Effects of intensive lipid lowering compared with moderate-intensity lipid lowering on coronary atherosclerotic plaque phenotype and major adverse cardiovascular events in adults with low to intermediate 10-year ASCVD risk (ILLUMINATION study): protocol for a multicentre, open-label, blinded-endpoint, randomised controlled trial

Jianan Zheng, Zhihui Hou, Jinqing Yuan, Xueyan Zhao, Yang Wang, Jia Li, Wenjia Zhang, Kefei Dou, Bin Lu

ABSTRACT

Introduction Current guidelines recommend moderate-intensity lipid lowering (low-density lipoprotein cholesterol, LDL-C of <2.6 mmol/L or 30%–49% reduction from the baseline) for patients with intermediate 10-year atherosclerotic cardiovascular disease (ASCVD) risk. The effects of intensive lipid lowering (LDL-C of <1.8 mmol/L) on coronary atherosclerotic plaque phenotype and major adverse cardiovascular events (MACE) in adults with both non-obstructive coronary artery disease (CAD) and low to intermediate 10-year ASCVD risk remain uncertain.

Methods and analysis Intensive Lipid-lowering for Plaque and Major Adverse Cardiovascular Events in Low to Intermediate 10-year ASCVD Risk Population is a multicentre, randomised, open-label, blinded endpoint clinical trial. Inclusion criteria are as follows: (1) patients with the age of 40–75 years within 1 month of coronary CT angiography (CCTA) and coronary artery calcium score (CACS) evaluation; (2) population with low to intermediate 10-year ASCVD risk (<20%) and (3) patients with non-obstructive CAD (stenosis <50%) using CCTA. 2900 patients will be randomly assigned to the intensive lipid lowering (LDL-C of <1.8 mmol/L or ≥50% reduction from the baseline) or the moderate-intensity lipid lowering (LDL-C of <2.6 mmol/L or 30%–49% reduction from the baseline) group in a 1:1 ratio. The primary endpoint is MACE (composite of all-cause death, non-fatal MI, non-fatal stroke, any revascularisation and hospitalisation for angina) within 3 years after enrolment. The secondary endpoints are changes in coronary total plaque volume (mm$^3$), plaque burden (%), plaque composition (mm$^3$, %), high-risk plaque characteristics detected using CCTA and CACS determined using CT.

Ethics and dissemination Ethics committee approval for this study was obtained from the review boards of Fuwai Hospital (No.2022-1787) and all other study sites. Written informed consent will be obtained from all participants. The results of this study will be published in peer-reviewed journals and reported at international conferences.

Trial registration number NCT05462262.

INTRODUCTION

Lowering lipids is very important in preventing atherosclerosis and thus, primary atherosclerotic cardiovascular diseases (ASCVDs), including coronary artery disease (CAD), stroke and peripheral vascular disease. The 2019 ACC/
AHA (the American College of Cardiology and American Heart Association) guidelines on the primary prevention of cardiovascular disease and the 2019 ESC/EAS (the European Society of Cardiology and European Atherosclerosis Society) guidelines for the management of dyslipidaemias recommend moderate-intensity lipid-lowering therapy (achieving an low-density lipoprotein cholesterol (LDL-C) of <2.6 mmol/L or a 30%-49% reduction of LDL-C from the baseline) for the primary prevention of ASCVDs in the population at 10-year ASCVD borderline and intermediate risk. Nevertheless, current guidelines advocate lipid-lowering therapy for the primary prevention of ASCVD based on clinical risk stratification. With the increased use of non-invasive tests in determining cardiovascular diseases in clinical practices, the application of risk-enhancing factors, besides clinical risk factors, detected by non-invasive tests remains to be explored.

Coronary CT angiography (CCTA) produces accurate images of early coronary atherosclerotic lesions and provides a wealth of anatomical and functional attributes, including plaque burden (total plaque volume, calcification score and segment involvement score), plaque composition, characteristics of high-risk plaque, luminal stenosis and CCTA-derived fractional flow reserve. Complete CCTA imaging-based information is used in risk stratification, guiding primary prevention of ASCVD and predicting major adverse cardiovascular events (MACEs) in non-obstructive CAD patients.

