making stability for stable complex CAD.

Stability is a potential metric of decision-making quality. As the expertise of individual specialists is specific to their professional training and experience, cardiologists and surgeons prefer PCI or CABG, respectively.[10] Prior data showed that 18.1% of the overall decision-making for stable angina patients was classified as inappropriate based on a single disciplinary decision, especially among patients undergoing PCI [32]. The heart team, a medium of communication to integrate the input of numerous specialists, can help to minimize fragmented communication between specialists and eliminate specialist bias in the decision-making process. It was reported that heart team recommendations differed from those of the original treating interventional cardiologist in approximately one-third of cases.[33] Sanchez et al convened 301 heart team meetings for complex CAD from 2012 to 2015 and reported the concordance of the heart team to appropriate use criteria was up to a 99.3% appropriate primary indication for coronary revascularization.[34] Therefore, qualified heart teams perform more evidence-based and neutral in revascularization decision-making. The success of the heart team approach is apparent in a growing number of optimal revascularization decisions made according to professional guidelines.

Notably, a dedicated and structured heart team has a potential benefit for patient survival. Peyman et al reported patients treated for mitral valve disease based on a dedicated heart team decision have significantly higher survival than a general heart team, which illustrated the establishment of a dedicated heart team consisting of experienced specialists with adequate

procedure volume benefits patient survival[35]. In addition, appropriate revascularization is associated with improved 1-year outcomes in patients with appropriate indications and has no benefit in those with uncertain or inappropriate indications.[19] Thus, we assume that revascularization recommendations of dedicated heart teams organized by the standardized heart team protocol would be more stable and appropriate compared with those of general heart teams based on guideline principles, which leads to better clinical outcomes.

Making the heart team approach well-structured and efficient contributes to a better quality of cardiovascular care. The current study is essential to answer the following questions: (1) Is it feasible to establish and organize heart team meetings with the guidance of the standardized heart team protocol? (2) Will the standardized heart team protocol improve the decision-making stability in patients with stable complex CAD compared with the fundamental principles of heart team organizing in guidelines? Moreover, it will enhance educational opportunities for all team members involved and provide experience in the practice of heart team meetings in prospective clinical scenarios.

Several novel designs underlie the strength of this study. Firstly, we use a randomized controlled design to demonstrate the structure and effect of an evidence-based standardized heart team protocol on decision-making stability against the controlled approach based on guideline principles, which fills the gap with no randomized data currently available in optimal heart team implementation[12 33]. Secondly, the study applies randomization three times. Eligible specialists are first randomly selected and assigned to different arms by stratification randomization. Then we establish heart teams with randomized membership to reduce social factors that may have

negative implications on individual decision-making[36]. Cases are also randomized into 6 sets of 80 cases each to ensure relatively equal heart team exposure to case complexity. Thirdly, all heart team training and meetings are held via video conference using an online decision-making support system, which makes it possible to involve specialists from multiple hospitals, reduce the negative influence of a few influential individuals on face-to-face decision-making, and eliminate the risk of viral spreading in COVID-19.[37] Fourthly, we provide the most up-to-date risk scores (such as SYNTAX Ⅱ 2020 score[23], sinoSCORE Ⅱ[27]) and QFR[20], a novel angiography-derived physiological assessment approach, in structured information for the specialists to adjudicate the optimal treatment strategy.

The study has several limitations. First, cases discussed are retrospectively selected rather than prospectively enrolled. All cases have already been treated from August 2016 to August 2017 in the original hospitalization, thus it is unable to reveal the causal link between heart team meetings and real-world decision-making and outcomes in routine clinical practice. Prospective design is needed for the next step. Second, the intervention in the standardized protocol group is an integrated approach and the potential differential outcomes associated with its use cannot be attributed to a single point of the process. Additional quantitative and qualitative analysis is needed to find out which steps work on the decision-making stability. Third, heart team decisions will be made independently of patient preferences, while in real-world clinical practice, patient preference is an important factor for the final treatment decision. Patient involvement in shared decision-making should be considered in future trials.

DECLARATIONS

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Contributors

ZZ contributed to study conception, funding obtaining, administration, and technical material support. HPM, SL, XL, BX, and ZZ contributed to the study design. HPM and SL drafted the manuscript. XL and YW contributed to statistical consultation. HPM, SL, and BX contributed to data collection and interpretation. All authors revised the manuscript for important intellectual content and approved the final version.

