Original Article

Coronary computed tomography angiography for risk stratification before noncardiac surgery

Ahmed Fathala
Cardiovascular Imaging and Nuclear Medicine, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia

ABSTRACT

Background: Currently, there are limited available data for coronary computed tomography angiography (CCTA) in the setting of the risk stratification before noncardiac surgery. The main purpose of this study is to investigate the role of CCTA in cardiac risk stratification before noncardiac surgery. **Materials and Methods:** Ninety-three patients underwent CCTA in the assessment of cardiac risk before noncardiac surgery. Patients with normal or mildly abnormal CCTA (<50% stenosis) underwent surgery without any further testing (Group 1). Patients with abnormal CCTA (17 patients) (more than 50% stenosis) and nondiagnostic CCTA (5%) underwent either stress myocardial perfusion scintigraphy or conventional coronary angiography, Group 2. **Results:** Group one consists of 71 patients who went for surgery without any further testing. 59 of 71 (83%) patients had no complications in the postoperative period, 9 patients had noncardiac complications, 1 had a cardiac complication (new onset atrial fibrillation), and 2 patients died in the postoperative period due to noncardiac complications. Group 2 comprises 22 (26%) patients, 16 patients had no postoperative complications, 5 patients had noncardiac complications, and one patient developed postoperative acute heart failure. **Conclusions:** CCTA is diagnostic in up to 95% in the preoperative setting, and it provides a comprehensive cardiac examination in the risk stratification before intermediate and high-risk noncardiac surgery. Therefore, CCTA may be considered as an alternative test for already established imaging techniques for preoperative cardiac risk stratification before noncardiac surgery.

Key words: Coronary computed tomography angiography; Postoperative complication; Preoperative risk stratification

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INTRODUCTION

Preoperative assessment before noncardiac surgery is common in the clinical practice of the medical consultant, anesthesiologist, and surgeon. Most noncardiac surgeries are performed for patients with advanced age with a high prevalence of cardiovascular disease particularly coronary artery disease (CAD); CAD is the primary cause of perioperative mortality and morbidity associated with noncardiac surgery.[1] In the evaluation of cardiac risk for noncardiac surgery, it is clear that CAD risk factors, noninvasive cardiac imaging, and invasive coronary angiography (ICA) can all provide useful information in the appropriate patient subgroup.[2] In most noncardiac surgery, the test of choice is exercise electrocardiogram (ECG). However, if patients are unable to perform adequate exercise pharmacological stress with adenosine, dipyridamole, or dobutamine stress myocardial perfusion scintigraphy (MPS) with single photon computed tomography (SPECT) or dobutamine echocardiography (DE) are

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Address for correspondence: Dr. Ahmed Fathala, King Faisal Specialist Hospital and Research Center, Medical Imaging Service, P.O. Box: 3354, Riyadh, Saudi Arabia. E-mail: ahm35799@hotmail.com

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recommended.[3,4] Both stress MPS and DE have several limitations such as limited availability, limited expertise, nondiagnostic or nonconclusive results, ionizing radiation exposure (only stress MPS), and cost.

Coronary computed tomography angiography (CCTA) with multidetector computed tomography has demonstrated the excellent accuracy of coronary artery stenosis. In addition, it provides early detection of coronary atherosclerosis, assessment of cardiac and great vessels morphology, and accurate assessment of left and right ventricular function.[5-7] Currently, there are several clinical indications of CCTA.[8] One potential application of CCTA may be a preoperative evaluation before noncardiac surgery. Few small studies showed the high diagnostic accuracy of CCTA in cardiac patients who referred for cardiac surgery.[9-14] CCTA has a very high negative predictive value that associated with very low posttest probability of CAD. CCTA is classified as uncertain indication before noncardiac surgery in a certain population based on the most recent appropriateness use criteria.[15] Currently, there are few data available investigating the role of CCTA in the setting of risk stratification before noncardiac surgery. Subsequently, the main purpose of the study is to investigate the role of CCTA in risk stratification before noncardiac surgery.