Statin therapy reduced myocardial infarction (MI) and adverse events through primary prevention interventions. Combining ezetimibe with statin also reduced the risk of MACE in patients, demonstrating the incremental benefits when adding other lipid-lowering drugs. In statin-intolerant patients, treatment with bempedoic acid could be considered for further LDL-C reduction, which was demonstrated to reduce the risk of MACE. In a previous study by Øvrehus et al., the benefit of statin treatment in the primary prevention of CAD was directionally proportional to CAD burden. Regarding different clinical risk stratifications, a study published in the *New England Journal of Medicine* demonstrated that a moderate-intensity statin therapy resulted in significantly lower adverse cardiovascular events than a placebo in intermediate-risk patients without cardiovascular disease. However, heterogeneity in the extent of coronary atherosclerosis exists in patients with low to intermediate risk, and CCTA imaging could differentiate these differences. Combining clinical risk stratification and CCTA findings in making precise risk re-stratification and primary prevention intervention, is presently lacking. Therefore, this study aims to use CCTA in exploring better strategies for the primary prevention of ASCVD. We predict that intensive lipid lowering in adults with low to intermediate 10-year ASCVD risk and non-obstructive CAD determined by CCTA will improve clinical outcomes compared with moderate-intensity lipid lowering.

### METHODS AND ANALYSIS

#### Study design

Intensive Lipid-lowering for Plaque and Major Adverse Cardiovascular Events in Low to Intermediate 10-year ASCVD Risk Population (ILLUMINATION; NCT05462262) is a prospective, randomised, open-label, blind endpoint clinical trial being conducted at 28 clinical centres in China. Recruitment will be competitive with no maximum limit for the patient from each centre. The onset of the enrollment was on 10 October 2022. The estimated end of the enrolment will be on 31 October 2023. A core laboratory will be responsible for image analysis, interpretation and quality control. The flow chart of the ILLUMINATION study is shown in figure 1.

#### Study objectives

The primary objective is to determine whether intensive lipid lowering could reduce the incidence of MACE in patients with non-obstructive CAD and low to intermediate 10-year ASCVD risk, compared with moderate-intensity lipid lowering. The secondary objectives are to compare the effects of intensive lipid lowering versus moderate-intensity lipid lowering on the plaque phenotype determined using CCTA.

#### Patient population

The study population includes patients between 40 and 75 years of age within 1 month of CCTA imaging and coronary artery calcium score (CACS) scan. The inclusion criteria are as follows: (1) population with low to intermediate 10-year ASCVD risk of <20% calculated using pooled cohort equations and (2) patients with non-obstructive CAD (stenosis of ≤50%) diagnosed on CCTA.

The exclusion criteria are as follows:

1. Patients who have comorbidities, such as serious cardiovascular diseases, including heart failure (ejection fraction of ≤30%), arrhythmias (persistent atrial flutter/atrial fibrillation and second-degree or third-degree atrioventricular block), haemodynamically important valvular disease, haemodynamically important congenital heart disease and stroke.
2. Patients with MI, coronary revascularisation or severe/unstable angina before or within 1 month of screening.
3. Patients with active liver disease or hepatic dysfunction (determined from alanine aminotransferase or aspartate aminotransferase level of >3 times the upper limit of normal).
4. Patients with unexplained creatine phosphokinase levels of >6 times the upper limit of normal.
5. Patients with nephrotic syndrome.
6. Patients with diabetes mellitus.
7. Patients with uncontrollable hypertension.
8. Patients with uncontrollable hypothyroidism.
9. Patients who are hypersensitive to statins.
11. Patients with gastrointestinal diseases affecting drug absorption or a history of gastrointestinal surgery.
12. Patients with survival-limiting diseases.
13. Patients who have concurrent long-term immunosuppressive therapy.
14. Patients participating in another clinical trial concurrently or within 30 days before screening.
15. Patients who are pregnant or breast feeding.
16. Patients who are unable to give informed consent.
17. Patients with other unsuitable situations that are deemed by physicians.