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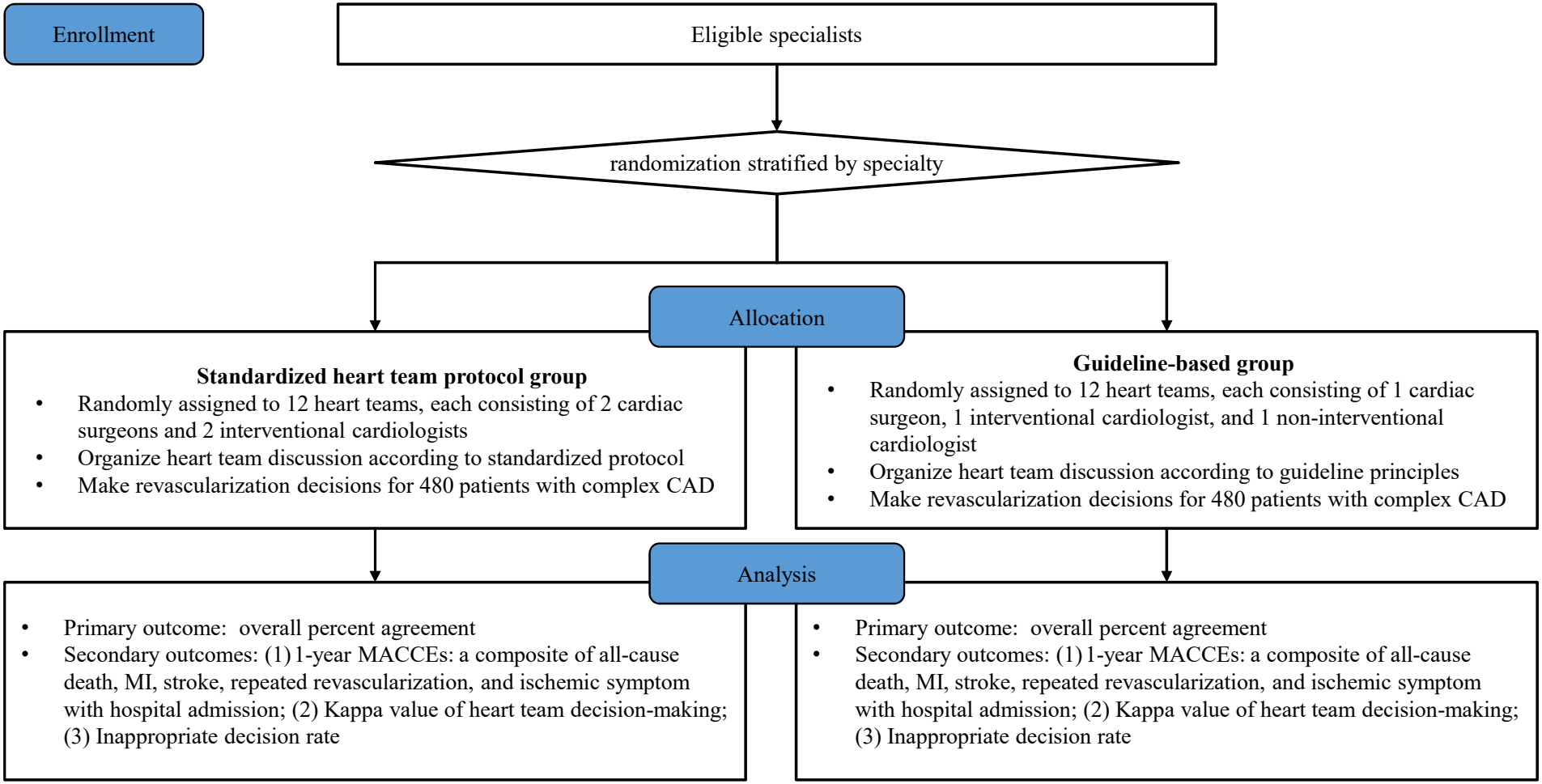
FIGURE TITLES AND LEGENDS

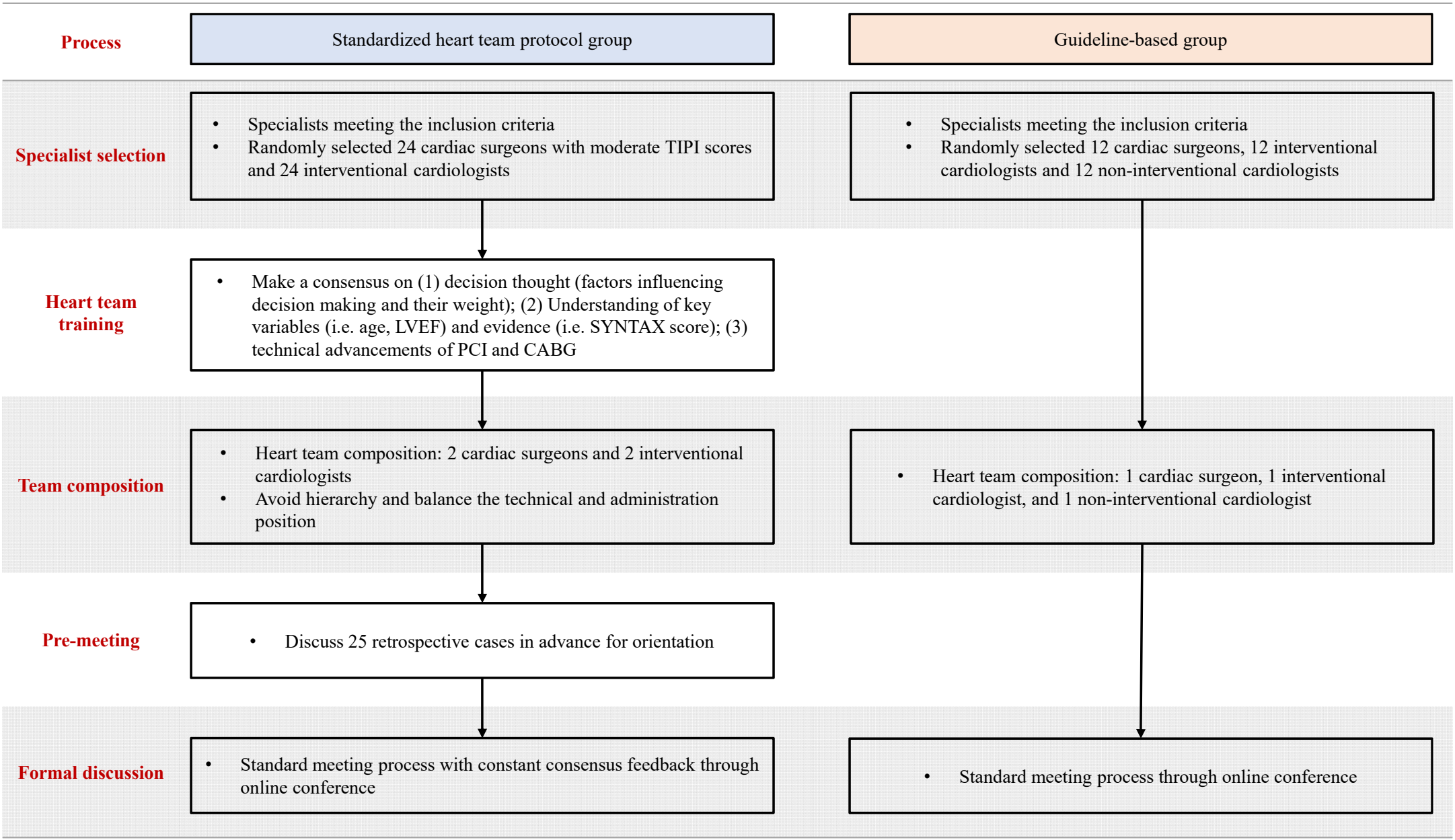
Figure 1. Study flowchart

Eligible specialists will be randomized to a standardized heart team protocol group or a guideline-based group and established 12 heart teams in each group to make revascularization decisions for 480 historic cases (from a prospective registry) with stable complex CAD. CAD indicates coronary artery disease; MACCE, major adverse cardiovascular and cerebrovascular event.

