

# Efficacy and Safety of the Computed Tomography Coronary Angiography Based Approach for Patients with Acute Chest Pain at an Emergency Department: One Month Clinical Follow-up Study

To evaluate the safety and efficacy of the computed tomography coronary angiography (CTCA) for evaluation of acute chest pain in real world population, we prospectively enrolled 296 patients with acute chest pain at emergency department (ED) from November 2005 to February 2007. The patients were grouped based on the clinical information and CTCA result. The patients with a low risk profile and no significant coronary stenosis (>50%) in CTCA were discharged immediately (Group 1, n=103). On the other hand, the patients with an intermediate risk profile without significant stenosis were observed in ED for 24 hr (Group 2, n=104). The patients with significant stenosis underwent further coronary evaluation and management accordingly (Group 3, n=89). While no false negative case was found in Group 1, seven cases (6.73%) were found in Group 2, mostly during the observation period. In Group 3, there were 54 (60.67%) cases of acute coronary syndrome including 10 myocardial infarctions. The overall accuracy of CTCA for acute coronary syndrome was 88.5% (sensitivity), 85.1% (specificity), 60.7% (positive predictive value) and 96.6% (negative predictive value). In conclusion, clinical decision based on CTCA is safe and effective for low risk patients. Further validation is needed in patients with intermediate risk profile.

**Key Words :** Angina; Diagnosis; Imaging; Angiography; Coronary Disease; Tomography

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## INTRODUCTION

The evaluation of acute chest pain is a challenging task for physicians who work in emergency departments (EDs). Although complex diagnostic algorithms that combine multiple diagnostic modalities were developed to minimize error (1-3), a high portion (2-6%) of acute coronary syndrome (ACS) patients are being mistakenly discharged from EDs (4-6). This is related to adverse clinical outcomes (4) and responsible for the largest portion of malpractice suits (7).

The recent development of computed tomography coronary angiography (CTCA) provides a high spatial and temporal resolution images non-invasively (8). It provides comprehensive information about the patency of coronary artery, the integrity of great vessels and the lungs (triple rule out) (9, 10). In many comparative studies, targeting a non-ED based population, CTCA already showed its high diagnostic accuracy and high negative predictive value (8).

The application to the patients with an acute chest pain in

ED environment is also being actively evaluated. Some recent studies had shown that CTCA is reliable for ruling out an ACS in low risk group. However, previous studies are mostly small observational studies and/or have a narrow spectrum of target population (11-17).

We tried to evaluate the safety and efficacy of the CTCA-based approach for the patients with acute chest pain in real world ED situation.

## MATERIALS AND METHODS

### Study population

This study was performed at the urban teaching hospital with more than 44 thousand visits per year (2007) in ED. A total of 1,125 adult patients who visited the ED with acute chest pain was screened from November 2005 to February 2007. Initial clinical evaluation included history taking, phys-

ical examination, chest radiography, electrocardiogram (ECG), cardiac biomarker and creatinine level. The patients with high risk clinical profile were excluded after initial evaluation. High risk clinical profile was defined to the following criteria: 1) ST-segment elevation or new onset LBBB, 2) Increased level of serum troponin or CK-MB, 3) Typical chest pain with ischemic ST-T change (ST segment depression >1 mm or T-wave inversion >3 mm), 4) Overt congestive heart failure, recurrent ventricular arrhythmia, 5) Ongoing or recurrent angina at rest or minimal effort, and 6) Proven significant coronary artery disease.

After exclusion of these high risk patients, we determined whether each patient has intermediate or low risk profile. Intermediate risk profile was defined as having any of the following characteristics: 1) Atypical chest pain with any possible ischemic ECG change (mainly ST-segment depression or T-wave inversion), 2) Typical chest pain with normal ECG. And all patients who do not have possible ischemic ECG change nor typical chest pain were considered to have low risk profile.

The cases with definite evidence of non-coronary etiology of chest pain (e.g., newly diagnosed pneumothorax, overt herpes zoster or evident history of acute chest trauma) or which are not eligible for the test (significant arrhythmia, uncontrollable heart rate, contraindication to beta-blocker or hypersensitivity to radiocontrast agent) were also excluded.