**Intervention and follow-up**

Eligible patients will be randomised into the intervention group (LDL-C of <1.8mmol/L or ≥50% reduction from the baseline) and control group (goal for LDL-C <2.6 mmol/L or 30%–49% reduction from baseline, according to current guidelines for ASCVD primary prevention) in a 1:1 ratio using computer-generated random allocation. The LDL-C values will be controlled to the target levels through lipid-lowering therapy and/or lifestyle modification in patients in both groups. The lipid-lowering therapies include statins, ezetimibe and proprotein convertase subtilisin/kexin type 9 inhibitors. Based on the tolerance in Chinese people, statin therapy will be started at a moderate intensity. If the target of LDL-C is not achieved in 1 month, the statin dose will be increased appropriately, or ezetimibe will be added. If the therapy still does not achieve the goal within 6 months, a proprotein convertase subtilisin/kexin type 9 inhibitor will be considered to lower the lipids. However, the type, dose and combinatory drugs need to be tailored to individual patients by physicians. Following dispensing of the study drug and/or giving healthy lifestyle recommendations, randomised patients will be clinically evaluated at 1, 3 and 6 months and then every 6 months thereafter. Within 6 months of randomisation, lipid-lowering therapy will be adjusted based on the treatment effect. Follow-up LDL-C values will be reported to the patients and physicians to adjust the drug regimen to ensure differences between the control and intervention groups. Patients will be clinically evaluated within 6 weeks after each adjustment of medication for efficacy and adverse drug reactions. Follow-up CCTA and CACS will be performed after about 3 years. MACE will be followed up for about 3 years. The details of the follow-up procedure are shown in online supplemental table 1.

**Study endpoints**

The primary endpoint is the incidence rate of MACE, and the secondary endpoints are the change in plaque burden, plaque composition, high-risk plaque characteristics and plaque progression determined using CCTA and CACS by CT. The details of study endpoints and definitions are shown in box 1.

**Sample size and statistical analysis**

All the statistical analyses will be performed using SPSS V.22.0 for Windows (SPSS) by an expert in medical statistics. For descriptive analysis, continuous variables will be represented as the mean±SD, and categorical variables will be presented as percentages. Categorical variables will be compared using χ2 statistics and continuous...
variables will be compared using a t-test. We will test the interobserver agreement of CCTA variables by k-statistic. Cumulative event rates as stratified by intervention and the control group will be estimated using the product limit (Kaplan-Meier) method and the log-rank test. A two-sided p<0.05 will be considered to indicate statistical significance.

According to 2012 literature, the incidence of 3-year MACE events in outpatients with non-obstructive coronary heart disease was 3.7%. It is expected that enhanced lipid-lowering will reduce the 3-year MACE events to 1.8%, which is a clinically acceptable positive cut-off value. The two-sided statistical significance level is 0.05, and the confidence level is 80%. The sample size (N1) in the intensive intervention group = the sample size (N2) in the control group = 1160. It is increased to 1450 in each group to account for a 20% loss during follow-up. A total sample size of 2900 patients is required.

**Patient and public involvement**

None.

**ETHICS AND DISSEMINATION**

The study adheres to the principles of the Declaration of Helsinki and the specifications of the International Conference on Harmonisation, and Good Clinical Practice. Ethics committee approval for this study was obtained from the Fuwai Hospital Institutional Review Board (No.2022-1787) and the institutional review boards/institutional ethics committees at all other sites. Written and verbal informed consent will be provided by all patients (see online supplemental material for consent form).

This trial is an investigator-initiated study with financial support from the Chinese Academy of Medical Sciences and Peking Union Medical College. The study has set up a management committee, an endpoints committee and a third-party independent imaging reading centre to ensure smooth progress. All completed electronic case report forms from each of the 28 sites will be collected from the Electronic Data Capture System (https://edc.fuwai.cn/reports) and transmitted to a central data repository to generate the master ILLUMINATION dataset. All study-related information will be stored securely at the study site. The third-party independent imaging reading centre is responsible for interpreting images and quality control. The results of this study will be published in peer-reviewed journals and reported at international conferences.

**DISCUSSION**

The ILLUMINATION study is the first randomised controlled trial to use the CCTA imaging information as a risk-enhancing factor in evaluating the effects of intensive lipid lowering in the primary prevention of ASCVD. Unlike previous studies, this trial uses LDL-C targets for grouping patients and interventions, which is more aligned with real-world primary prevention strategies. The outcomes due to intensive lipid lowering will be both evaluated using both plaque phenotype and MACE to elucidate the development and prognosis of atherosclerosis. However, this is an open-label and assessor-blinded trial, and the patients and physicians will not be blinded to the randomisation. Further, the study will not strictly follow the types of lipid-lowering drugs or lifestyle changes recommended to patients, which may introduce some confounding effects.