Figure 2. Implementation strategies for the standardized protocol group and guideline-based group

In the standardized protocol group, the heart team will be implemented based on an evidence-based protocol including specialist selection, specialist training, team composition, team training, and a standardized meeting process. In the guideline-based group, the heart team will be implemented according to the key principles mentioned in clinical guidelines, including team composition and standardized meeting process. TIPI indicates a ten-item personality inventory; LVEF, left ventricular ejection fraction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; SYNTAX, Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery.


Enrollment
Eligible specialists
randomization stratified by specialty
Allocation
Standardized heart team protocol group
Randomly assigned to 12 heart teams, each consisting of 2 cardiac surgeons and 2 interventional cardiologists
Organize heart team discussion according to standardized protocol
Make revascularization decisions for 480 patients with complex CAD
Guideline-based group
Randomly assigned to 12 heart teams, each consisting of 1 cardiac surgeon, 1 interventional cardiologist, and 1 non-interventional cardiologist
Organize heart team discussion according to guideline principles
Make revascularization decisions for 480 patients with complex CAD
Analysis
Primary outcome: overall percent agreement
Secondary outcomes: (1) 1-year MACCEs: a composite of all-cause death, MI, stroke, repeated revascularization, and ischemic symptom with hospital admission; (2) Kappa value of heart team decision-making; (3) Inappropriate decision rate
Primary outcome: overall percent agreement
Secondary outcomes: (1) 1-year MACCEs: a composite of all-cause death, MI, stroke, repeated revascularization, and ischemic symptom with hospital admission; (2) Kappa value of heart team decision-making; (3) Inappropriate decision rate


Process
Standardized heart team protocol group
Guideline-based group
Specialist selection
• Specialists meeting the inclusion criteria
• Randomly selected 24 cardiac surgeons with moderate TIPI scores and 24 interventional cardiologists
• Specialists meeting the inclusion criteria
• Randomly selected 12 cardiac surgeons, 12 interventional cardiologists and 12 non-interventional cardiologists
Heart team training
• Make a consensus on (1) decision thought (factors influencing decision making and their weight); (2) Understanding of key variables (i.e. age, LVEF) and evidence (i.e. SYNTAX score); (3) technical advancements of PCI and CABG
Team composition
• Heart team composition: 2 cardiac surgeons and 2 interventional cardiologists
• Avoid hierarchy and balance the technical and administration position
• Heart team composition: 1 cardiac surgeon, 1 interventional cardiologist, and 1 non-interventional cardiologist
Pre-meeting
• Discuss 25 retrospective cases in advance for orientation
Formal discussion
• Standard meeting process with constant consensus feedback through online conference
• Standard meeting process through online conference

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	4
	2b	All items from the World Health Organization Trial Registration Data Set	see clinicaltrials.gov
Protocol version	3	Date and version identifier	8
Funding	4	Sources and types of financial, material, and other support	27
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1-2, 27
	5b	Name and contact information for the trial sponsor	see clinicaltrials.gov
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	27
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	15-16

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	6-7
	6b	Explanation for choice of comparators	6-7
Objectives	7	Specific objectives or hypotheses	8
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	7-8
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7-8
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	NA
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	13
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	14-15
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	see clinicaltrials.gov

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	17-18
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	9
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	10
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	NA
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8-14
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	10
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10-11,16-17
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	15-16
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	16-17
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	18
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	NA
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	15-16
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	NA
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	15-16
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	23
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	23

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	9, 11
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15-16
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	27
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	23
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	23
	31b	Authorship eligibility guidelines and any intended use of professional writers	27
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	27
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Supplemental file 2
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	3-4
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	6-7
	2b	Specific objectives or hypotheses	8
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	7-8
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	7-8
	4b	Settings and locations where the data were collected	7-8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	12-14
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	14-15
	6b	Any changes to trial outcomes after the trial commenced, with reasons	NA
Sample size	7a	How sample size was determined	17-18
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	10
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	10
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	NA
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	10
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	10

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	14
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	16-17
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	18
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	10
	13b	For each group, losses and exclusions after randomisation, together with reasons	NA
Recruitment	14a	Dates defining the periods of recruitment and follow-up	8-9
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	20-22
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	NA
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	NA
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	NA
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	NA
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	NA
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	NA
Other information			
Registration	23	Registration number and name of trial registry	4
Protocol	24	Where the full trial protocol can be accessed, if available	See ClinicalTrial.gov
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	27

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

The TIDieR (Template for Intervention Description and Replication) Checklist*:

Information to include when describing an intervention and the location of the information

Item number	Item	Where located **	
		Primary paper (page or appendix number)	Other † (details)
	BRIEF NAME		
1.	Provide the name or a phrase that describes the intervention.	12-14	
	WHY		
2.	Describe any rationale, theory, or goal of the elements essential to the intervention.	12-14	Ma H, Lin S, Li X, et al. Optimal Heart Team Protocol to Improve Revascularization Decisions in Patients with Complex Coronary Artery Disease: A Sequential Mixed Method Study. Eur Heart J Qual Care Clin Outcomes 2022; 8(7):739-749. doi: 10.1093/ehjqcco/qcab074
	WHAT		
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (e.g. online appendix, URL).	11-12	Online table 1
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention, including any enabling or support activities.	12-14	
	WHO PROVIDED		

5.	For each category of intervention provider (e.g. psychologist, nursing assistant), describe their expertise, background and any specific training given.	12-14	
	HOW		
6.	Describe the modes of delivery (e.g. face-to-face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group.	13-14	
	WHERE		
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.	13-14	
	WHEN and HOW MUCH		
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity or dose.	13-14	
	TAILORING		
9.	If the intervention was planned to be personalised, titrated or adapted, then describe what, why, when, and how.	N/A	
	MODIFICATIONS		
10.‡	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).	N/A	
	HOW WELL		
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them.	13	
12.‡	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned.	N/A	

** **Authors** - use N/A if an item is not applicable for the intervention being described. **Reviewers** – use '?' if information about the element is not reported/not sufficiently reported.