Initial evaluation, enrollment and data collection were performed prospectively by trained emergency physician. The data also were reviewed by a cardiologist every week.

### CTCA scanning and analysis

The patients with low to intermediate clinical profile and without other exclusion criteria underwent CTCA evaluation with 16 or 64-channel multi-detector computed tomography (MDCT) with ECG gating capability. Heart rate was controlled under 65 bpm with metoprolol. Scan results were analyzed by a radiologist specialized in cardiovascular imaging. CTCA criterion of significant stenosis was defined as more than 50% diameter stenosis of any major coronary arteries.

### Management protocol at ED for the patients with acute chest pain

The patients were classified into three groups according to their clinical characteristics and CTCA reading (Fig. 1): 1) Group I (Immediate discharge group)-No significant coronary stenosis in the CTCA with low risk profile, 2) Group II (ED observation group)-No significant coronary stenosis in the CTCA with intermediate risk profile, 3) Group III (Further work up group)-Any CTCA evidence of significant coronary stenosis with low to intermediate risk profile.

The patients in Group I were immediately discharged from ED with a short-term out-patient department (OPD) follow-

up arrangement. The patients in Group II were observed in ED chest pain unit with serial ECG and cardiac biomarker assay. During the observation period, if a patient had recurrent chest pain or dynamic ST-T change or rising cardiac biomarker level, he was admitted and had coronary angiography. When a patient showed no above-mentioned sign and ACS still could not be ruled out, patients underwent further diagnostic test such as treadmill test (TMT) or myocardial single photon emission computed tomography (SPECT). The patients in Group III underwent the coronary angiography in most cases. However, in the cases with intermediate coronary lesions in CTCA, the myocardial SPECT or TMT was also considered.

### Clinical follow-up

The follow-up evaluation was done by a cardiologist at out-patient department within one week for all patients discharged from ED. On the follow-up visit, the cardiologist reviewed every detail about ED evaluation and clinical courses after the discharge. If there was any doubt about patient's diagnosis, additional diagnostic modalities were followed accordingly. Any occurrence of major adverse cardiovascular events (MACE), which is defined as death, myocardial infarction, unplanned coronary revascularization, and repeat ED visits or hospitalization for unstable angina, were also monitored during one month of clinical follow-up. After this period, the cardiologist determined whether the patient had ACS or not.

### Statistical analysis

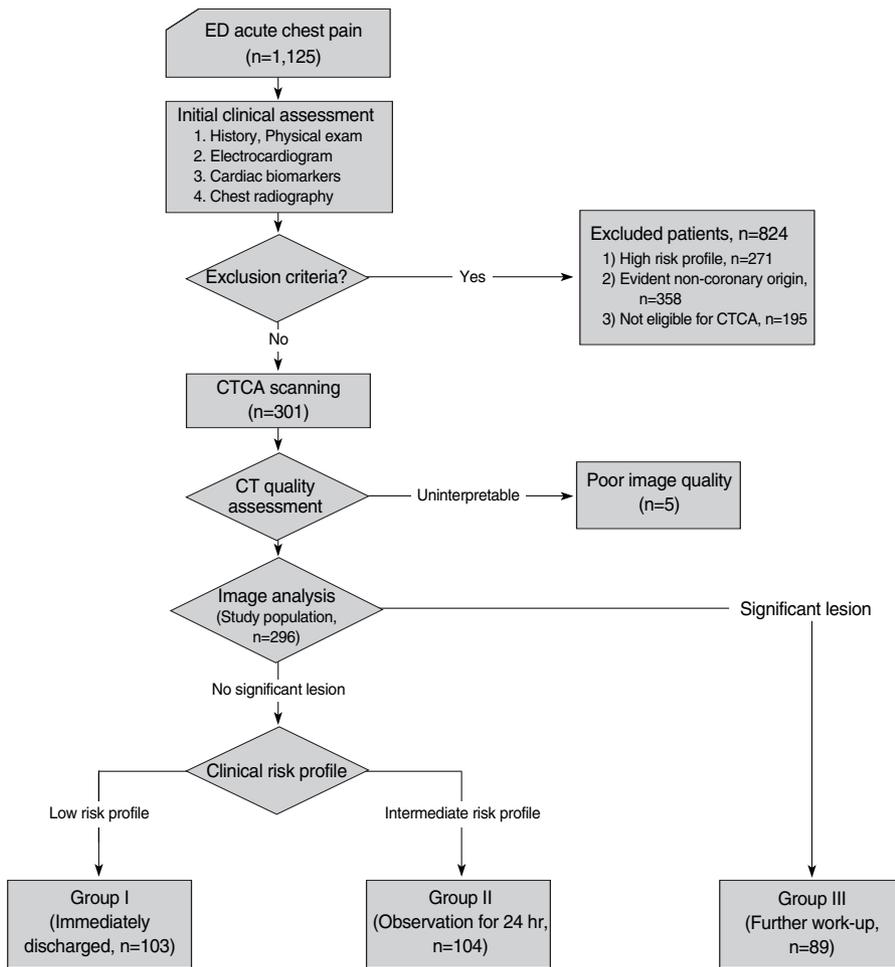
The statistical analysis was performed with the use of STATA 10 software package (StataCorp LP, College Station, TX, USA). We calculated sensitivity, specificity, and positive and negative predictive values of MDCT findings for diagnosis of ACS in whole study group and each clinical risk group. Categorical variables were analyzed with chi-square test. Continuous variables were analyzed with ANOVA. A *P* value <0.05 was considered significant.

