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ORIGINAL RESEARCH

Coronary Evaluation Before Heart Valvular Surgery by Using Coronary Computed Tomographic Angiography Versus Invasive Coronary Angiography

Xinshuang Ren, MD; Kun Liu, MD; Heng Zhang, MD; Ying Meng, MD; Haojie Li, MD; Xiaogang Sun, MD; Hansong Sun, MD; Yunhu Song, MD; Liqing Wang, MD; Wei Wang, MD; Chuangshi Wang, PhD; Yang Wang, PhD; Zhihui Hou, MD; Yang Gao, MD; Weihua Yin, MD; Zhe Zheng, MD; Bin Lu, MD

BACKGROUND: Coronary computed tomography angiography (CCTA) is a noninvasive, less expensive, low-radiation alternative to invasive coronary angiography (ICA). ICA is recommended for coronary evaluation before heart valvular surgery, and the supporting evidence for CCTA is insufficient. Our study is a single-center, prospective cohort study designed to evaluate the feasibility of CCTA instead of ICA in detection of coronary artery disease before surgery.

METHODS AND RESULTS: Heart valvular surgery candidates were consecutively enrolled between April 2017 and December 2018. Nine hundred fifty-eight patients in the CCTA group underwent CCTA primarily, and those with ≥50% coronary stenosis or uncertain diagnosis underwent subsequent ICA. One thousand five hundred twenty-five patients in the ICA group underwent ICA directly before surgery. Coronary artery bypass grafting decision was made by surgeons according to CCTA or ICA results. Most of the patients (78.8%) in the CCTA group avoided invasive angiography. Thirty-day mortality (0.7% versus 0.9%, P=0.821), myocardial infarction (6.4% versus 6.9%, P=0.680), and low cardiac output syndrome (4.2% versus 2.8%, P=0.085) were similar in the CCTA and ICA groups. Median duration of follow-up was 19.3 months (interquartile range, 14.2–30.0 months), cumulative rates of mortality (2.6% versus 2.6%, P=0.882) and major adverse cardiac events (9.6% versus 9.0%, P=0.607) showed no difference between the 2 groups. Coronary evaluation expense was lower in the CCTA group ($149.6 versus $636.0, P<0.001).

CONCLUSIONS: The strategy of using CCTA as a doorkeeper in coronary evaluation before heart valvular surgery showed noninferiority in identification of candidates for coronary artery bypass grafting and postoperative safety.

Key Words: computed tomography angiography ■ coronary artery disease ■ heart valvular surgery

Coronary artery disease (CAD) predicts worse clinical outcomes in patients who underwent heart valvular surgery.[1–4] Preoperative detection of CAD by invasive coronary angiography (ICA) is recommended in patients scheduled for valvular surgery with any of the following situations: male >40 years of age or postmenopausal woman, patients with symptoms of angina, objective evidence of ischemia, decreased left ventricular function, history of CAD, or coronary risk factors ≥1 according to current American Heart Association/American College of Cardiology guidelines.[5] Because the majority of patients undergoing surgery for valvular heart disease (VHD) are >50 years old, most patients are evaluated for CAD before surgery. However, a considerable proportion of patients recommended for ICA had low-to-intermediate probability of

Correspondence to: Bin Lu, MD, Department of Radiology, Fuwai Hospital, National Center for Cardiovascular Diseases, No. 167 Beilishi St, 100037 Beijing, China. E-mail: blu@vip.sina.com

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CLINICAL PERSPECTIVE

What Is New?

- This is the first large-scale cohort study evaluating the feasibility of using coronary computed tomography angiography (CCTA) instead of invasive coronary angiography as a coronary artery disease screening tool before heart valvular surgery worldwide.
- Nearly 80% of patients can avoid invasive coronary angiography by undergoing CCTA first. Safety of the CCTA protocol is confirmed according to long-term follow-up results.

What Are the Clinical Implications?

- The protocol of using CCTA first for coronary evaluation is sufficient in the majority of patients scheduled for valvular surgery.
- Coronary artery disease risk factors should be evaluated and plain computed tomography scan should be performed first.
- Patients with <4 coronary artery disease risk factors and calcium score <400 have a low-to-intermediate risk of coronary artery disease and benefit most from a CCTA strategy.

Nonstandard Abbreviations and Acronyms

ICA	invasive coronary angiography
VHD	valvular heart disease

CAD, and ICA results do not show significant CAD.[6–9] Although ICA is considered a safe procedure, it still carries a small risk of major (death, stroke, or vascular dissection) and minor (inguinal hematoma) complications.[10] Furthermore, the catheterization procedure is rather expensive, because its invasive nature involves admission to the hospital and requires surveillance by an experienced team.

Coronary computed tomography angiography (CCTA) as an alternative diagnostic procedure shows promising performance. Several studies had reported high negative predictive value (93%–100%) of CCTA in patients with VHD,[11–13] which confirmed that CCTA is a suitable noninvasive procedure to reliably rule out CAD before cardiac surgery. Furthermore, CCTA is a noninvasive procedure with low risk and cost, and it can be easily performed at the clinic for outpatients before hospital admission. Except for coronary evaluation, CCTA can also provide information about lung, mediastinum, and cardiac structure, which may help physicians make an early diagnosis and treatment. CCTA has been applied gradually in recent years for patients with VHD before surgery as a potential alternative to ICA.