† If the information is not provided in the primary paper, give details of where this information is available. This may include locations such as a published protocol or other published papers (provide citation details) or a website (provide the URL).

‡ If completing the TIDieR checklist for a protocol, these items are not relevant to the protocol and cannot be described until the study is complete.

* We strongly recommend using this checklist in conjunction with the TIDieR guide (see *BMJ* 2014;348:g1687) which contains an explanation and elaboration for each item.
* The focus of TIDieR is on reporting details of the intervention elements (and where relevant, comparison elements) of a study. Other elements and methodological features of studies are covered by other reporting statements and checklists and have not been duplicated as part of the TIDieR checklist. When a **randomised trial** is being reported, the TIDieR checklist should be used in conjunction with the CONSORT statement (see www.consort-statement.org) as an extension of **Item 5 of the CONSORT 2010 Statement.** When a **clinical trial protocol** is being reported, the TIDieR checklist should be used in conjunction with the SPIRIT statement as an extension of **Item 11 of the SPIRIT 2013 Statement** (see www.spirit-statement.org). For alternate study designs, TIDieR can be used in conjunction with the appropriate checklist for that study design (see www.equator-network.org).

复杂冠心病心脏团队决策一致性对比研究（随机对照试验）

知情同意书

我们邀请您参加由中国医学科学院阜外医院发起的一项“复杂冠心病心脏团队决策一致性对比研究”，本研究已通过中国医学科学院阜外医院伦理委员会审批（电话 010-8839****）。请仔细阅读说明，了解您在研究中的权利和义务，明确研究性质和风险。参加研究属完全自愿。当研究人员向您说明和讨论知情同意书时，您可以随时提问并让研究人员向您解释您不明白的地方。若您目前正参加其他临床研究，请告知研究人员。本项研究的项目负责人是郑**（中国医学科学院阜外医院），本项研究的资助方是中国医学科学院阜外医院。

为什么进行这项研究？

当前复杂冠心病心脏团队实践流程存在标准不统一及决策一致性欠佳的问题。前期的一项序贯解释性混合方法研究探索出了一套优化流程的标准化心脏团队实践方案，其对改善心脏团队决策一致性的效果有待验证。本研究拟通过随机对照设计，评价标准化心脏团队实践方案改善复杂冠心病心脏团队决策一致性的效果。

为什么邀您请参加这项研究？

因为您（作为介入医生）具备年介入手术量至少 200 例、左主干病变介入年手术量至少 25 例，且可独立完成慢性完全性闭塞病变的介入手术的能力；或（作为心脏外科医生）具备总搭桥手术量至少 200 例，且可熟练完成体外循环和非体外循环搭桥手术的能力；或（作为非介入手术医生）具备副主任医师及以上的技术资格。此外，您还需具备相关临床研究经验及循证医学素养。因此，我们邀请您参加本项研究。是否最终入选由研究者根据您的实际情况来判断。

多少人将参与这项研究？

本研究计划在内外科合作良好的医院中最终招募 84 位心血管病医生，其中包含介入医生 36 位、心外科医生 36 位及非介入手术医生 12 位。

参加本项研究，需要您做什么？

您需要在项目组的引导下，学习使用心脏团队会议系统、接受会议培训，并参与心脏团队会议讨论，为回顾性病例提供最优诊疗决策推荐。同时，需对项目组为您提供的任何形式的包括但不限于研究方案、病例基本临床信息、心电图图片、超声心动图报告、造影图像、未公开发表的临床文件或其他保密信息进行保密，不得通过拍照、录音、录像、截图等形式泄露、告知、公开、发布、出版、传授、转让或其他任何方式使任何第三方知悉项目提供的数据或利用项目组数据分析的成果数据。

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本项研究将持续 12 个月。

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本研究仅邀请您参与心脏团队并进行既往病例会议讨论。研究不会干预您正常的临床诊疗工作，研究过程中无任何风险和不良反应。

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本研究仅邀请您参与心脏团队并进行既往病例会议讨论，不影响您正常的临床工作，不会发生研究相关伤害。

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是否一定要参加并完成本项研究？

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是否愿意参加未来研究？

如果您同意，我们希望保留您在研究期间的资料和数据。您的匿名研究数据将继续用于后续经审批的心血管相关医学研究。如果您不同意，在本项研究完成之后，您的研究数据将根据国家规定保存至指定年限，并严格保密。参与未来研究不会增加您额外的风险与经济负担，所有未来研究的样本及资料都将妥善保存于中国医学科学院阜外医院并严格保密。您可以自愿选择是否参加未来研究，并可以在任何时间联系研究人员以书面文件形式退出研究。

如果有问题或困难，该与谁联系？

您可以在任何时间提出有关本项试验的任何问题，并得到相应的解答，请联系研究人员，电话：010-8839****。如果您对自己的权益有任何疑问，请联系阜外医院伦理委员会，电话：010-8839****。感谢您花时间阅读本知情同意书。如果您通过充分考虑之后同意参加本临床试验，希望您能按照研究人员的要求完成本次临床试验。参加本试验前，请与您的研究人员共同完成并签署此文件最后一页（签署页），一式两份，您和医院各保留一份签署的文件。