## RESULTS

From November 2005 to February 2007, a total of 1,125 patients visited our ED with chief complaint of acute chest pain. High risk patients (n=271), evident non-cardiac etiology of chest pain (n=358) and patients having contraindication for CTCA (n=195) were excluded. As a result, 301 patients were initially enrolled in the registry and underwent CTCA scan. Five (1.7%) cases were excluded from the final analysis according to the poor image quality of CTCA (Fig. 1).

### Demographics

Of the 296 enrolled patients, 103 (34.8%) were classified



**Fig. 1.** Study protocol of CTCA based approach for acute chest pain patients. This flowchart shows CTCA based approach for patients with acute chest pain in our ED. Every patient without contraindication who visited our ED had CTCA and managed according to clinical risk profile and result of CTCA analysis. CTCA, computed tomography coronary angiography; ED, emergency department.

**Table 1.** Baseline characteristics according to the discharge group

	Group I (n=103)	Group II (n=104)	Group III (n=89)
Age* (yr)	53.8±12.8	56.9±10.6	64.5±11.1
Male (%)	50 (49.0%)	46 (44.2%)	50 (56.2%)
DM (%)	7 (6.8%)	13 (12.5%)	13 (14.6%)
Hypertension (%)	42 (40.8%)	47 (45.2%)	45 (50.6%)
Dyslipidemia (%)	15 (14.6%)	12 (11.5%)	13 (13.5%)
Previous CAD	5 (4.9%)	12 (11.5%)	13 (14.6%)
Previous CVA	5 (4.9%)	3 (2.9%)	7 (7.9%)
Smoker, current	15 (14.6%)	12 (11.5%)	14 (15.7%)

\*Age showed statistically significant difference between three groups ( $P<0.001$ ).

DM, diabetes mellitus; Previous CAD, previous coronary revascularization, myocardial infarction; Previous CVA, previous cerebrovascular accident.

as Group I, 104 (35.1%) classified as Group II, and 89 (30.0%), as Group III. Table 1 shows the demographic information of enrolled patients. There was little difference in the baseline characteristics between the three groups except mean

**Table 2.** Diagnostic accuracy of CTCA according to clinical risk profile

	Clinical risk profile			
	Low risk		Intermediate risk	
	ACS (-)	ACS (+)	ACS (-)	ACS (+)
CTCA (-)	103	0	97	7
CTCA (+)	18	11	17	43
	PPV, 37.9%; NPV, 100% Sens, 100%; Spec, 85.1%		PPV, 71.7%; NPV, 93.3% Sens, 86.0%; Spec, 85.1%	

ACS, final diagnosis of acute coronary syndrome; PPV, positive predictive value; NPV, negative predictive value; Sens, Sensitivity; Spec, Specificity.

age which was significantly higher in Group III.