The hypothesis of this study is that CCTA as a gatekeeper for CAD detection before heart valvular surgery is sufficient and safe. To our knowledge, this study is the first prospective trial to assess the feasibility and safety of CCTA in evaluating CAD before valvular surgery of the heart.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Population

There are 11 surgical wards in our institution and ICA was routinely used before heart valvular surgery previously. The strategy of using CCTA in preoperative coronary evaluation was approved in 4 surgical wards and ICA was preferred in the other 7 surgical wards after discussion with the surgical center. CCTA protocol was performed in all eligible patients in 4 surgical wards (CTA group), while ICA was routinely used for coronary evaluation in patients in the other 7 wards (ICA group). Heart valvular surgery candidates were prospectively and consecutively enrolled in our study between April 2017 and December 2018. Inclusion criteria were as follows: (1) Man ≥40 years old; postmenopausal woman; (2) Patient scheduled to undergo valvular replacement or repair; (3) Patient providing written informed consent. Exclusion criteria were as follows: (1) patient has definite CAD history (prior myocardial infarction, percutaneous coronary intervention, or coronary artery bypass grafting [CABG]); (2) patient has objective evidence of myocardial ischemia (typical angina with ST-T change simultaneously, positive result in exercise treadmill test, or perfusion defect in radionuclide myocardial perfusion imaging); (3) Patient has undergone CCTA or ICA within 6 months; (4) Patient has contraindications to CCTA/ICA (allergic history for iodine contrast medium, peripheral arterial occlusive disease, or chronic kidney disease with estimated glomerular filtration rate <15 mL/min per 1.73 m^2).

Study Protocol

Our study was a single-center, prospective cohort study (2016-zx-054) with ethical approval of Fuwai hospital and informed consent. Eligible patients enrolled in the ICA group underwent ICA before surgery to evaluate the coronary lesions, while patients in the CCTA group underwent CCTA primarily, and those with positive findings (≥50% diameter stenosis in main coronary arteries) or uncertain diagnosis caused by motion artifact or calcium blooming artifact underwent

subsequent ICA before surgery. Coronary evaluation reports were sent to surgeons, and they decided whether or not to perform CABG. Unplanned CABG was defined as CABG performed in patients without obstructive coronary stenosis (≥50%) diagnosed by CCTA or ICA.

CCTA Scan Protocol and Analysis

Dual-source computed tomographic scanner (SOMATOM Definition Flash, Siemens Healthcare, Forchheim, Germany) or 256-slice wide volume coverage CT scanner (Revolution CT; GE Healthcare, Milwaukee, WI) was used in the CCTA group. Acquisition parameters were 2×64×0.6 mm detector collimation and 280 ms gantry rotation time of the dual-source computed tomographic scanner and 256×0.625 mm collimation and 280 ms gantry rotation time of wide volume coverage CT scanner. All scans were acquired in a cranio-caudal direction in end-inspiration. Attenuation-based tube current modulation was applied per default. For contrast medium enhancement, automated bolus-tracking was used in a region-of-interest within the ascending aorta, with a signal attenuation trigger threshold of 100 Hounsfield units and a 6-second scan delay.

A triple phase contrast medium injection protocol was used in the study, which consisted of 50 to 60 mL of undiluted contrast agent (iopromide [Ultravist] 370 mg I/mL, Bayer Healthcare, Berlin, Germany) followed by a 30 mL 30%/70% mixture of contrast medium and a 40-mL saline chaser bolus at flow rates of 4 to 5 mL/s. All prospectively ECG-triggered scans were performed between 35% and 80% of the R-R interval. All images were reconstructed with the Iterative Reconstruction (ASiR or SaFire) technique.

Patients with an average heart rate >70 beats/min and no contraindication to β blockade received 25 mg of metoprolol before the examination. A wide volume coverage CT scanner was used in patients with uncontrolled heart rate. Prospective ECG triggering was performed, and coronary images in systolic and diastolic phases were acquired and analyzed on a dedicated workstation (Advantage Workstation VolumeShare 4.6, GE Healthcare). CT interpretation conformed to Society of Cardiovascular Computed Tomography guidelines.[14] Coronary artery calcium score was quantified with the Agatston score. Each lesion was identified as the hyper-attenuating region exceeding the CT density of 130 Hounsfield units. The coronary artery calcium score was calculated by multiplying the detectable calcification lesion with a 1 to 4 rating dictated by the maximum CT density within that region (130–199, 200–299, 300–399, and >399 Hounsfield units). The total coronary artery calcium score was then calculated by summing up the coronary artery calcium score from all lesions. The Society of Cardiovascular Computed Tomography 18-segment coronary model was used to describe stenosis of the coronary artery. The degree of coronary stenosis was judged as normal (0%), minimal (1%–24% diameter stenosis), mild (25%–49%), moderate (50%–69%), and severe (≥70%), in accordance with Society of Cardiovascular Computed Tomography guidelines.[15] All CCTA examinations were interpreted by 2 readers (radiologists B. L., Y. G.); if the diagnosis was inconsistent, the 2 readers had a discussion and made a final decision.

ICA Protocol and Analysis

ICA was performed by certified interventional cardiologists following usual clinical indications and imaging standards set forth by the American College of Cardiology Foundation/Society Consensus on cardiac catheterization.[16] ICA images were transmitted to and read by independent blinded readers (cardiologists). If the diagnosis was inconsistent, discussion between the 2 readers was held and a final decision was made. Similar to CT images, an 18-segmental model was used for the coronary evaluation.

Procedural Complications and Radiation Exposure Collection

Procedural complications including allergic reaction, vascular complications (leakage of contrast medium at puncture site, hemorrhage, or thromboembolism), acute myocardial infarction, arrhythmia (onset atrioventricular block, atrial or ventricular flutter and fibrillation) and vasovagal reaction (defined as a reflex of the involuntary nervous system that causes the heart to slow down and blood pressure to drop) were evaluated and recorded.