MATERIALS AND METHODS

Patients

Ninety-three patients (48 men; mean age 60 ± 9 years) were referred for CCTA for preoperative risk stratification before noncardiac surgery between January 2011 and December 2014. Patients classified as candidates for further noninvasive cardiac testing based on CAD risk factors, type of surgery (intermediate or high-risk surgery), exercise capacity, abnormal Electrocardiography (ECG), or nondiagnostic stress ECG. The final decision for further testing based on the referral physicians judgment and recent guidelines for preoperative evaluation. Patients with normal CCTA or nonobstructive CAD (mild coronary artery lesion <50% stenosis) with normal left ventricular ejection function (LVEF) were cleared for surgery. Patients with moderate CAD (50–70% stenosis), severe CAD (more than 70% stenosis), or nondiagnostic CCTA (such as excessive calcification or motion artifact) underwent either conventional coronary angiography (CCA) or stress MPS. Exclusion criteria include patients with known CAD, contraindication to CCTA or intravenous (IV) iodinated contrast, unstable patients, patients with a known cardiac condition such as heart failure or valve diseases, or patients who will have cardiac surgery. The research protocol was approved by institutional review board.

Postoperative complications

Postoperative complications were observed and recorded from the operative room until hospital discharge. Postoperative complications were classified into three categories:

- Cardiac complications such as myocardial ischemia, myocardial infarction, sudden cardiac death, heart failure, and new onset arrhythmias
- Noncardiac complications such as sepsis, renal failure, and gastrointestinal bleeding
- Cardiac death
- Noncardiac death.

Computed tomographic coronary angiography

Patients without contraindications received metoprolol targeting a heart rate of ≤65 bpm and nitroglycerin 0.8 mg sublingually before image acquisition. A bolus tracking technique was used to calculate the time interval between IV contrast (Visipaque 320, GE Healthcare; Milwaukee, Wisconsin, USA) infusion and image acquisition. Final images were acquired with a triphasic protocol (100% contrast, 40/60% contrast/saline, and 40 cc saline). The contrast volume and infusion rate (5–6 cc/s) were individualized according to scan time and patient body habitus. Retrospective ECG-gated data sets were acquired with the GE high-definition CT (GE Healthcare; Milwaukee, Wisconsin, USA) with 64 mm × 0.625 mm slice collimation and a gantry rotation of 350 ms (mA = 300–800, kV = 120). Pitch (0.16–0.24) was individualized to the patient's heart rate. The CCCTA data sets were reconstructed with an increment of 0.4 mm using the cardiac phase with the least cardiac motion.

Computed tomography angiography image analysis

Images were processed using the GE Advantage Volume Share Workstation (GE Healthcare, Milwaukee, Wisconsin, USA) and visually interpreted by two expert observers blinded to all clinical data. A 17 segment model of the coronary arteries and 4 point grading score (normal, mild [<50%], moderate [50–69%], severe [≥70%]) were used for the evaluation of coronary stenosis.[16] Similar to ICA, obstructive CAD was defined as coronary diameter stenosis ≥50% [Figure 1].

Conventional coronary angiography

All CCA reports were reviewed and results were categorized as normal if there was no significant

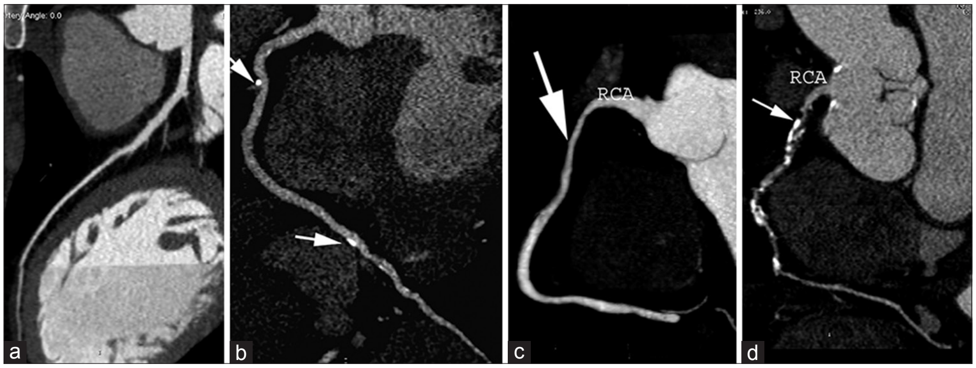

Figure 1: Multiplanar reformatting images of coronary computed tomography angiography in four different patients are demonstrated. (a) Normal left anterior descending artery, (b) nonobstructive calcified plaques (arrows) in the right coronary artery, (c) moderate stenosis of long segment of proximal right coronary artery (arrow), and (d) severe stenosis of multiple lesions in right coronary artery (arrows)

obstructive CAD (diameter stenosis <50%) or abnormal if there was ≥1 coronary segment with diameter stenosis ≥50%.[17]

Stress myocardial perfusion scintigraphy acquisition and analysis

Stress MPS imaging was performed by using a 1-day ECG-gated rest-stress protocol.