签署页

我已经认真阅读、理解并同意本知情同意书全部条款。

我已被告知此项研究/临床试验的试验目的、内容、程序，研究/试验可能有的不良反应，研究补偿，以及我的权益等；我有足够的时间和机会进行提问，并得到了令我满意答复。

我承诺我提供的信息是真实的；如提供了虚假信息，我承诺对其后果负责。

我确认签名处所留联系方式为我本人有效联系方式，如变更联系方式应及时告知你院，否则，我愿意承担无法联系及无法收到通知的相应后果。

我知道我可以随时退出此项试验，并不影响我正常临床工作。

我将得到这份知情同意书的正本，上面包含我和研究者的签名。

我同意参加本项研究。

是否同意参与未来研究□同意□不同意（请您选择）研究数据用于未来研究，授权研究者及相关医学研究项目的共同研究单位在被批准的心血管相关医学研究中使用并且处理我本人的匿名数据。

受试者姓名	签名：
	日期：
研究者	签名：
	日期：

A comparative study on the stability of heart team decision-making in complex coronary artery disease (a randomized controlled trial)

INFORMED CONSENT

We invite you to participate in a " comparative study on the stability of heart team decision-making in complex coronary artery disease (a randomized controlled trial)" initiated by Fuwai Hospital, Chinese Academy of Medical Sciences. This study has been approved by the Ethics Committee of Fuwai Hospital, Chinese Academy of Medical Sciences (Tel: 010-8839****). Please read the instructions carefully to understand your rights and obligations in the research and to clarify the nature and risks of the research. Participation in research is entirely voluntary. When the researcher explains and discusses the informed consent form to you, you can always ask questions and ask the researcher to explain to you what you don't understand. If you are currently participating in other clinical studies, please inform the investigators. The project leader of this research is Zheng ** (Fuwai Hospital, Chinese Academy of Medical Sciences), and the sponsorof this research is Fuwai Hospital, Chinese Academy of Medical Sciences.

Why do this research?

The current practice processes of coronary revascularization heart team have problems with inconsistent standards and poor consistency of decision-making. A previous sequential explanatory mixed methods study explored a standardized heart team implementation protocol to optimize the process, and its effect on improving the consistency of heart team decision-making remains to be verified. This randomized controlled trial aims to evaluate the effect of a standardized heart team implementation protocol on improving decision-making consistency in complex coronary artery disease.

Why are you invited to participate in this study?

Because you (as an interventional cardiologist) have the ability to have annual PCI volume ≥ 200, annual left main (LM)-PCI volume ≥ 25, and is capable of chronic total occlusion (CTO)-PCI; or (as a cardiac surgeon) have total CABG volume ≥ 200, and is proficient in both on-pump and off-pump CABG; or (as a non-interventional surgeon) have the technical qualifications of associate chief physician or above. In addition, you need to have relevant clinical research experience and evidence-based medicine literacy. Therefore, we invite you to participate in this study. Whether you are finally selected or not will be judged by the researcher based on the actual situation.

How many people will be involved in this study?

This study plans to eventually recruit 84 specialists from hospitals with good cooperation in internal medicine and surgery, including 36 interventional cardiologists, 36 cardiac surgeons, and 12 non-interventional cardiologists.

What do you need to do to participate in this study?

Under the guidance of the project team, you need to learn to use the heart team meeting system, receive team training, and participate in the heart team meeting discussions to provide optimal treatment decisions for retrospective cases. At the same time, it is necessary to keep confidential of any form of information provided to you, including but not limited to research protocols, basic clinical information of cases, electrocardiogram pictures, echocardiography reports, angiography images, unpublished clinical documents or other confidential information. Any means (photographing, audio recording, video recording, screenshots, etc.) to make any third party aware of the data provided by the project or the results of data analysis by the project team is forbidden.

How long will this study last?

The study will last for 12 months.

Risks and adverse effects of participants in this study?

This study only invites you to participate in the heart team and make decisions for retrospective cases. The study will not interfere with your normal clinical practice, and there will be no risks and adverse effects during the process.

What are the possible benefits of participating in this study?

You will not directly benefit from participating in this study, but your participation will help promote the exchange of disciplines and techniques between cardiologists and cardiac surgeons, and provide valuable information and experience for real-world optimization and improvement of heart team practice.

If not participating in this study, are there other options?

You can choose not to participate in this study, which will not have any impact on your normal clinical work.

Fees and Compensation for Participation in the Study

This study only invites you to participate in the heart team and make decisions for retrospective cases, and there is no related cost and compensation.

What happens to research-related injuries?

This study only invites you to participate in the heart team and make decisions for retrospective cases, which will not interfere with your normal clinical work and will not cause research-related injuries.

Will my information be kept private?

Yes, your information will be kept strictly confidential during the study. When your research data is used in this trial, your personal information is kept confidential, and all your information will be kept securely and used for research purposes only. The information in the research database will be strictly desensitized to eliminate personally identifiable characteristics, and information that may identify you will not be disclosed to anyone other than the researcher without your permission. Without violating the principle of confidentiality and relevant regulations, the reviewers of the ethics committee can consult the original medical records of the subjects to verify the process and data of the clinical trial. If the research results are published publicly, your personal information will not appear in any publications, and we will not disclose this information to anyone or any institution.

Do I have to participate in and complete this study?

Participation in this study is voluntary, and you are free to decide to participate or refuse to participate in this study. Whether you agree to participate in this research or not will not affect your normal clinical work. If you want to participate in this research, you need to read this informed consent form carefully and sign this informed consent form after confirming that you fully understand the relevant issues. You will not lose any legal rights conferred on you by law by signing this document. You may refuse to participate at any time or have the right to withdraw from the research at any time during the research period without any reason, without discrimination or retaliation, and the corresponding rights will not be affected. If you want to withdraw from the research project during the participation, please notify the researcher, complete the relevant procedures before withdrawal as required by the researcher, and complete the relevant withdrawal procedures in writing as required; after withdrawal, the researcher will no longer continue to collect and use your trial data, but data collected anonymized prior to your opt-out cannot be deleted or withdrawn.

Would you like to participate in future research?

With your consent, we wish to retain your data during the study period. Your anonymous research data will continue to be used for subsequent approved cardiovascular-related medical research. If you do not agree, after the completion of this research, your research data will be kept for a specified period of time in accordance with national regulations and will be kept strictly confidential. Participating in future research will not increase your additional risk and financial burden. All future research samples and materials will be properly stored in FuwaiHospital, Chinese Academy of Medical Sciences and will be kept strictly confidential. You may voluntarily choose to participate in future research and to withdraw from research at any time in writing by contacting the researcher.