**Diagnostic accuracy of CTCA**

The prevalence of ACS was 20.6%. Diagnostic accuracy of CTCA for ACS was 88.5% (sensitivity), 85.1% (specificity).

ty), 60.7% (positive predictive value) and 96.6% (negative predictive value). However, according to the risk profile, the positive and negative predictive values were 37.9% and 100% in the low risk profile group, while 71.7% and 93.3% in intermediate risk profile group (Table 2).

**Table 3.** Result of clinical follow-up

	Group I (n=103)	Group II (n=104)	Group III (n=89)
CAG (Positive/All tested)	0/13	5/21	43/56
Revascularization (PCI/CABG)	0	5	33
Myocardial infarction	0	0	10
Death	0	0	0
ACS as final diagnosis	0	7	54

CAG, Coronary angiography; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass graft; ACS, Acute coronary syndrome.

**Safety of CTCA based approach to the patients with acute chest pain**

Table 3 shows the result of clinical follow-up for each group. None of the Group I patients had MACE during follow-up period. In some cases additional tests were performed during follow-up period, but no ACS case was found in this group. Among Group II patients, seven (6.73%) were finally categorized as ACS, although there was no case of myocardial infarction or mortality (Table 4). Six of the seven were identified during the ED observation period and were admitted directly from ED. Among the six was a case of 65 yr old male who was diagnosed with microvascular angina. He had reproducible ischemic symptom and ECG change during a treadmill test which was performed during his ED observation period. He was admitted and his invasive coronary angiography showed no significant stenosis. Although he had no definite lesion found, he was considered as one of the seven

**Table 4.** Seven false negative cases of Group II

Sex	Age (yr)	MDCT finding	Reason for invasive angiography	Angiography finding	Treatment	Final diagnosis
F	59	Motion artifact, almost non-calcified lesion	Poor image quality, Positive SPECT	3 VD	STENT	Unstable angina
F	61	Small calcified plaque, mid LAD, Diagonal branch, RCA	Dynamic ST-T change	1 VD (LAD 50%)	No PCI	Stable angina
F	52	Mid-LAD calcification	Dynamic ST-T change	1 VD (LAD 90%)	STENT	Unstable angina
M	65	No significant stenosis, calcified plaque at proximal LAD	Dynamic ST-T change, Positive treadmill test	Normal*	No PCI	Microvascular angina
F	78	Calcified plaque at proximal and mid LAD	Blooming effect, Positive Myocardial SPECT	1VD (LAD 80%) <sup>†</sup>	STENT	Unstable angina
M	42	Multiple calcified stenosis	Blooming effect, Unknown significance of LCx. Lesion	1 VD (LCx 75%)	STENT	Unstable angina
F	73	Normal, multiple tiny calcified plaque at LAD	Recurrent symptom, Positive Myocardial SPECT	1 VD (LCx 95%) <sup>†</sup>	STENT	Unstable angina

\*He had reproducible exertion-related dynamic ST-T change with chest pain without coronary lesion; <sup>†</sup>The Lesion was located at the distal part of the coronary artery.

LAD, Left anterior descending coronary artery; LCx, Left circumflex coronary artery; RCA, Right coronary artery; PCI, Percutaneous coronary intervention.

**Table 5.** Diagnostic accuracies of CTCA for patients with acute chest pain syndromes

Authors (Ref. No.)	Reported year	No. of cases	Modality	Sens	Spec	PPV	NPV	ACS prevalence	Inadequate images excluded	STENT evaluation
White et al. (11)	2005	69	16-MDCT	83%	96%	83%	96%	18.84%	No	No
Ghersin et al. (12)	2006	59	16-MDCT	80%	89%	52%	97%	n/a	Yes	Yes
Hoffmann et al. (13)	2006	40	16/64-MDCT	100%	74%	38%	100%	12.50%	No	Yes
Hoffmann et al. (14)	2006	103	64-MDCT	100%	82%	47%	100%	14%	No	Yes
Olivetti et al. (15)	2006	31	MSCT	71.4%	99.6%	93.7%	97.7%	58.06%	No	No
Gallagher et al. (16)	2007	85	64-MDCT	86%	92%	50%	99%	8%	Yes	No
Rubinstein et al. (17)	2007	58	64-MDCT	92%	76%	52%	97%	34.48%	No	Yes