The dose length product, defined as total radiation energy absorbed by the patient's body, were measured in milliGray (mGy)×cm in patients in whom CCTA was performed. The effective radiation dose was calculated as dose length product times a conversion coefficient for the chest (κ=0.014 mSv/mGy×cm).[17] For ICA, the effective radiation dose was calculated by multiplying the dose area product by a conversion factor (κ=0.21 mSv/mGy×cm^2) for postero-anterior and lateral radiation exposure in the chest area.[17]

Outcomes and Follow-Up

Cardiovascular complications[18] within 30 days after surgery were set as the early outcomes to evaluate perioperative safety of using CCTA for screening CAD before heart valvular surgery. The composite early outcomes included all-cause mortality, myocardial infarction,[19] postoperative low cardiac output syndrome defined as hemodynamic collapse with systolic

pressure <90 mm Hg requiring continuous application of vasoactive agent (dopamine, noradrenaline) ≥7 days or mechanical support (extracorporeal life support, intra-aortic balloon pump, or extracorporeal membrane oxygenation) and acute kidney injury.[20] Patients were followed up postoperatively with clinical reviews, CTA imaging, or ultrasound at 6 months, 12 months, and annually thereafter. All-cause mortality and major adverse cardiac events including all-cause mortality, myocardial infarction, and coronary revascularization were recorded.

Length of postoperative hospital stay, total hospitalization expense (including clinical test, drugs, iatric consumptive material, surgery expense), and coronary evaluation procedure expense were also recorded.

Statistical Analysis

Continuous variables were expressed as mean value±SD or medians with quartiles after the assessment of a normal distribution. Categorical variables were presented as frequencies or percentages. The assumption of normality for continuous variables was assessed with the Shapiro–Wilk test. Based on the test result for each variable, independent *t* test or Mann–Whitney *U* test was used for comparison. Chi-square test or Fisher exact test was used to compare categorical variables in 2 groups. Kaplan–Meier graphs were used to analyze time-related events, and log-rank tests were used to compare intergroup differences in such event rates. A 2-tailed $P<0.05$ was considered statistically significant. Data analysis was performed using SPSS version 16.0 (SPSS Inc., Chicago, IL).

RESULTS

Study Population

A total of 2626 patients were enrolled and 143 patients were excluded by CAD history (n=74), objective evidence of myocardial ischemia (n=31), underwent CCTA or ICA within 6 months (n=28), with contraindications to CCTA/ICA (n=10). Two thousand four hundred eighty-three patients were finally included, with 958 patients in the CCTA group and 1525 patients in the ICA group.

Baseline Clinical Characteristics in the CCTA and ICA Group

Baseline clinical characteristics in the 2 groups are shown in Table 1. The value of age, sex distribution, body mass index, left ventricle ejection fraction, incidence rate of CAD risk factors, and STS score showed no significant differences between the 2 groups. Rheumatic heart disease and degenerative valvular disease were the main cause diagnosed in 40.1% and 45.7% of patients, respectively. Mitral valve replacement and aortic valve replacement were the main valve procedures, accounting for 41.1% and 28.5%. The distribution of valvular disease and surgery

Table 1. Basic Clinical Characteristics of Patients in 2 Groups

	CCTA Group (n=958)	ICA Group (n=1525)	*P* Value
Age (y)	58.9±8.2	59.4±7.8	0.073
Male patients (%)	517 (54.0%)	813 (53.3%)	0.772
BMI, kg/m^2	24.4±3.4	24.5±3.3	0.873
Smoking (%)	296 (30.9%)	526 (34.5%)	0.066
CVD family history (%)	41 (4.3%)	55 (3.6%)	0.395
Hypertension (%)	367 (38.3%)	622 (40.8%)	0.222
Diabetes mellitus (%)	76 (7.9%)	124 (8.1%)	0.880
Hyperlipidemia (%)	346 (36.1%)	576 (37.8%)	0.418
Heart failure (III/IV) (%)	456 (47.6%)	754 (49.4%)	0.199
Atrial fibrillation (%)	405 (42.3%)	613 (40.2%)	0.315
Stroke (%)	80 (8.4%)	136 (8.9%)	0.661
Peripheral artery disease (%)	13 (1.4%)	19 (1.2%)	0.856
COPD (%)	20 (2.0%)	36 (2.4%)	0.680
Chronic kidney disease (stage ≥3) (%)	68 (7.1%)	119 (7.8%)	0.533
LVEF (%)	58.3±11.6	59.5±12.1	0.104
STS score (%)	4.6±1.2	4.4±0.8	0.552
Degenerative valvular disease (%)	435 (45.4%)	700 (45.9%)	0.849
Rheumatic valvular disease (%)	382 (39.9%)	613 (40.2%)	0.885
Congenital valvular disease (%)	94 (9.8%)	127 (8.3%)	0.133
Infective endocarditis (%)	11 (1.1%)	21 (1.4%)	0.860
Secondary valvular disease (%)	36 (3.8%)	64 (4.2%)	0.794
Valve surgery			
AVR (%)	293 (30.6%)	415 (27.2%)	0.075
MVR (%)	391 (40.8%)	629 (41.2%)	0.834
AVR+MVR (%)	132 (13.8%)	255 (16.7%)	0.053
MVP (%)	111 (11.6%)	182 (11.9%)	0.848
AVR+MVP (%)	12 (1.3%)	22 (1.4%)	0.727
TVP (%)	19 (2.0%)	22 (1.4%)	0.333
Concomitant surgery			
Aorta replacement (%)	60 (6.3%)	108 (7.1%)	0.461
CABG (%)	152 (15.9%)	273 (17.9%)	0.208

AVR indicates aortic valve replacement; BMI, body mass index; CABG, coronary artery bypass grafting; CCTA, coronary computed tomography angiography; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; ICA, invasive coronary angiography; LVEF, left ventricular ejection fraction; MVP, mitral valvuloplasty; MVR, mitral valve replacement; STS, the Society of Thoracic Surgeons; and TVP, tricuspid valvuloplasty.

types showed no significant difference between the 2 groups.