Rest images were acquired after a dose of 350 MBq of technetium 99m-tetrofosmin.

This was followed by pharmacologic stress induced by infusion of adenosine at a standard rate of 140 µg/kg of body weight per minute, and a dose of 1100 MBq of technetium 99m-tetrofosmin was injected 3 min into the state of pharmacologic stress according to a standard protocol.[18] Patients were told to refrain from ingesting caffeine-containing beverages for at least 12 h, nitrates and calcium channel blockers for 24 h, and β-blockers for 48 h before the myocardial perfusion imaging study. Gated SPECT studies were performed with a dual-head gamma detector camera (CardioMD; Phillips Medical System, Netherlands); a low-energy, high-resolution collimator; a 20% symmetric window at 140 keV; a 64 × 64 matrix; an elliptic orbit with step-and-shoot acquisition at 3° intervals over 180°; and a 20-s dwell time per stop. Acquisitions were gated at 16 frames per R-R cycle with a 50% window of acceptance. For all patients, the summed nongated SPECT image set was reconstructed on a dedicated workstation by using an iterative reconstruction algorithm (ordered-subset expectation maximization with two iterations and 10 subsets) with radionuclide source-based attenuation correction into short-axis, vertical long-axis, and horizontal long-axis sections encompassing the entire left ventricle. In addition, polar maps of perfusion, wall motion, and wall thickening were produced by using a commercially available software package (Cedars QGS/QPS; Cedars-Sinai Medical Center, Los Angeles, California, USA).[19] No serious adverse events following radionuclide injection or pharmacologic stress agent administration were reported. Image quality of myocardial perfusion images was amenable to visual interpretation in all patients.

Stress myocardial perfusion scintigraphy image interpretation

Stress MPS image interpretation was visually performed in consensus by two nuclear medicine physicians with more than 10 years of clinical experience in nuclear cardiology both of whom were blinded to the clinical history and to the findings from CCTA and ICA. Images were reviewed on short-axis, horizontal long-axis, and vertical long-axis sections and semiquantitative polar maps of perfusion. Anterior and septal wall perfusion defects were allocated to the left anterior descending coronary artery, lateral defects were allocated to the left circumflex coronary artery, and inferior defects were allocated to the right coronary artery. Stress MPS was considered abnormal in the presence of one or more abnormal segment (reversible, partially reversible, or fixed with abnormal wall thickening).

Statistical analysis

Statistical analysis was performed using SPSS for Windows, version 13.00 (SPSS Inc., Chicago, Illinois, USA); continuous variables were expressed as a mean ± standard deviation or median and range where appropriate; categorical data were expressed as percentages. Student test with Levene test for assessing homoscedasticity or Mann–Whitney U-test and Chi-square test or Fisher exact test were used to compare continuous and categorical variables between

Table 1: Patients characteristic, type of surgery, postoperative complications, and CCTA result

	Number/ percentage(%)
Patients characteristic, population *n*=93	
Men	48 (52)
Age (years)	60±9
High cholesterol	29 (31)
Hypertension	63 (67)
Diabetes mellitus	60 (64)
Obesity	29 (31)
Smoking	20 (22)
Family history of CAD	15 (16)
Type of surgery	
Oncologic surgery (major oncologic surgery such as lung and liver resection)	39 (42)
Vascular surgery (aortic and peripheral vascular surgery)	25 (27)
General surgery (hepatobiliary surgery, gynecological surgery, and genitourinary surgery)	13 (14)
Orthopedic surgery (joint replacement, fracture femur)	9 (10)
Neurosurgery (brain tumor, spinal cord, and spine surgery)	7 (7)
Postoperative complications, total 18 (19%)	
Noncardiac (e.g., sepsis, gastrointestinal bleeding, renal failure)	14 (78)
Cardiac (atrial fibrillation and heart failure)	2 (11)
Death (respiratory failure and intracranial hemorrhage)	2 (11)
CCTA results	
Group 1	71 (76%) normal or nonobstructive CAD
Group 2	22 (24%) moderate CAD, severe CAD, nondiagnostic CCTA

CAD: Coronary artery disease, CCTA: Coronary computed tomography angiography

groups, respectively. All *P* values refer to two-tailed tests of significance. A $P = 0.05$ was considered significant.