Many previous studies found that lowering lipids by statin therapy prevented coronary atherosclerotic plaque progression. Statin therapy reduced the total plaque burden, diminished plaque volume progression and attenuated the characteristics of high-risk plaque. Statin transformed atherosclerotic plaque compositions towards high-density calcium. In addition, a systematic review and meta-analysis by Andelius et al showed that statin therapy reduced non-calcified plaque volume and low-attenuation plaque volume but increased calcified plaque volume and calcium signal intensity. Intensive statin therapy showed more pronounced effects than moderate statin therapy. Studies that used optical coherence tomography found more effects from intensive statin therapy on plaque phenotypes, such as an increase of minimum fibrous cap thickness, reduction of macrophage accumulation and regression of thin cap fibroatheroma. Besides statin therapy, intensive lifestyle interventions had benefits in slowing plaque progression and reducing non-calcified plaque volume in non-obstructive CAD. Although there are many studies of statin therapy and
coronary atherosclerotic plaque, allocating statin dosages and selecting lipid-lowering target values for the primary prevention of ASCVD based on CCTA remains unknown.

Previous studies of cholesterol lowering mostly focused on secondary prevention and were drug-based randomised controlled trials, neglecting early prevention of atherosclerotic lesions and accurate stratification based on non-invasive imaging tools. In contrast to the previous studies, the ILLUMINATION study identifies early coronary atherosclerotic lesions detected by CCTA for early primary prevention using drugs and intervention by adopting a healthy lifestyle, thereby delaying plaque progression and reducing the risk of long-term MACE, thus achieving complete prevention of early disease.

The ILLUMINATION study is designed to address the question of whether intensive lipid lowering further delays plaque progression and reduces MACE compared with moderate-intensity lipid lowering in adults with low to intermediate 10-year ASCVD risk. When results are available, more information on the effects of lipid lowering will be provided on coronary atherosclerotic plaque phenotype and adverse cardiovascular events in primary prevention. If a clinically worthwhile benefit is detected, the ILLUMINATION study is expected to provide new insights into CCTA-based detection and prevention of early coronary atherosclerotic lesions and further risk stratification to reduce the risk of MACE in patients with non-obstructive CAD.

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Contributors Conception and design of the study: BL, ZH and JZ. Methodology: JY and XZ. Acquisition of data: JL and WZ. Analysis of data: YW. Writing—original draft: PH and KF. Writing—reviewing and editing: BL and ZH. Funding acquisition: KD and BL. All authors approved the final version of the manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES


Supplemental Table 1. Measures and frequency during the follow-up procedure in ILLUMINATION trial

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**Abbreviations:** MACE, major adverse cardiovascular events; EQ-5D, EuroQol Five Dimensions Questionnaire; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LP(a), lipoprotein(a); apoA1, apolipoprotein A-1; apoB, apolipoprotein B; Cr, creatinine; BUN, blood urea nitrogen; UA, uric acid; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BIL, bilirubin; CK, creatine kinase; Glu, glucose; Hs-CRP, hypersensitive c-reactive protein; HCY, homocysteine; CT, computed
tomography; CACS, coronary artery calcium score; CCTA, coronary computed tomography angiography.
中国医学科学院医学与健康科技创新工程

强化降脂治疗对冠状动脉粥样硬化斑块表型及心血管结局影响的多中心随机对照研究

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我们邀请您参加由中国医学科学院创新工程项目资助的一项研究“强化降脂治疗对冠状动脉粥样硬化斑块表型及心血管结局影响的多中心随机对照研究”，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)。请仔细阅读本知情同意书，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，无论是否参加本研究都不会影响您在医院期间的治疗。当研究者向您说明和讨论知情同意书时，您可以随时提问并要求他/她向您解释您不明白的地方。您可以与家人、朋友以及您的经治大夫讨论之后再做决定。

本项研究的项目负责人是吕滨，主任医师，中国医学科学院阜外医院。

1. 为什么进行本项研究？

应用10年动脉粥样硬化心血管病风险（ASCVD）评估模型，评估为中危患者在我国具有很庞大的患者群，对于这些中危患者施行冠心病一级预防，是降低我国冠心病事件的根本措施。但是，临床上对于中危患者是否启动降脂药物治疗，以及降脂治疗强度的临床策略及实践仍缺乏循证医学证据，同时缺乏对中危患者进行进一步危险分层的工具和精准化干预的一级预防证据。我国因疑诊冠心病行冠状动脉CT血管成像（CCTA，为注射对比剂的CT扫描，能够观察钙化和非钙化斑块）的患者中，发现早期冠状动脉粥样硬化病变（有斑块，但管腔狭窄<50%）的患者约占23.1%，随访显示，其3年MACE事件(包括全因死亡、急性心肌梗死、冠状动脉血运重建)发生率约为3.7%。本项目入组中危患者，但冠状动脉存在粥样硬化斑块，狭窄率<50%的患者，随机分为强化降脂干预组及对照组，通过3年的主要不良心血管事件随访，旨在证明强化降脂是否可以降低中危早期冠状动脉粥样硬化病变患者主
要心血管不良事件的发生率，为中危早期冠状动脉粥样硬化病变患者的风险再分层及 I 级预防提供循证医学证据。