Clinical Pathway in CCTA and ICA Groups

All of the patients underwent coronary evaluation before surgery. Seven hundred fifty-five (78.8%) patients in the CCTA group avoided subsequent invasive angiography, while 203 (21.2%) patients underwent subsequent ICA as follows: 178 (18.6%) patients diagnosed with moderate or severe coronary stenosis and 25 (2.6%) patients with uncertain diagnosis (motion artifact: n=9; calcification artifact: n=16). Among the 9 patients with motion artifact, 6 patients had atrial fibrillation. One hundred forty-one patients were finally diagnosed with ≥50% stenosis by ICA. Concomitant CABG surgery was performed in 152 patients (15.9%) including 18 unplanned CABG because of intraoperative coronary complications despite negative results by CCTA (n=16) or ICA (n=2). Furthermore, 1 patient was found to have lung cancer incidentally by CT examination. In the ICA group, 266 patients (17.4%) were diagnosed with ≥50% stenosis and 273 patients (17.9%) underwent CABG including 34 unplanned CABG. The pathway of the CCTA group and the ICA group is shown in Figure 1.

Unplanned CABG was performed because of difficulty in cardiac repulse (n=29) or visible regional wall motion abnormality (n=23) appeared during the surgery. All the CCTA and ICA images of patients with unplanned CABG were re-evaluated. Two patients in the CCTA group were misdiagnosed with severe stenosis in the left circumflex artery and posterior descending artery, respectively, and 1 patient underwent CABG because of myocardial bridge at the left anterior descending artery mentioned in the CCTA report. The other 15 patients in the CCTA group were diagnosed with no stenosis (n=4), mild stenosis in the anterior descending artery (n=8) and right coronary artery (n=3) respectively. Three patients in the ICA group were diagnosed with no stenosis and 31 patients were diagnosed with mild stenosis in the anterior descending artery (n=25), circumflex artery (n=4), and right coronary artery (n=6). The clinical characteristics of patients with unplanned CABG (n=49) are shown in Table S1.

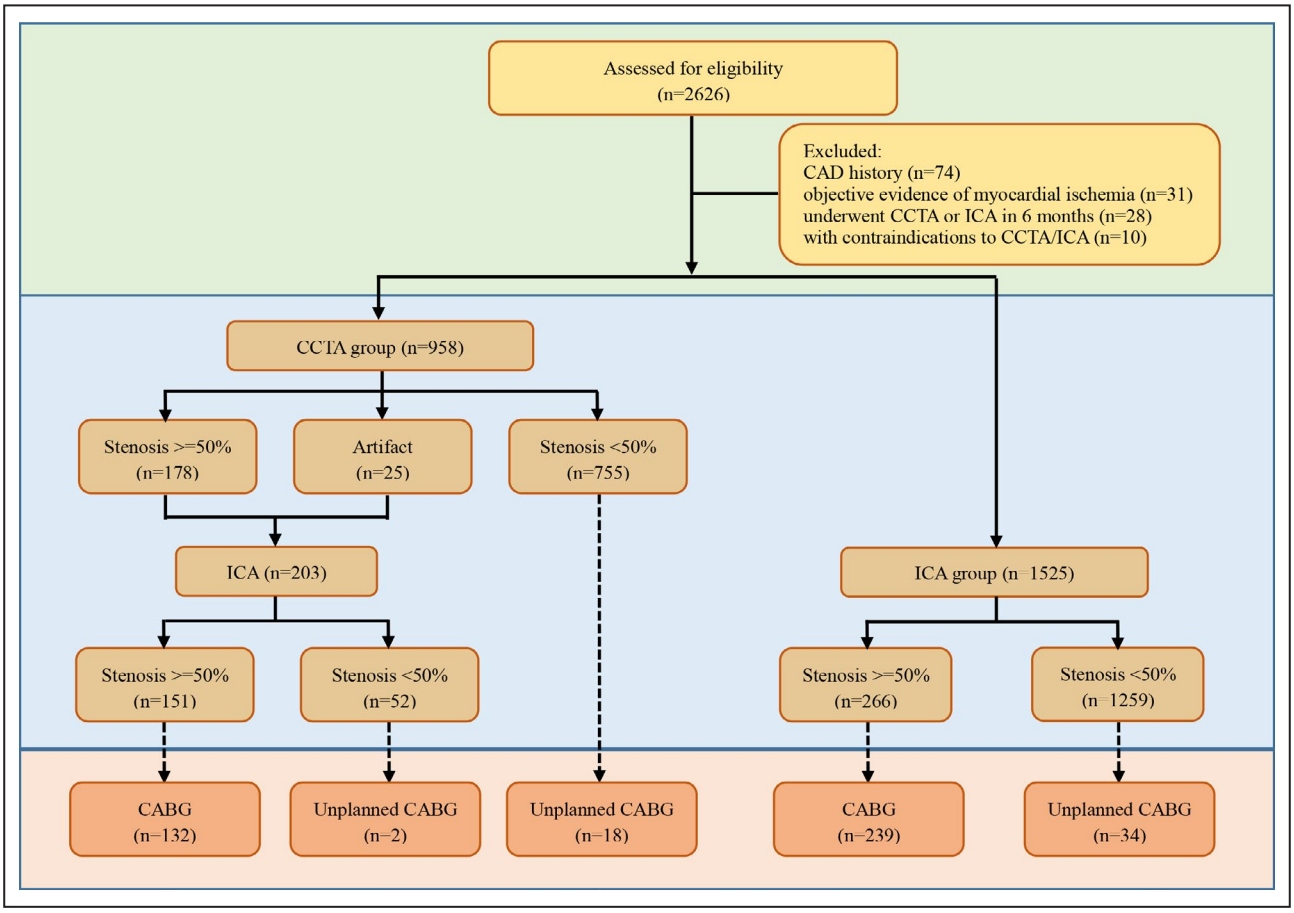

Figure 1. Clinical flow diagram of patients who underwent CCTA (n=958) and ICA (n=1525) initially for coronary evaluation. CABG indicates coronary artery bypass grafting; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; and ICA, invasive coronary angiography.