RESULTS

Ninety-three patients referred for risk stratification before noncardiac surgery. Age, gender, and other demographic data in Table 1. Based on the result of CCTA patients were divided into two groups. Group 1 patients who have normal CCTA or nonobstructive CAD (<50% stenosis), and Group 2 patients with either moderate coronary artery stenosis (50–70%), severe stenosis (stenosis more than 70% to total occlusion), and nondiagnostic CCTA (5% patients in total population study) due to excessive calcification, poor quality images from motion artifact, or any other artifacts that interfere with evaluation of the images. Group 2 patients underwent either stress MPS or CCA (based on the availability of either test or referring physician preference).

Group 1 consists of 71 patients who went for surgery without any further testing. 59 (83%) patients had no complications in the postoperative period, 9 patients had noncardiac complications, 1 had a cardiac complication (new onset atrial fibrillation), and 2 patients died during the postoperative period; these deaths were unrelated to cardiac complications. One patient died from intracranial bleeding which is related to his primary diagnosis of brain tumor, and the second death due to respiratory failure.

Group 2 comprises of 22 (26%) patients of whom 16 (72%) patients had no postoperative complications, 5 patients had noncardiac complications, and 1 patient developed postoperative acute heart failure and pulmonary edema. CCTA of this patient demonstrated severe stenosis and low ejection fraction of 40% and, unfortunately, cardiac catheterization failed due to severe peripheral arterial calcification. The patient went for surgery as a high-risk patient without any further preoperative testing because he had total aortic occlusion.

- Abnormal CCTA and stress MPS: 13 patients with abnormal CCTA underwent stress MPS, 8 (61%) had normal stress MPS, and 5 (39%) have abnormal MPS
- Abnormal CCTA and CCA: Total 9 patients with abnormal CCTA had CCA, 2 patients had normal CCA, and remaining 7 patients have abnormal CCA.

The mean CACS for Group 1 was 103 ± 18, and for Group 2 were 555 ± 74 ($P < 0.001$). However, there was no statistical significance between CAD risk factors (including age, diabetes mellitus, hypertension, dyslipidemia, or obesity) findings between Group 1 and 2. Moreover, there was no statistical significance between LVEF and CCTA results in either group.

DISCUSSION

The main finding of this study can be summarized as follows: First, CCTA is reliable preoperative testing before noncardiac surgery. It is diagnostic in approximately 95% of patients, and only 25% of patients (total of nondiagnostic and abnormal CCTA with more than 50% coronary artery stenosis) will need additional testing. Second, normal or mildly abnormal (<50%) stenosis excludes significant CAD and predicts favorable postoperative outcomes. Third, abnormal or nondiagnostic CCTA will benefit from either stress MPS or CCA. Fourth, high CACS is highly predictive of abnormal and nondiagnostic CCTA. Fifth, preoperative CCTA and CACS determination provide both short-term and long-term coronary artery risk stratification.

Stress echocardiography using exercise or pharmacological stress and stress MPS for preoperative risk stratification is well established. CCTA allows accurate detection of coronary artery calcification, presence and extent of CAD, cardiac function, and long-term CAD risk stratification by adding CACS. Based on this study, CCTA may be used as alternative test for already established techniques for risk stratification before noncardiac surgery, although currently there is no enough data available regarding the role of CCTA in the setting of preoperative evaluation. Our study suggests that CCTA is diagnostic in most patients with <25% of patients will need further testing.

Prior studies

Several small studies have reported the high diagnostic accuracy of CCTA for preoperative evaluation of cardiac patients who are referred for noncoronary cardiac surgery (e.g., aortic valve surgery). Gilard *et al*., confirmed the high ability of CCTA to rule out significant coronary artery stenosis in patients undergoing noncoronary cardiac surgery with negative predictive value of 100%.[9] CCA was performed in all patients as a gold standard reference. Russo *et al*. showed that no cardiovascular perioperative complications such as myocardial ischemia, myocardial infarction, or heart failure occurred in any patients with normal CCTA. 30 out of 36 patients with significant coronary artery stenosis (more than 50% luminal stenosis) by CCTA underwent bypass surgery or coronary angioplasty, but in 8 patients CCTA overestimates the severity of coronary artery stenosis.[14] Most recently, a prospective study consists of 133 patients showed that CCTA was diagnostic in 108 of 133 patients. Of these, 93 of 108 had no significant CAD (<50% stenosis) and noncoronary cardiovascular surgery was performed without preoperative ICA. No patient in this group had postoperative ischemic events at follow-up. CCTA was not diagnostic in 25 of 133 patients who were referred for preoperative ICA.[20] Interestingly, in this study total CACS was the most independent predictor for nondiagnostic CCTA a finding that is consistent with our study. However, CCTA was not diagnostic in 81% of cases compared with our study; CCTA was diagnostic in up 95% of total study population.