Who should I contact with questions or difficulties?

Please contact the researchers at 010-8839**** . If you have any questions about your rights, please contact the Ethics Committee of Fuwai Hospital, Tel: 010-8839****.

Thank you for taking time to read this informed consent form. If you agree to participate in this clinical trial after due consideration, I hope you can complete this clinical trial in accordance with the requirements of the researchers. Before participating in this trial, please complete and sign the last page (signature page) of this document together with your investigator in duplicate, with one signed document each for you and the hospital.

SIGN PAGE

I have carefully read, understood and agreed to all the terms of this informed consent form.

I have been informed of the purpose, content, procedures of this research/clinical trial, possible adverse effects of the research/trial, research compensation, and my rights and interests; I have enough time and opportunity to ask questions, and have received satisfactory answers.

I promise that the information I provide is true; if false information is provided, I promise to be responsible for the consequences.

I confirm that the contact information left in the signature office is my valid contact information. If I change the contact information, I should inform your hospital in time. Otherwise, I am willing to bear the corresponding consequences of not being able to contact and not being notified.

I know that I can withdraw from this trial at any time without affecting my normal clinical work.

I will get the original copy of this informed consent form, signed by me and the researcher.

I agree to participate in this study.

I agree to participate in the future study. ☐Agree ☐Disagree

SUBJECT'S NAME	sign: date:
RESEARCHER	sign: date:

SUPPLEMENTAL MATERIALS

Effect of a standardized heart team protocol versus a guideline-based protocol on revascularization decision stability in stable complex coronary artery disease: rationale and design of a randomized trial of cardiology specialists using historic cases

Contents

Supplemental Methods

Full Definitions of key variables and clinical endpoints

1. **Three-vessel disease:** three lesions with a percent diameter stenosis (DS%) between 50%-99% or total occlusion in a coronary artery with a ≥ 2.5 mm reference vessel diameter by visual assessment.
2. **Left main desease:** left main coronary artery is visually assessed DS% ≥ 50%.
3. **Major adverse cardiovascular and cerebrovascular events (MACCEs):** a composite of death, myocardial infarction, stroke, repeated revascularization, and rehospitalization due to ischemic symptoms.
4. **Death:** death from any cause. The cause of death will be adjudicated as being due to cardiac death or non-cardiac death.
5. **Myocardial infarction (MI)**

   (1) In-hospital MI: Defined as the occurrence during hospitalization after PCI, CABG or coronary angiography meeting at least 1 of the following criteria:

   1) The rise in cardiac troponin I (cTnI) is ⩾ 70 times the 99th percentile URL (where the baseline is lower than the URL, elevated and stable, or falling).
   2) If cTnI was not available, MI was defined with at least one of the following:
      i. New ischaemic ECG changes;
      ii. Development of new pathological Q waves;
      iii. Imaging evidence of loss of viable myocardium that is presumed to be new and in a pattern consistent with an ischaemic etiology;

iv. Angiographic findings consistent with a procedural flow-limiting complication such as coronary dissection, occlusion of a major epicardial artery or graft, side-branch occlusion-thrombus, disruption of collateral flow or distal embolization.

(2) Spontaneous MI: Defined as detection of a rise and/or fall of cTn values with at least one value above the 99th percentile URL after discharge and with at least one of the following:

1) Symptoms of acute myocardial ischemia;
2) New ischaemic ECG changes;
3) Development of pathological Q waves;
4) Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic etiology;
5) Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy.

6. Stroke was confirmed by a neurologist on the basis of imaging studies and was defined as follows:

1) A focal neurologic deficit of central origin lasting >72 hours, or
2) A focal neurologic deficit of central origin lasting >24 hours, with imaging evidence of cerebral infarction or intracerebral hemorrhage, or
3) A non-focal encephalopathy lasting >24 hours with imaging evidence of cerebral infarction or hemorrhage adequate to account for the clinical state.

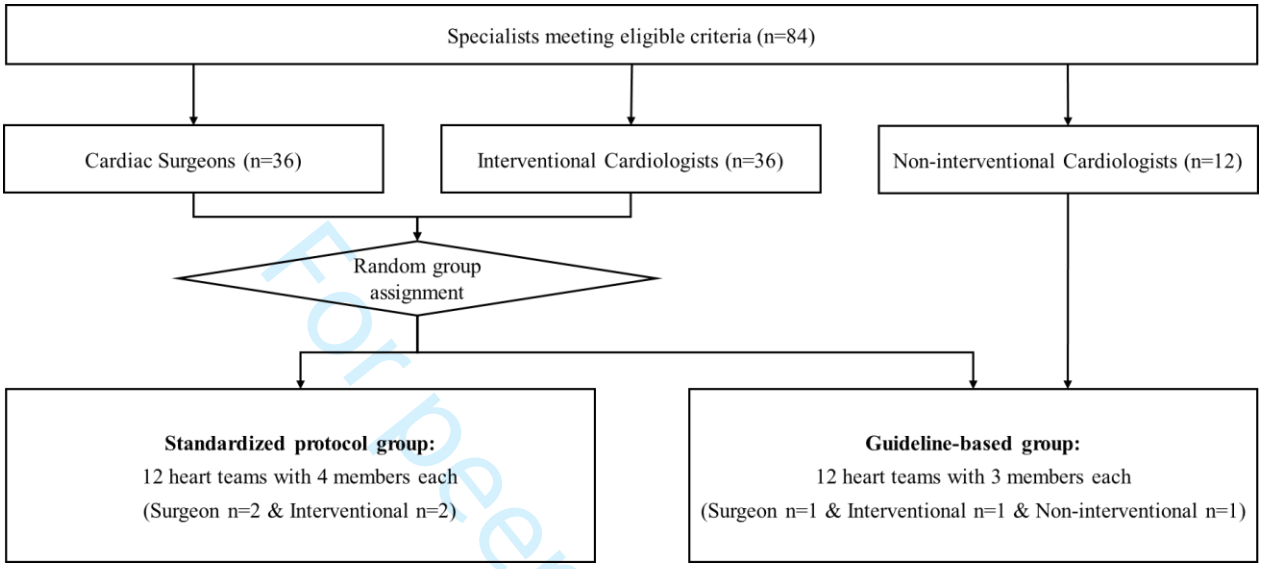
7. **Repeat revascularization** was defined as any repeat coronary artery bypass graft (CABG) or PCI.
    1) Target Lesion: Lesions were revascularized in the index procedure (or during a planned or provisional staged procedure).
    2) Non-Target Vessel: Lesions were not treated by either PCI or CABG at the index procedure.
8. **Rehospitalization due to ischmic symptoms:** rehospitalization because of ischemic discomfort (angina or symptoms thought to be equivalent).