Clinical Characteristics and CT Results in Patients in the CCTA Group

Patients in the CCTA group were classified into 5 groups according to numbers of CAD risk factors including man ≥50 years old or woman ≥55 years old; male patient; smoking; hypertension; diabetes mellitus; hyperlipidemia; and CAD family history. CAD was diagnosed in 4.8% patients with 0 to 1 risk factors, and ICA was avoided in 91.2% of patients. Incidence of CAD increased with added risk factors; CAD was found in 11.9%, 17.4%, 22.1%, and 34.8% patients with 2, 3, 4, and >4 risk factors, and 81.5%, 75.7%, 69.3%, and 56.1% patients avoided subsequent ICA, respectively, in each group. Details are shown in Figure 2.

Patients who underwent subsequent ICA were older (62.4±9.0 versus 57.9±7.4, *P*=0.001), had a higher male proportion (63.5% versus 51.4%, *P*=0.003) and higher incidence of smoking (38.9% versus 28.7%, *P*=0.006), hypertension (54.2% versus 34.0%, *P*<0.001), diabetes mellitus (15.3% versus 6.0%, *P*<0.001), hyperlipidemia (45.3% versus 33.6%, *P*=0.002), and atrial fibrillation (52.7% versus 39.5%, *P*=0.001) than those who underwent CCTA only. The distribution of the calcium score differed significantly between the patients who underwent CCTA only and those who underwent subsequent ICA. ICA was avoided in 87.2% patients with calcium score of zero, while the proportion decreased to 75.4%, 48.8%, and 25.0%, respectively, in patients with a calcium score of 1 to 100, 100 to 400, and >400. The details are shown in Table 2.

Procedural Complications and Radiation Exposure

Two hundred fifty-nine patients in the ICA group underwent coronary angiography from a femoral approach (17.0%) and 1266 patients from a radial approach (83.0%). Seven patients from the femoral approach experienced vascular complications: 4 patients with hematoma at puncture site, and 3 patients with femoral artery thrombosis including 1 patient who underwent femoral artery thrombectomy. Six patients from the radial approach experienced hematoma at the puncture site. Four patients in the CCTA group experienced leakage of contrast medium at the puncture site. Even though there was no significant difference in the incidence of vascular complications between the ICA group and the CCTA group (0.9% versus 0.4%, *P*=0.224), symptoms and treatments in patients who underwent ICA from femoral approach were severe and complex. No significant difference was found in the rate of mild allergic reaction or side effects (nausea, vomiting, headache, hot, and skin rash) between the CCTA group and the ICA group (0.8% versus 0.6%, *P*=0.466). No severe allergic reaction happened in any of the patients. Cumulative radiation exposure showed no statistical difference between the ICA group and the CCTA group (5.3±2.4 mSv versus 5.7±3.0 mSv, *P*=0.142).

Follow-Up Evaluation

There were no significant differences in the rate of 30-day mortality (0.7% versus 0.9%, *P*=0.821), 30-day myocardial infarction (6.4% versus 6.9%; *P*=0.680), low cardiac output syndrome (4.0% versus 2.8%, *P*=0.085), and acute kidney injury (4.0% versus 3.8%; *P*=0.882) between the 2 groups. Details of 30-day outcomes are shown in Table 3.

The final confirmation rates of significant (≥50%) coronary stenosis showed no difference between the CCTA group and the ICA group (15.8% versus 17.4%, *P*=0.295). Patients with degenerative valvular disease had a higher rate of CAD than those with rheumatic valvular disease in CCTA (20.2% versus 11.0%, *P*<0.001) and ICA (23.6% versus 10.3%, *P*<0.001) group. Concomitant CABG was performed in 425 patients, and no significant difference was shown between the CCTA and ICA groups (15.9% versus 17.9%, *P*=0.208).

Twelve-month follow-up was completed in 2044 patients (82.3%). The median duration was 19.3 months (interquartile range, 14.2–30.0 months). During follow-up, 64 deaths occurred with no significant difference between the 2 groups. Two hundred twenty-nine cases of major adverse cardiac events including 64 deaths, 13 cases of coronary revascularization, and 152 myocardial infarctions mostly occurred within 30 days after surgery and no significant difference was shown between the 2 groups. Details are shown in Figure 3.

Postoperative hospital stay (7.6±2.1 days versus 8.0±2.5 days, *P*=0.490) showed no difference in the 2 groups. Total in-hospital cost ($18 768±7680 versus $19 481±7074, *P*=0.071) showed no significant difference between the 2 groups, while the coronary evaluation procedure expense was significantly lower in the CCTA group ($149.6 versus $636.0, *P*<0.001).

DISCUSSION

This is the first large-scale cohort study evaluating the feasibility of using CCTA instead of ICA as a CAD screening tool before heart valvular surgery worldwide. The capacity for identification of candidates for CABG by using CCTA was verified because confirmation rates of significant (≥50%) coronary stenosis and incidence of CABG in the 2 groups showed no significant difference. Furthermore, safety of the new pathway strategy was confirmed because no significant difference was found in the rate of 30-day events and long-term mortality and major adverse cardiac events.

