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Improving the diagnostic performance of the real world coronary computed tomography angiography including uninterpretable segments

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ABSTRACT

Objectives: The purpose was to investigate the diagnostic performance of coronary computed tomography angiography (CTA) when non-calcified uninterpretable segments were determined as either obstructive or patent. We also investigated the factors that could improve the diagnosis of CTA.
Methods: A total of 268 patients without known coronary artery disease who were clinically indicated for coronary angiogram (CAG) within 50 days of coronary CTA were retrospectively included. The diagnostic performance of CTA was assessed with CAG as a reference, whereas stenosis of ≥50% was considered obstructive. We compared the results when non-calcified uninterpretable segments were determined as obstructive or patent. Coronary risk factors as well as contrast medium arrival time adjusted by heart rate (CAT_{HR}) were investigated for improvement of CTA diagnosis.
Results: Area under the receiver operating characteristic curve (AUC) improved when uninterpretable segments were determined as patent rather than obstructive (0.79 vs 0.73, $p = 0.02$). Multivariate analysis showed that CAT_{HR} was a predictor of CAG stenosis (odds ratio 1.13, $p = 0.046$) while other risk factors were not. Adding CAT_{HR} further improved the AUC to 0.82 ($p = 0.003$). The accuracy, sensitivity, specificity, positive predictive value and negative predictive value of CTA stenosis (uninterpretable segments as obstructive) were 72%, 99%, 32%, 68% and 95%. The values were 78%, 89%, 61%, 77% and 80% when CAT_{HR} was added and uninterpretable segments determined as patent.
Conclusions: The diagnostic performance of coronary CTA improved when non-calcified uninterpretable segments were determined as patent rather than obstructive. Adding CAT_{HR} could further improve the specificity.

1. Introduction

Coronary computed tomography angiography (CTA) has been proposed as a noninvasive test to determine obstructive coronary artery disease (CAD) with its high sensitivity and negative predictive value [1–3]. However, motion artifacts due to high heart rates [4,5], ectopic heart beat [6] or poor breath holding could degrade the image quality and therefore segments may not be interpretable. When an intention to diagnose strategy is applied, uninterpretable segments are determined as obstructive and invasive coronary angiography (CAG) is necessary to rule out CAD. Most studies which assess the diagnostic accuracy of coronary CTA apply the intention to diagnose strategy, but little is known about the diagnostic performance when uninterpretable segments were determined as patent. It is difficult to rule out obstructive CAD when calcified segments have artifacts. However, we hypothesized that non-calcified segments which are uninterpretable due to artifacts have low probability of obstructive CAD, thus diagnostic performance might improve by interpreting these segments as patent.

Hypertension, diabetes mellitus, dyslipidemia, smoking and familial history are known conventional risk factors of obstructive CAD. Reduced cardiac function by CAD could result in delayed circulation time with longer contrast medium arrival time (CAT) during the bolus tracking scan [7]. These factors might have a potential to improve the diagnostic performance of coronary CTA.

The purpose of this study was to investigate the diagnostic performance of coronary CTA without known CAD when non-calcified uninterpretable segments were determined as either obstructive or patent with CAG as a reference standard. We also assessed whether

Abbreviations: CTA, computed tomography angiography; CAD, coronary artery disease; CAG, coronary angiography; HU, Hounsfield unit; CAT, contrast medium arrival time; ROC, receiver operating characteristics; AUC, area under the curve.

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the conventional coronary risk factors as well as CAT could further improve the diagnostic performance of coronary CTA.

2. Methods

This retrospective study was approved by the local ethics committee, and the requirement for informed consent to participate in this study was waived.

2.1. Patients

The records of 1637 consecutive patients who underwent coronary CTA from November 2012 to November 2013 were retrospectively examined. These patients had several risk factors of CAD with chest pain and/or dyspnea, abnormal results of electrocardiogram, cardiac echo or treadmill test. A total of 348 patients were scheduled for CAG because ischemic heart disease was suspected according to the results of the CTA. The exclusion criteria were as follows: patients with known CAD (n = 32); arrhythmia (n = 23); known valvular disease (n = 4); duration period of >50 days between coronary CTA and CAG (n = 19); bolus tracking at the ascending aorta (n = 1); contrast medium arrival time not recorded (n = 1). The final study group included 268 patients (Fig. 1).

Clinical history was obtained by the referring physician, and the following conventional cardiovascular risk factors were assessed: 1) hypertension (blood pressure > 140/90 mm Hg and/or use of antihypertensive drugs); 2) diabetes mellitus (fasting glucose level ≥ 126 mg/dl or HbA1c ≥ 6.5% or need for insulin or oral antidiabetic drugs [8]); 3) dyslipidemia (low-density lipoprotein ≥ 140 mg/dl or high-density lipoprotein < 40 mg/dl or triglyceride ≥ 150 mg/dl or need for antilipidemic drugs [9]); 4) smoking (currently or previously); 5) family history of CAD. The pretest cardiovascular risk was assessed by the Morise pre-test score [10]. The Morise pretest score is a clinical risk score including age, gender, angina history, estrogen status in women, diabetes mellitus, dyslipidemia, hypertension, smoking, family history and obesity.

2.2. CT data acquisition

All patients underwent CTA with the 64-row CT (Brilliance 64; Philips, Tokyo, Japan). Retrospectively electrocardiogram-gated helical scans were performed in all patients. The scanning parameters were as follows: detector configuration, 64 × 0.625 mm; tube potential, 120 kVp; tube current-time product, 800–1050 mAs, depending on the body weight; gantry rotation time, 420 ms; and helical pitch, 0.2.