MDCT, Multi-detector computed tomography; Sens, Sensitivity; Spec, Specificity; PPV, Positive predictive value; NPV, Negative predictive value; ACS, Acute coronary syndrome.

false negative cases. The one missed ACS case was about a 73 yr old female who was discharged from ED after 24 hr observation period and had recurrent exertional chest pain at home. She was admitted and had coronary angiography (CAG) which showed 75% stenosis at the left circumflex artery. However there was no evidence that she suffered myocardial infarction. Neither myocardial infarction nor mortality case was missed in Group II.

In Group III (n=89), 53 patients (59.6%) had coronary angiography of which 43 patients (48.3%) showed significant stenosis and 33 (37.1%) were treated with interventions including PCI or CABG. Of the 53 patients examined by coronary angiography, 10 (18.9%) patients were diagnosed as myocardial infarction. There was no mortality.

## DISCUSSION

Previous non ED-based studies of 64-channel MDCT reported very high diagnostic accuracy of CTCA (8). Both sensitivity and specificity were about 95% and negative predictive value was about 99% (8). In two meta-analyses, 64-channel MDCT showed sensitivity and specificity of 92% and 95% respectively for segment analysis. For patient analysis, both sensitivity and specificity reached 100% (18, 19). These excellent results of CTCA diagnosis, however, may not be applicable in patients with acute chest pain in ED. In recent small studies, 64 channel MDCT showed rather low discriminatory power compared to the previous non-ED based studies (Table 5) (13, 14, 16, 17). And the American College of Cardiology Foundation guideline 2006 mentioned that the clinical application of CTCA for acute chest pain can only be considered "appropriate" when its application is limited to patients with intermediate pre-test probability without ECG and serial biomarker change (20).

Our intention in this study was testing the clinical applicability of CTCA in the real world ED situation. We had to exclude high risk patients from the study population because application of CTCA to diagnose or exclude an ACS for the population is considered to be neither safe nor efficient. And we also excluded patients whose diagnoses were overtly evident at the beginning of clinical evaluation.

The remaining 'low to intermediate risk' patients group underwent rapid diagnostic evaluation by CTCA. Conventional stress tests require 4 to 8 hr of pre-test observation period and impose cardiovascular loading to patients which can be potential danger to them occasionally. In contrast, we could obtain CTCA image right after the brief initial clinical evaluation without causing the potentially undesirable cardiovascular loading. And immediate discharge from ED was safe in low risk profile group which was also reported to be safe in one previous study (21). In terms of time and effort to evaluate the patients with acute chest pain at ED, the CTCA-based algorithm we applied in this study can be considered

more efficient than conventional approaches based on the stress tests. And it was also safe at least for low risk patients. However, there was seven false negative cases found in the intermediate risk group even though six out of the seven were successfully identified during observation period. It signifies the importance of clinical risk profiling. Until further technical advancement is to be made, judicious selection of patients and proper period of observation will remain important for most clinicians.

In terms of 'cost-effectiveness' there is possibility that CTCA may lead additional healthcare cost when used as a primary evaluation tool for acute chest pain. Otero and Rybicki evaluated cost-effectiveness of CTCA, stress echocardiography and myocardial SPECT for 10,000 simulated patients using reported imaging test characteristics, prevalence and risk of coronary heart disease, and medicare reimbursement schedules (22). They reported that the clinical application of CTCA may significantly reduced the overall observation period, negative CAG rate and total healthcare cost (22). However, injudicious use of CTCA can result in increased healthcare cost and develop undesirable health effect, such as radiation exposure, anaphylaxis and nephropathy that can also increase overall cost.

This study has some limitations. This study was conducted in a single, tertiary referral hospital. And more than 70% of initially screened patients were excluded. The results of this study could be applicable only for the "CTCA eligible" patients with "low to intermediate clinical risk profile". It is impossible to compare the result of this study with that of previous studies involving other popular diagnostic methods (e.g., myocardial SPECT, TMT), as this study is a single arm observational study. And the aspect of cost-effectiveness was not assessed in this study.

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