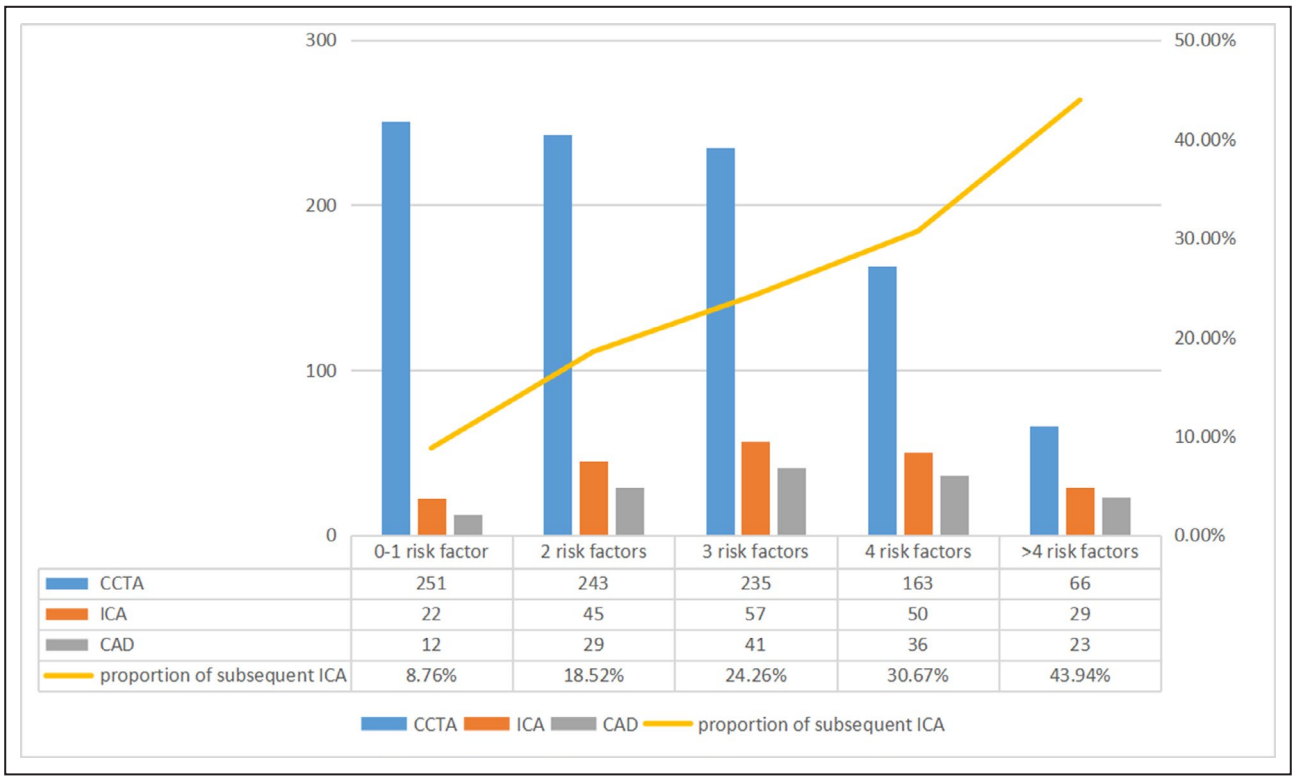

Figure 2. Proportion of subsequent ICA in patients with different number of CAD risk factors in the CCTA group.
CAD indicates coronary artery disease; CCTA, coronary computed tomography angiography; and ICA, invasive coronary angiography.

Coronary angiography is routinely used before heart valvular surgery, while the positive rate of coronary stenosis is low in the population recommended for this procedure. Prior study showed the positive CAD rate was only 5% to 10% in patients with rheumatic heart disease, which was the most common cause of valvular damage in China.[6,21] While the incidence of degenerative valvular disease increased as a result of the enlarged aging population, the prevalence of CAD increased in patients with VHD. Degenerative process and rheumatic heart disease were both main causes of valvular damage in our study, and the CAD rate was only 16.8%. The current guideline suggests that CCTA can be an option to exclude CAD in patients considered at low or intermediate pretest risk of CAD, but the score system frequently used to estimate probability

Table 2. Clinical Characteristic and Calcium Score in CCTA Group (CCTA-Only Versus CCTA and ICA)

	CCTA Only (n=755)	CCTA+ICA (n=203)	*P* Value
Age, y	57.9±7.4	62.4±9.0	0.001
Male patients (%)	388 (51.4%)	129 (63.5%)	0.003
BMI, kg/m^2	24.4±3.0	24.7±3.5	0.655
Smoking (%)	217 (28.7%)	79 (38.9%)	0.006
CVD family history (%)	30 (4.0%)	11 (5.4%)	0.433
Hypertension (%)	257 (34.0%)	110 (54.2%)	<0.001
Diabetes mellitus (%)	45 (6.0%)	31 (15.3%)	<0.001
Hyperlipidemia (%)	254 (33.6%)	92 (45.3%)	0.002
Atrial fibrillation (%)	298 (39.5%)	107 (52.7%)	0.001
Calcium score of 0 (%)	609 (80.7%)	89 (43.8%)	<0.001
Calcium score of 1–100 (%)	92 (12.2%)	30 (14.7%)	0.343
Calcium score of 101–400 (%)	40 (5.3%)	42 (20.7%)	<0.001
Calcium score>400 (%)	14 (1.9%)	42 (20.7%)	<0.001

BMI indicates body mass index; CCTA, coronary computed tomography angiography; CVD, cardiovascular disease; and ICA, invasive coronary angiography.

