Rationale, design, and baseline characteristics of Chinese registry in early detection and risk stratification of coronary plaques (C-STRAT) study

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To the Editor: Coronary computed tomographic angiography (CCTA) has been considered as one of the most important noninvasive imaging modalities in diagnosing coronary artery disease (CAD).[1] Modern scanner of CCTA can provide precise coronary atherosclerotic plaque information, showing improved diagnostic accuracy and sensitivity for identifying obstructive CAD with a preferable temporal and spatial resolution. Several studies have demonstrated the prognosis value of CCTA for the prediction of future adverse CAD events.[2] However, these findings were mostly based on old scanner of CCTA and from developed countries. On the other hand, artificial intelligence (AI) and machine learning are poised to influence the diagnosis and treatment.[3] It definitely requires a huge dataset for cardiovascular imaging, especially CT imaging, to incorporate AI technology to further enhance the management of CAD.

C-STRAT (Chinese regiStry in early detecTion and Risk strAtificaTion of coronary plaques) study was registered in the Chinese clinical trial registry authority (registry number: ChiCTR1800015864) and approved by Ethical Committees of Chinese PLA General Hospital (No: S2018-033-01). This registry study includes four hospitals located in North China, four hospitals in East China, two hospitals in Central China, two hospitals in South China, and one hospital in West China. All participated sites are tertiary hospitals across the country. They have considerable medical diagnostic and therapeutic capability, updated hospital information system, and a large number of outpatients. Consecutive patients, who meet the inclusion criteria and plan to undergo CCTA by order of physicians, will be enrolled in this multisite registry study. Subjects were prospectively recruited from May 2017 to October 2019. Inclusion criteria were designed to capture at risk individuals with stable chest pain or chest pain equivalent syndromes, aged between 18 and 75 years, and who had no history of CAD. Exclusion criteria were designed to exclude any individual with unstable hemodynamics or requiring urgent evaluation for suspected acute coronary syndrome (ACS), with a history of CAD.

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All the subjects enrolled in C-STRAT study underwent CCTA examination according to the guidance of clinicians. Before examination, the patient's information was collected prospectively by investigators, including demographic data and medical history, and documented in the case report forms (CRFs). The project allows each site to supplement and collect additional content not limited to CRFs. An encrypted website platform (www.ct-registry.cn) was established in order to collect, manage, and monitor relative big data. The operation of this website was approved and authorized by the principal investigator and institutional review board.

CCTA was interpreted in accordance with SCCT (Society of Cardiovascular Computed Tomography) guideline.[4] A coronary artery tree model was used, which contains visual estimation of three major coronary arteries and branches. According to the 17 segments of the coronary tree proposed by the AHA (American Heart Association), all coronary arteries with diameter ≥2 mm were analyzed. Coronary artery disease-reporting and data system (CAD-RADS) was used to illuminate coronary artery stenosis. CAD-RADS 0 represents no coronary stenosis, CAD-RADS 5 represents totally occlusive lesions, and CAD-RADS 1–4 correspond to the degree of lumen stenosis of 1%–24% (minimal stenosis), 25%–49% (mild stenosis), 50%–69% (moderate stenosis), and 70%–99% (severe stenosis), respectively. The location, length, and feature of plaque lesions were also recorded. CAD-RADS 3–5 are considered as obstructive CAD. If the evaluated result was inconsistent by two interpreters, a discussion was necessary to reach an agreement.

Follow-up of enrolled subjects will be performed by dedicated physicians or research nurses. C-STRAT database was locked in December 2019 to identify the subjects for long-term follow-up. The follow-up interval is 24 to 36 months, and long-term (at least 2 years) follow-up will be carried out with an anticipated 5% lost and the follow-up data will be recorded. All included subjects are followed for a primary endpoint of major adverse cardiovascular event. Ascertainment of death and other ascertainments will be determined by direct interview or telephone contact with the patient's immediate family or review of medical records, while case records need to be photocopied for data retention. The primary objective of C-STRAT study aims to identify the association of CCTA image findings with long-term prognosis in a large Chinese population with suspected CAD and further improve risk stratification in combination with imaging indicators and clinical characteristics. The secondary objectives of the C-STRAT study will also include:

I. The current status of CCTA application in China.
II. The rate of invasive testing and utilization of other examination resources in downstream after undergoing CCTA examination.
III. The accuracy of the probability of CAD in Chinese population based on the pretest probability model established by European and American guideline.
IV. A rapid detection technology of plaque feature and lumen stenosis by using AI and machine learning technology.