Inclusion and exclusion criteria of cases to be discussed

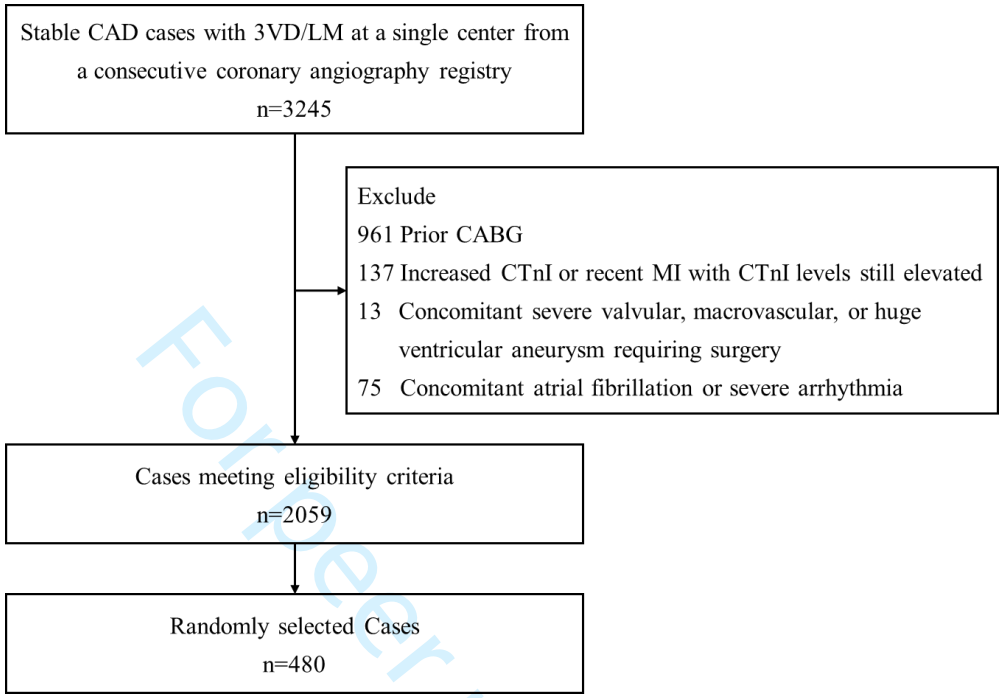
Adult patients with stable CAD according to the National Cardiovascular Data Registry (NCDR) CathPCI criteria (stable angina, no or silent myocardial ischemia) and angiographically confirmed 3-vessel disease or left main (3VD/LM) disease will be eligible for inclusion in the study. The exclusion criteria included: (1) prior coronary artery bypass grafting (CABG); (2) cardiac troponin I (CTnI) greater than the local laboratory upper limit of normal or recent myocardial infarction with CTnI levels still elevated; (3) concomitant severe valvular disease, macrovascular disease, or huge ventricular aneurysm requiring surgery; (4) concomitant atrial fibrillation or severe arrhythmia; or (5) unavailable de novo angiography images of the current hospitalization. Eligible cases will be randomly selected from a prospective registry of consecutive patients who underwent coronary angiography between August 2016 and August 2017.