Table 3. Procedural Complications and Follow-Ups of Cardiovascular Events

	CCTA Group (n=958)	ICA Group (n=1525)	*P* Value
Procedural complications			
Vascular complications (%)	4 (0.4%)	13 (0.9%)	0.224
Mild allergic reaction (%)	8 (0.8%)	9 (0.6%)	0.562
Procedural radiation dose (mSv)	5.7±3.0	5.3±2.4	0.142
Early follow-up (30 d)			
Mortality (%)	7 (0.7%)	13 (0.9%)	0.821
MI (%)	61 (6.4%)	105 (6.9%)	0.680
MI in patients underwent CABG (%)	13/152 (8.6%)	22/273 (8.1%)	0.856
AKI (%)	38 (4.0%)	58 (3.8%)	0.882
LCOS (%)	40 (4.2%)	43 (2.8%)	0.085
Late follow-up			
Cumulative mortality (%)	25 (2.6%)	39 (2.6%)	0.882
Cumulative MACE (%)	92 (9.6%)	137 (9.0%)	0.607

AKI indicates acute kidney injury; CABG, coronary artery bypass graft; CCTA, coronary computed tomography angiography; ICA, invasive coronary angiography; LCOS, low cardiac output syndrome; MACE, major adverse cardiovascular events; and MI, myocardial infarction.

of CAD,[22–24] such as the Diamond–Forrester model and Duke Clinical Score, focus on patients with angina, which is a poor predictor of obstructive CAD in patients with valvular disease.[25] Studies investigating the CAD risk score model in VHD were rare and some studies only focused on a single valvular disease or rheumatic valvular disease. Hasselbalch et al[26] investigated a risk score (CT-valve score) to identify CAD in patients with VHD through a cohort of 2221 patients. Seven points was a reasonable cutoff to achieve a goal of less than one quarter of patients re-evaluated with ICA after CCTA. Numbers of CAD risk factors were used to evaluate the probability of CAD in our study. Some patients (11.2%) with <4 risk factors were diagnosed with CAD, and nearly 75% of patients can avoid ICA by using CCTA primarily. The results confirmed a simple way of selecting patients who can benefit from the CCTA strategy. Coronary calcium score should also be considered because 75% of patients with calcium score >400 underwent subsequent ICA. Plain CT scan should be suggested, and patients with calcium score >400 underwent ICA immediately. Patients who underwent subsequent ICA following CCTA experienced an increased radiation dose and elevated risk of acute kidney injury. Though these patients represent a small percentage of the population, it would be helpful if we could distinguish them before the examination. Discovering the target population who could benefit from our new evaluation protocol is what we will investigate in the future.

Nearly 80% of patients avoided ICA evaluation by coronary screening with CCTA in this study. The patients (78.2%) who underwent subsequent ICA were finally diagnosed with CAD. Since the rate of unplanned CABG in the CCTA group may raise questions about the accuracy of CCTA, we re-evaluated

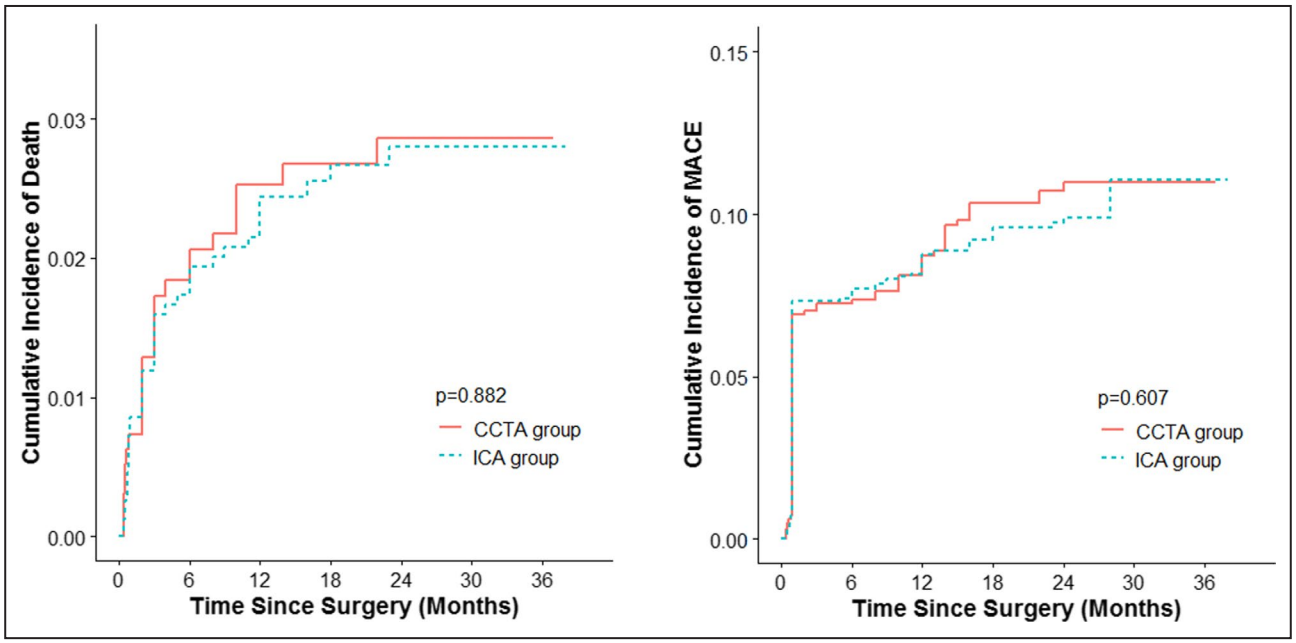

Figure 3. Kaplan–Meier graphs for cumulative incidences of death (left) and MACE (right) in the cohort.
CCTA indicates coronary computed tomography angiography; ICA, invasive coronary angiography; and MACE, mortality and major adverse cardiac events.