A total of 30,039 subjects (55.3% male) were finally recruited in this study with an average age of 58.8 years. The prevalence of hypertension, hyperlipidemia, diabetes, stroke, peripheral vascular disease, and CAD family history is 43.4%, 32.5%, 15.4%, 4.5%, 5.8%, and 16.9%, respectively. There are 35.5% of subjects smoking currently and 40.8% of drinking alcohol. With regard to the proportion of examinational aims, 23.7% subjects underwent CCTA examination with typical chest pain and 34.5% with atypical chest pain overall. 41.8% of subjects are of non-chest pain symptom. The prevalence of obstructive CAD in different regions of China is shown in Figure 1. Subjects with obstructive CAD (CAD-RADS 3–5) account for 22.0% of the total, while the rate of nonobstructive CAD (CAD-RADS 0–2) is 76.6% overall. 36.4% of them are without any coronary artery stenosis. Notably, only 1.4% of subjects could not be diagnosed due to the poor uninterpretable CCTA image.

In view of a tremendous rise in CCTA examination numbers in China, it becomes an unmet need to handle the

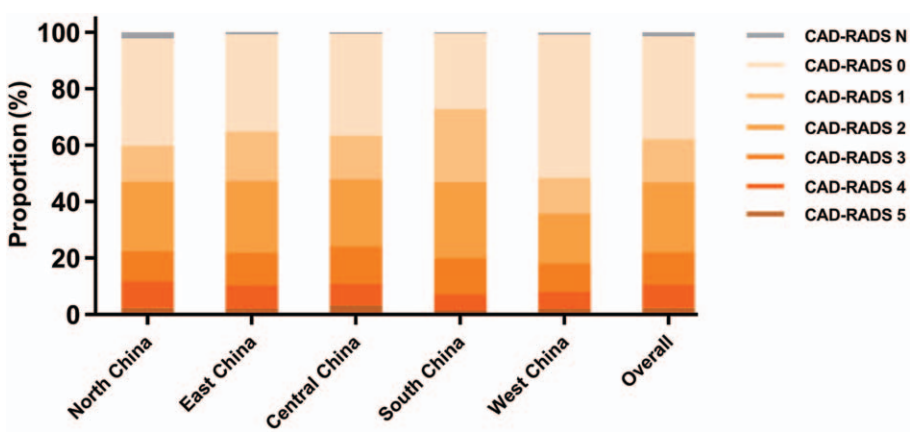

Figure 1: Distribution of CAD severities in C-STRAT study. CAD-RADS 0 represents no coronary stenosis. CAD-RADS 1–4 correspond to the degree of lumen stenosis of 1%–24% (minimal stenosis), 25%–49% (mild stenosis), 50%–69% (moderate stenosis), and 70%–99% (severe stenosis), respectively. CAD-RADS 5 represents totally occlusive lesions. CAD-RADS N represents undiagnosed due to the poor uninterpretable CCTA image. CAD-RADS: Coronary artery disease-reporting and data system.

increasing CCAT-derived information to better improve risk stratification and management based on a large prospective multisite patient cohort. Through the generalizability and reliability of its data collection, C-STRAT study will help to establish and validate new models to provide robust pretest prediction for stable chest pain patients and optimize decision-making of diagnosis and treatment for stable chest pain in clinical practice. CONFIRM study revealed that CCTA finding could add incremental value for prognosis beyond demographic and clinical characteristics. However, CONFIRM study was finished decades ago, and the imaging quality has been improved for quantitatively analysis by new generation CT scanner in recent year. In typicality of symptom, there were more asymptomatic patients (34.2%) in CONFIRM study than C-STRAT study (24.6%), suggesting that CCTA is less likely to be recommended for asymptomatic patients in clinical practice of China. In per patients CT findings, C-STRAT study was somewhat in line with CONFIRM study, illustrating the similar prevalence of CAD between China and its counterpart in decades ago. Another significant difference is the use of prospective gating, with mostly 100% in C-STRAT study and only 13% in CONFIRM study. Recently, China-PAR project (Prediction for arteriosclerotic cardiovascular disease [ASCVD] Risk in China) has developed and validated a 10-year risk prediction equation for ASCVD based on Chinese population.[5] On the other hand, it has been demonstrated that some CT imaging findings could add incremental prognosis value to traditional prediction models. Therefore, further investigation can be warranted to examine whether combining CT imaging findings with current China-PAR equations could have better performance in C-STRAT cohorts with certain durations of follow-up.

Recently, cardiovascular imaging is increasingly gaining interest of AI field, which may be particularly beneficial in optimized image acquisition, efficient image post-processing, accurate segmentation, and novel prognostic biomarkers exploration. C-STRAT study is also aiming to provide high-quality imaging and clinical relevant big data on this potential field, which can assist on modern technology to automatically identify and explore more plaque features, to illustrate more information for risk assessment, and to facilitate the detection of true "vulnerable patients."

In conclusion, C-STRAT registry is, to date, the largest prospective multisite observational study related to CCTA imaging in the world. The main purpose of C-STRAT study is to assist on exploring new early diagnostic technology and to find the associations between CT imaging findings and the clinical prognosis. This registry study is also expected to evaluate the current situation of noninvasive image utilization in China through the establishment of large-scale Chinese population cohort, providing new ideas and focus for the future randomized controlled study, and further optimize and improve the current risk stratification strategy in China.

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Conflicts of interest

None.

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