2. 为什么邀请您参加本项研究？

根据您提供的信息，我们依据 PCE 10 年主要不良心血管事件概率计算公式，您 10 年内发生事件的风险为 5% - 20%，为指南定义的中危（含临界）患者。且您的冠状动脉 CT 显示主干血管（直径 >2mm）冠状动脉存在非钙化斑块，且管腔狭窄率 < 50%，属于早期动脉粥样硬化病变。且您的年龄为 40-75 岁。上述 3 点符合该研究的入选标准。并且您不符合以下排除标准：(1) 患者合并其他严重心血管疾病，如心力衰竭、心律失常（持续性房扑/房颤、II 度或 III 度房室传导阻滞）、严重瓣膜病、先天性心脏病。 (2) 有急性冠状动脉综合征、心肌梗死或脑卒中病史的患者。(3) ALT、AST > 正常值高限 3 倍。(4) 无法解释的肌酸激酶>正常值高限 6 倍。(5) 肾病综合征患者。(6) 糖尿病患者及不可控制的高血压患者。(7) 不可控制的甲状腺功能减退。(8) 对他汀药物有过敏史者。(9) 拟进行手术的患者。(10) 影响药物吸收的胃肠道疾病或胃肠道手术病史。(11) 影响生存期的恶性肿瘤患者。(12) 长期免疫抑制剂治疗。(13) 酒精滥用史的患者。(14) 同时或 30 天内参加其他临床试验的患者。(15) 其他主管医师认为不适合参加该研究的患者。故邀请您参加本项研究。

3. 多少人将参与本项研究？

根据统计学样本量的计算，本研究预计招募 2900 例患者，分别在全国 11 家医院完成患者入组。本中心拟入选 1500 例患者。

4. 参加本项研究，需要您做什么？

您加入本研究按照中央随机分配进入强化干预组和对照组，分到两组的概率为 1:1。无论您被分配至哪组，您需要配合完成以下内容：

首先，我们需要您提供您的个人基本信息资料：包括您的年龄、身高、体重、家庭住址、联系方式等；冠心病危险因素信息：包括高血压、糖尿病、高血脂症、吸烟、家族史等；目前服药信息，生活方式，心理认知水平评估。
其次，在您服用药物后，我们会定期随访您的危险因素控制情况，不良生活方式改变情况，药物不良反应。由于我们需要严格监控您血脂水平，需要您配合在入组1个月、3个月、12个月、24个月、36个月分别进行血生化检查。

再者，您入选时已完成一次冠状动脉CT检查，为了观察3年后您冠状动脉斑块的变化，需要您在入组36个月时，再进行一次冠状动脉CT复查。另外，我们会在您入组6个月、18个月及36个月时，对您进行电话随访，询问是否出现主要不良心血管事件。

5. 本项研究会持续多久？

本研究预计3年，需要您参与3年的研究。

6. 参加本项研究的风险是什么？

（1）本项研究药物干预方案使用的药物均为临床常规用药（他汀、依折麦布），如果您被随机分配至对照组，医师给予您相应治疗，本研究不做额外干预，如果您被随机分配到强化干预组，将会给您他汀或者联合依折麦布等降脂药物以达标；研究过程中的血脂管理、血生化检查为临床常规操作，不会对您造成额外伤害；但强化治疗组可能增加药物用量，将严格按照药物说明书用药，风险可控。