Coronary computed tomography angiography and coronary artery calcification

One of the major advantages of CCTA in the setting of preoperative evaluation is adding coronary calcium score scanning to measure CACS. CACS has provided to be a major predictor of future coronary events in both asymptomatic and symptomatic population. Several studies have shown the ability of CACS to predict future coronary events in symptomatic persons. A multicentral study of 491 patients undergoing ICA and CACS found that high CACS were associated with an increased risk of coronary events over the next 30 months, as compared to patients in the lowest quartile of the score (odds ratio 10.8, 95% confidence interval 1.4–85.6).[21] CACS was a stronger independent predictor of future events than a sum of all of the conventional risk factors combined.[22] The extent of CAC has shown to predict a cardiac event in asymptotic population as well. In a large cohort study consists of 10,377 asymptomatic individuals, CACS was an independent predictor of death ($P < 0.001$) and the risk increased proportionally to the baseline calcium score.[23] Our data showed that patient with high CACS has high likelihood to have abnormal (moderate or severe stenosis) or nondiagnostic CCTA. It is well known that arterial wall calcification may adulterate the result of CCTA. One study showed that number of segments with nondiagnostic image quality increased from 3% to 13% in patients with high CACS.[24] Another study concluded that in the presence of heavy coronary artery calcification, CCTA becomes less reliable due to high false positive CCTA due to overestimation of coronary stenosis secondary to blooming artifacts.[25] This is an important observation, and we strongly suggest cancelation of CCTA in the presence of heavy calcification and instead refer the patients for other testing such as stress MPS, stress echocardiography, or ICA.

Interrelationship between coronary computed tomography angiography and stress myocardial perfusion scintigraphy and conventional coronary angiography

Thirteen patients with abnormal or nondiagnostic CCTA underwent stress MPS. Thirty-eight percentage of those patients had an abnormal MPS. Although this is a relatively small number of patients, it confirms the relationship between stress MPS and CCTA. It is well known that abnormal CCTA is a poor predictor of ischemia, and further imaging with stress MPS is warranted in patients with abnormal CCTA who might benefit from revascularization procedure and those in whom conservative management and risk factor modification may be justified.[26] Fathala *et al*. studies 157 patients without known coronary disease and clinically proven indication for positron emission tomography/computed tomography (PET/CT) underwent PET/CT and stress MPS as a routine preoperative workup. The frequency of abnormal MPS was compared with the presence or absence of CAC. CAC was evaluated visually. The authors concluded that visual detection of CAC in the CT component of PET/CT was a strong predictor of MPS results. The presence of CAC is associated with a high likelihood of abnormal MPS, but the absence of CAC is rarely associated with abnormal MPS.[27] However, there is a high percentage of patients with abnormal CCTA 7/9 (77%) who have abnormal CCA. The possible explanations of this finding include most patients with abnormal CCTA, who referred to CCA have severely abnormal CCTA, both CCTA and CCA are anatomical imaging, and relatively few number of patients in this group and finding needs further validation.

Study limitations

The study is nonrandomized, observational, and retrospective study. CCA and stress MPS were not performed in patients with normal or mildly abnormal CCTA based on the well-known high negative predictive value of CCTA. Postoperative follow for the occurrence of cardiovascular complication was evaluated mainly during hospital admission and for only 6 months postoperatively. The relative number of patients (22 of 93 patients) who need additional testing with either CCA or stress MPS could also be considered as a limitation of the study. As with any other X-ray CT examination, ionizing radiation exposure is a major concern. The estimated ionizing radiation during CCTA is in the range of 10–10 mSv depending on scan length and sex. All studies were performed utilizing retrospective ECG gating with dose modulation to assess left ventricular function. Prospective ECG gating could limit radiation exposure and overcome these limitations.[28]

CONCLUSION

CCTA provides a comprehensive cardiac examination in the risk stratification before intermediate and high-risk noncardiac surgery. CCTA offers assessment of coronary artery calcification, coronary artery stenosis, and cardiac morphology and function; all these elements are necessarily for short- and long-term risk stratification, it is diagnostic in most preoperative patients, and normal or mildly abnormal CCTA predict no postoperative cardiac morbidity or mortality. Therefore, CCTA may be considered as an alternative test for already established imaging techniques for preoperative cardiac risk stratification before intermediate or high-risk noncardiac surgery.

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Conflicts of interest

There are no conflicts of interest.

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