Supplementary Figures

Online Figure 1. Specialist Enrollment Flowchart

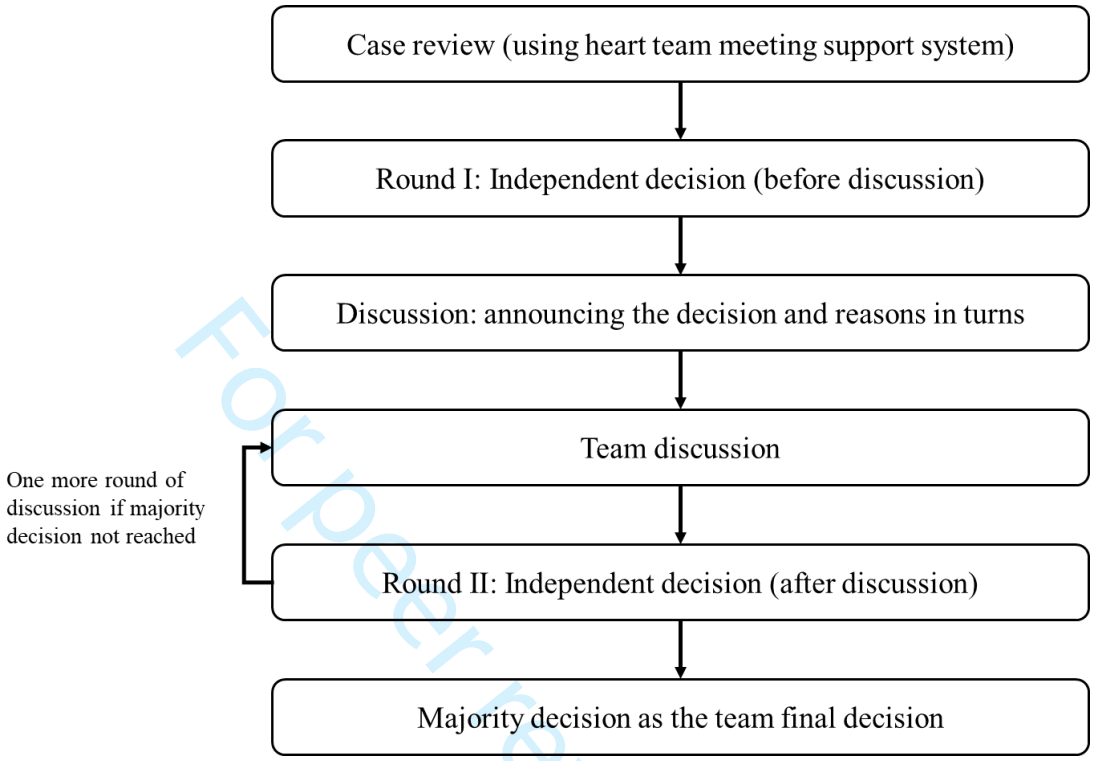


Online Figure 2. Cases Selection Flowchart



3VD indicates 3-vessel disease; CTnI, cardiac troponin I, LM, left main; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Online Figure 3. Standard heart team meeting procedure



Supplementary Tables

Online Table 1. Structured patient information

Heart Team Patient Information Sheet

A. Demograpgics

Patient ID:_____ Gender: ☐Male ☐female Age:_____y BMI :_____kg/m ^{2}

B. Medical history and risk factors

Diabetes	☐ Yes ☐No	
History of myocardial infarction	☐ Yes ☐No	Time: _____
History of heart failure	☐ Yes ☐No	EF value: _____%
History of stroke	☐ Yes ☐No	
renal insufficiency	☐ Yes ☐No	Creatinine: _____umol/L (44-133) Creatinine clearance: _____ml/min
Chronic obstructive pulmonary disease	☐ Yes ☐No	
Other comorbidities: *congenital mitral valve prolapse, hypertension, post-operative hypothyroidism, kidney stones*		

C. Coronary heart disease symptoms

Coronary heart disease symptoms	☐Unstable Angina ☐stable angina ☐Asymptomatic
Home antianginal medication	☐ Long-acting nitrates ☐ β -blockers ☐ Ca2+ channel blockers
CCS classification (stable angina)	☐I ☐II ☐III ☐IV ☐Asymptomatic
NYHA classification	☐I ☐II ☐III ☐IV

D. Laboratory test

Hemoglobin: _____g/L	White blood cells:_____ *10^9/L	Platelets:_____*10^9/L
PT: _____s (11.5-14.5)	APTT: _____s (28.5-43.5)	INR: _____(0.8-1.2)
Troponin I: _____ng/ml (ll_____:ul_____)		

E. Preoperative non-invasive examination

	Result
Admission ECG	*Sinus bradycardia 58 beats/min*
Echocardiography	*Mitral valve posterior leaflet prolapse, mitral valve regurgitation*
Stress Testing and Nuclear Medicine	
Coronary CTA	
Cardiac MRI	

F. Invasive coronary examination

Anigiography	FFR:	IVUS:	OCT:
QFR	LM (left main artery): _____		LAD (left anterior descending artery:_
	LCX (left circumflex artery):_____		RCA (right coronary artery):_____
	Obtusemarginal:_____		Diagonal:_____
	Posterior descending artery:_____		Left posterior artery:_____
	Ramus medianus:_____		

G. Clinical risk scores

SYNTAX	Score:_____

S YNTAX II	PCI Score: 30.0(9.8%)	CABG Score: 32.5(10.2%)	Recommended:/
SYNTAX II 2020	PCI score: 9.8%	CABG Score: 10.2%	
EuroScore II	Mortality: 0.7%		
SinoScore II	Mortality: 0.7%		
STS Score	Mortality: 0.49%	Mortality and complication rate: 9.95%	
	Renal failure rate: 0.39%	Stroke rate: 1.27%	
	Prolonged ventilation rate: 5.8%	Deep sternum infection rate: 0.36%	
	Reoperation rate: 2.37%	Extended hospital stay rate: 4.34%	

* Guidelines recommend STSscore mortality >2% with higher surgical risk

H. Decision result (single choice)

Independent decision before discussion	☐PCI ☐CABG ☐PCI /CABG ☐Drugs ☐Further inspection
Independent decision after discussion	☐PCI ☐CABG ☐PCI /CABG ☐Drugs ☐Further inspection

Online Table 2. Ten-Item Personality Inventory in China (TIPI-C)

Question No.*	Original items (Gosling et al., 2003)	Rating Scale						
		Absolutely disagree	Quite disagree	Almost disagree	Uncertain	Almost agree	Quite agree	Absolutely agree
		1	2	3	4	5	6	7
1	Extraverted, enthusiastic							
2	Critical, quarrelsome							
3	Dependable, self-disciplined							
4	Anxious, easily upset							
5	Open to new experience, complex							
6	Reserved, quiet							
7	Sympathetic, warm							
8	Disorganized, careless							

9	Calm, emotionally stable							
10	Conventional, uncreative							

*Scale scoring ("R" denotes reverse-scored items): Extraversion: 1, 6R; Agreeableness: 2R, 7; Conscientiousness: 3, 8R; Emotional Stability: 4R, 9; Openness to Experiences: 5, 10R.

Online Table 3. Tabular analysis of inter-team agreement

Case ID	Interventional group			Guideline group		
	Hear team 1 decision	Hear team 2 decision	agreement	Hear team 1' decision	Hear team 2' decision	agreement
001	CABG	CABG	Yes	PCI	CABG	No
002	CABG	PCI	No	PCI	PCI	Yes
003	Medication	PCI	No	Further testing	PCI	No
…	…	…	…	…	…	…
…	…	…	…	…	…	…
480	PCI	PCI	Yes	PCI	Medication	No

Online Table 3. Tabular analysis of inter-team agreement. Each case will be discussed by two assigned heart teams. The pairwise comparison between the heart team's decision on each case provides data on the agreement. CABG indicates coronary artery bypass grafting; PCI, percutaneous coronary intervention.