the images and found that the stenosis in the left circumflex branch and posterior descending artery in 2 patients were underestimated, while the residual coronary re-evaluation results were consistent with previous reports. Unplanned CABG was performed because of difficulty in cardiac repulse or visible regional wall motion abnormality appeared during the surgery. Patients with unplanned CABG were aging men; thus cardiac insufficiency could be the cause of unplanned CABG because severe heart failure was found in 65.3% of patients and mild coronary stenosis can lead to ischemia because myocardial microcirculation was dysfunctional in these patients. CCTA has been widely used in CAD detection and shows excellent diagnostic accuracy, especially its high negative predictive value. Sixty-four-row CT had been confirmed with a sensitivity of 85%, and a specificity of 90% 10 years earlier.[27] A recent meta-analysis showed patient-level CCTA sensitivity of 0.99 and specificity of 0.88 in 1375 patients.[28] CCTA has been suggested to exclude CAD in patients with low or intermediate pretest risk of CAD, but the level of supporting evidence was fairly low. Several studies evaluated the value of CCTA in ruling out significant CAD and suggested it as an alternative to ICA before surgery, but they only focused on the diagnostic accuracy of CCTA, and rare studies evaluated whether CCTA could replace ICA as a doorkeeper for coronary evaluation before heart valvular surgery by comparing clinical outcomes in a large-size cohort. An observational study in Korea[29] investigated CCTA as a screening tool before valvular heart surgery because CT was routinely used in their institute. Although participants in that study did not undergo the pathway as strictly as our study did, the result proved the safety of using CCTA for coronary evaluation before heart valvular surgery.

Even though no significant difference was found in the incidence of vascular complications between the ICA group and the CCTA group, patients in the ICA group, especially those selecting the femoral approach, had severe vascular complications such as femoral artery thrombosis, and 1 patient underwent artery thrombectomy. Prior studies showed that ICA was associated with a 2% to 6% vascular complication rate historically, since higher morbidity and mortality was associated with bleeding complications and blood transfusions.[30] The radiation dose showed no significant difference between the 2 groups in this study. Radiation dose of CCTA has been declining in the past decades because of a combination of improvements in data acquisition protocols and patient preparation. Several studies showed the radiation dose of CCTA was only 1 to 3 mSv in patients with controlled heart rate and 2 to 5 mSv in patients with atrial fibrillation.[31,32] Radiation dose in the CCTA group was higher than that reported by prior studies because 203 patients (21.2%) underwent subsequent ICA and the average radiation dose in these patients was 6.3 to 17.5 mSv.

All the patients in our study underwent coronary evaluation during hospitalization. Coronary evaluation cost decreased by $486.4 in the CCTA group compared with that in the ICA group, mainly because of the large cost difference between CCTA and ICA examinations in China. The cost of an ICA was at least double the cost of a CCTA in most countries, with the highest price difference in the United Kingdom,[33] where the cost of an ICA amounted to around 6 times the cost of a CCTA. The strategy of using CCTA first would be cost-effective in most countries.

Study Limitations

This study has limitations. Our study is a prospective cohort study. Randomization has not been performed because of management difficulties and staff shortages, because we have 11 surgical wards and more than 30 surgical teams. The CCTA strategy was decided on in 4 wards and ICA was in 7 wards after discussion with the surgical center. In order to reduce selection bias, the number of heart operations, operation success rates, and in-hospital mortality rates in different wards was compared and the results showed no obvious difference. In addition, the sample size was sufficient and no significant differences were found in basic clinical data between the 2 groups, thus verifying comparability of the data.

CONCLUSIONS

The strategy of using CCTA first in coronary evaluation before heart valvular surgery shows good performance in identification of candidates for CABG and postoperative safety. Patients with <4 CAD risk factors and calcium score <400 have low-to-intermediate risk of CAD and benefit most from the CCTA strategy.

ARTICLE INFORMATION

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Affiliations

Department of Radiology, Fuwai Hospital, National Center for Cardiovascular Diseases (X.R., K.L., Z.H., Y.G., W.Y., B.L.), Department of Surgery, Fuwai Hospital, National Center for Cardiovascular Diseases (H.Z., Y.M., H.L., X.S., H.S., Y.S., L.W., W.W., Z.Z.) and Medical Research and Biometrics Center (C.W., Y.W.), State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China.

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Disclosures

None.

Supplementary Material

Table S1

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SUPPLEMENTAL MATERIAL

Table S1. Clinical characteristics in patients with unplanned CABG.

n=49	
Age (years old)	62.7±7.3
Male patients (%)	29(59.2%)
BMI (kg/m2)	23.7±3.2
Smoking (%)	30(61.2%)
CVD family history (%)	1(2.0%)
Hypertension (%)	20(40.8%)
Diabetes Mellitus (%)	3(6.1%)
Hyperlipidemia (%)	17(34.7%)
Heart failure (III/IV) (%)	32(65.3%)
LVEF (%)	53.5±8.6
Valve surgery	
AVR (%)	17(34.7%)
MVR (%)	17(34.7%)
AVR + MVR (%)	9(18.4%)
MVP (%)	3(6.1%)
AVR + MVP (%)	2(4.1%)
TVP (%)	1(2.0%)
Coronary artery lesions	
LAD	33(67.3%)
LCX	4(8.2%)
RCA	9(18.4%)

BMI, body mass index; CVD, cardiovascular disease;AVR, aortic valve replacement; MVR, mitral valve replacement; MVP, mitral valvuloplasty; TVP, tricuspid valvuloplasty; LAD, left anterior descending artery; LCX,left circumflex artery; RCA, right coronary artery.