The patients received 21.0 mg I/kg/s of iopamidol 370 mg I/ml (Iopamiron 370; Bayer, Osaka, Japan). Contrast medium was injected for acquisition duration plus 7 s, followed by a 30-ml saline flush. Bolus tracking method was performed to determine the scan timing. The scan started 6 s after the descending aorta reached 100 Hounsfield Unit (HU). The time from the start of the injection to the threshold of 100 HU was recorded (CAT).

Thirty-seven patients were receiving an oral β-blocker as part of baseline medication, and an oral β-blocker (20–40 mg of metoprolol) was administered to 397 outpatients with heart rate (HR) >65 beats per minute (bpm). The patients were told to take the medicine 1 h prior to CTA. If the HR was over 65 bpm, as many as 2 mg of propranolol (Inderal; AstraZeneca, Osaka, Japan) or 12.5 mg of landiolol (Corebeta; Ono Pharmaceutical, Tokyo, Japan) was given intravenously. No patient had contraindications for β-blockers, and no β-blocker side effects were observed or reported. All patients received 0.3 mg sublingual nitroglycerin (Nitropen; Nippon Kayaku, Tokyo, Japan) before imaging.

For each patient, a senior technologist determined the phase with minimum artifacts at the CT console. Multiple phases were reconstructed when artifacts resisted in the image. The HR during the scan was recorded. The reconstructed slice thickness was 0.67 mm, and the increment was 0.33 mm. Images were reconstructed by using a cardiac sharp kernel. For processing, images were transformed to a workstation (Syanpse Vincent; Fuji, Tokyo, Japan).

2.3. Image analysis of CTA

The Society of Cardiovascular Computed Tomography 18-segment classification was applied for analysis of CTA data [11]. All segments with a diameter of at least 1.5 mm at their origin were included. We excluded vessels distal to total occlusions. The reconstructed images were evaluated and classified by two cardiovascular radiologists. Each segment was determined interpretable or uninterpretable. Causes of image degradation were recorded such as severe motion artifacts, intense noise or low opacification. We did not determine severe calcification as uninterpretable because severe calcification could cause significant stenosis. Anatomically obstructive CAD was defined as ≥50% stenosis.

2.4. Invasive coronary angiography

Left and right CAG was performed according to standard techniques. Angiograms were assessed by an experienced cardiologist and a radiologist blinded to the results of CTA. The same classification for CTA was applied for CAG analysis [11]. Each segment was visually evaluated for the presence of significant stenosis by determining the presence of ≥50% luminal diameter reduction with most severe luminal narrowing.

2.5. Statistical analysis

Continuous variables are shown as mean ± standard deviation and categorical variables as number (%). The Student's *t*-test was used to compare continuous variables and the Fisher's exact test or the chi-squared (χ^2) test was used to compare categorical variables.

Pearson correlation analysis was used to investigate the relationships between the HR and CAT. We adjusted the CAT by HR using regression analysis (CAT_{HR}).

Univariate and multivariate logistic regression analyses were used to assess the relationship of conventional cardiovascular risk factors, Morise risk score, CAT_{HR}, and CTA stenosis of ≥50% with CAG stenosis of ≥50% as a reference standard. Covariates with a *p* value of <0.05 in the univariate model were used in the multivariate model.

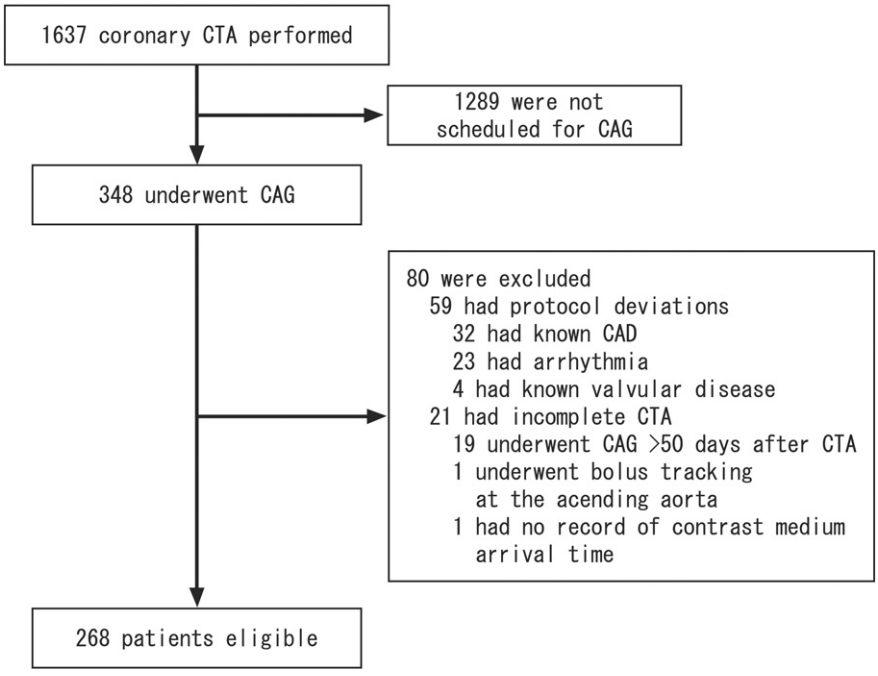

Fig. 1. A total of 1637 patients were screened and 348 patients were scheduled for invasive coronary angiography. The final study group included 268 patients. CAD, coronary artery disease; CTA, computed tomography angiography; CAG, coronary angiogram.