（2）冠状动脉CTA复查对判定病变进展非常有价值，但增加碘过敏风险（严重过敏发生概率极低）。

（3）本研究涉及的电话随访，为常规的临床事件随访，不会对患者带来不适。

7. 参加本项研究的获益是什么？

（1）严格的医疗管理：我们会按照既定方案，对您的危险因素控制、生活方式改变及用药方案进行指导，有助于您疾病的控制。

（2）由于本研究项目有经费支持，我们可以免除您的冠状动脉CT复查费用，以及部分强化干预组患者的药物费用。

8. 参加该项研究的费用和补偿与赔偿

（1）费用：强化干预组患者降脂治疗过程中为达标额外增加的药物费用由课题组承担，冠状动脉CT复查费用由课题组承担。

（2）补偿：本课题不给予补偿。
(3) 赔偿：当患者因复查冠状动脉 CT 出现严重不良反应（死亡）时，将根据实际情况及我国法律规定予以赔偿。

9. 发生研究相关损害的处理？

本研究涉及的检查及药物均为临床常规诊疗；强化治疗组部分患者需要增加药物，产生药物不良事件的风险，严格按照药物产品说明书执行。

本研究进行冠状动脉 CT 的随访检查，有产生碘对比剂过敏的风险，但严重不良事件风险极低。如果发生严重不良事件，将及时上报并按临床常规治疗措施救治患者，费用由课题组承担。入组前患者签署 CT 检查的知情同意书。

10. 我的信息会保密吗？

是的，您的信息在研究中将严格保密。本研究中使用您的研究数据时，您的个人信息都是保密的，您的所有信息资料将得到妥善保存并仅供研究使用。

研究数据库中的信息会严格脱敏消除个人身份识别特征，可能识别您身份的信息将不会透露给研究人员以外任何人，除非获得您的许可。

在不违反保密原则和相关法规的情况下，伦理委员会、卫生健康主管部门的检查人员可以查阅受试者的原始医学记录，以核实临床研究的过程和数据。

如果您研究结果公开发表，您的个人信息不会出现在任何公开病历资料和出版物中，我们也不会向任何人、任何机构透露此信息。

11. 是否一定要参加并完成本项研究？

是否参加本项研究是自愿的，您可以自由决定参加或拒绝参加此项研究。无论您是否同意参与此项研究，均不会影响您在我院就诊期间所应享有的临床常规诊疗措施。如果您不参与本研究将按临床常规诊疗进行治疗。

如果您想参加此项研究，您需要认真阅读本知情同意书，确认充分了解相关问题后签署本知情同意书。您不会因为签署本文件而失去法律赋予您的任何合法权利。
如果您同意签署本文件，中国医学科学院阜外医院将无偿获得您的研究数据，本院研究者可出于本研究目的使用您匿名研究数据。

您可以在任何时间拒绝参加或有权在研究期间的任何阶段随时退出研究，而不需要任何理由，也不会受到歧视或者报复，相应的医疗待遇与权益均不受影响。

如果您参加过程中想退出研究项目，请通知研究人员，按研究人员要求完成退出前相关检查，并根据要求以书面形式完成有关退出手续；退出后研究人员将不再继续收集并使用您的研究数据，但在您退出前已匿名化采集的数据将无法删除或撤回。若您退出后，发现新的与您健康和权益相关的信息时，我们可能会再次与您联系。

12. 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数据资料。此外，我们还希望在研究结束后对您后续长期持续随访，了解您的健康状况。您的匿名研究数据、临床诊疗数据（包括但不限于病历、影像资料、临床检验与监测数据，包括外院检查数据等）及随访数据将继续用于后续经审批的心血管类疾病的遗传学与非遗传学研究。如果您不同意，在本项研究完成之后，您的研究数据及临床诊疗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形式退出研究。

13. 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研究的任何问题，并得到相应的解答，包括临床研究期间可能出现的任何不适，请联系研究人员，侯志辉，电话：15011451210，或郑嘉男18810682390。

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：010-88396281。

知情同意书_V5.0_2022.11.14
感谢您花时间阅读本知情同意书。如果您及您的家属通过充分考虑之后同意参加本临床研究，希望您及您的家属能按照研究人员的要求完成本次临床研究。参加本研究前，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的研究目的、内容、程序，研究可能的风险，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。

我同意参加本研究并授权你院采集我的研究数据用于本研究。

我承诺我提供我的信息是真实的；如提供了虚假信息，我承诺对其后果负责。

我确认我提供的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研究，并不影响我应该得到的医疗待遇与权益，也知道研究者可能会根据医生的意见与建议随时中止/终止我继续参加此项研究。

我将得到这份知情同意书的正本一份，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）捐赠临床诊疗、研究数据及长期随访数据用于未来研究，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的遗传学与非遗传学医学研究中使用并且处理我本人的数据。

患者姓名                签名：

电话：

（如受试者为无行为能力人或限制行为能力人时，需监护人签署）

监护人姓名                签名：

与受试者的关系                日期：
我确认，在知情同意书中的信息是被正确解释了的并且受试者和/或受试者合法代表明白理解了这些信息。受试者自愿同意参加本研究。

公正见证人签名【如适用】：

日期：

研究者

签名：

日期：