

# Predictive value of Computed Tomography Coronary Angiography for the evaluation of acute chest pain: single center preliminary experience

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**Abstract.** *Aim:* To assess the predictive value of CT coronary angiography (CT-CA) in the stratification of patients with acute chest pain. *Materials and methods:* We enrolled 48 patients (31 males and 17 females, mean age 61.0±14yrs) with acute chest pain of suspected coronary origin, without diagnostic alterations of the ECG and/or increase of the myocardial biomarkers. Sixty-four slice CT-CA was performed within 48-72 hours. Depending on the clinical judgment, the patients were dismissed or underwent conventional coronary angiography (CAG). Patients underwent clinical follow-up at 6 months, recording the prevalence of major cardiovascular events. *Results:* One patient was excluded from the analysis because of poor image quality. CT-CA showed no coronary artery disease in 38.3% (18/47) of the patients, no significant coronary artery disease (<50% lumen reduction) in 31.9% (15/47) of the patients, significant coronary artery disease (≥50% lumen reduction) in 29.8% (14/47) of the patients. In 87.2% (41/47) of the patients no indication for CAG was present. In 6 (12,8%) patients with significant stenosis at CT-CA indication for CAG was present. In 50% (3/6) of these patients, CAG showed no significant coronary artery disease and in the remaining 50%(3/6) CAG was followed by percutaneous coronary angioplasty. At follow-up no major cardiovascular events were observed. *Conclusions:* CT-CA showed high sensitivity for the detection of significant coronary artery disease and a negative predictive value at 6-month follow-up. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** Multislice computed tomography, conventional coronary angiography, coronary artery disease, 64-slice CT, Acute Chest Pain, Prognostic Value

## Introduction

In Western Countries, cardiovascular disease is the main cause of morbidity and mortality. In the United States, 5 millions of people are hospitalized every year with acute chest pain and two millions are not affected by acute coronary syndrome (1).

In low risk symptomatic patients, invasive procedures (i.e. CAG) are not appropriate, however, 2-4% of patients with Acute Myocardial Infarct (ACS/

AMI) are inappropriately dismissed from the emergency department (2). The diagnosis of ACS is mandatory because a missed diagnosis determines a doubling of the mortality index (3).

Only in a limited group of patients, the diagnosis and therapeutic strategies are decided based on initial ECG alterations and/or increase of myocardial biomarkers (4).

Non-invasive Computed Tomography Coronary Angiography (CT-CA) showed high sensitivity and

specificity for the detection of coronary artery stenoses and a lower but interesting accuracy for the identification of coronary artery plaques (5-14).

In particular, CT-CA showed a very high negative predictive value (~100%) for the exclusion of stenoses and “culprit” lesions (5, 6, 8-11, 13). This high negative predictive value could be used in patients with atypical chest pain and low-to-intermediate probability of disease (15-21).

Several studies reported the effectiveness of 64-slice CA-CT as useful tool for the management of suspected ACS (16).

Recent studies also report the high negative predictive value of CT-CA at follow-up (22).

The purpose of this study is the assessment of the predictive value of CT coronary angiography (CT-CA) in the stratification of patients with acute chest pain with a follow-up for cardiovascular events of 6 months.

## Materials and methods

### Patient Population

We prospectively enrolled 48 patients (31 male, 17 female, mean age =  $61.0 \pm 14$  yrs) with acute chest pain reaching our Emergency Department. The two groups were stratified based on cardiovascular risk parameters (Table 1-2-3):

In Group 1 CT-CA was performed within 24-72 hours after admission, while in Group 2 CT-CA was performed 3-4 days after admission.

Depending on CT-CA results, patients were divided as follows: CAG not recommended (absence of significant coronary artery stenosis and/or CT finding of other causes justifying the symptoms), and CAG recommended (presence of significant coronary artery stenosis).

In the patients with border-line stenosis (~50% lumen reduction) or poor CT-CA image quality due to severe coronary calcifications, stress-ECG/SPECT was performed for the evaluation of the ischemic impact of the stenosis.

The chest pain symptoms were evaluated on a per-patient basis and classified as typical, atypical.

All patients underwent clinical follow-up at 6 months, recording the prevalence of major cardiovascular events, as: death, re-hospitalization, recurrence of angina pectoris, CAG, PCI or CABG, changes in medical therapy, stress-test performed.

### CT-CA protocol

#### Coronary Calcification

All patient underwent standard calcium scoring protocol (11) in order to allow the quantification of

**Table 1.** Exclusion and inclusion criteria

	Inclusion criteria	Exclusion criteria
Group 1	<ul style="list-style-type: none"> <li>• non previous angina pectoris and Percutaneous Coronary Intervention (PCI) with stenting or Coronary Artery Bypass Graft (CABG);</li> <li>• atypical chest pain (Geleijnse and coll. chest pain scoring)[2];</li> <li>• without diagnostic ST-alterations of the ECG</li> <li>• without increase of the myocardial biomarkers (myoglobine &lt; 70ng/ml, CK-MB &lt;4 ng/ml, troponine I &lt;0.05ng/ml) after 6h in 3 consecutive draft;</li> <li>• low ACS risk (TIMI score <math>\leq 2</math>)[23];</li> <li>• Coronary Angiography CT was performed within 24-72 hours after symptoms.</li> </ul>	<ul style="list-style-type: none"> <li>• ST elevation of the ECG, in 2 or more derivations;</li> <li>• increase of the myocardial biomarkers;</li> <li>• hemodynamic alterations (cardiac failure NYHAI/ IV);</li> <li>• pregnant or presumed;</li> <li>• kidney failure (creatinine &gt;1.4mg/dl);</li> <li>• iodinated contrast-agent allergy;</li> <li>• non sinus rhythm or heart rate &gt;70bpm;</li> <li>• <math>\beta</math>-blockers contraindications;</li> <li>• the ability to perform a breath-hold of at least 12s.</li> </ul>
Group 2	<ul style="list-style-type: none"> <li>• atypical chest pain (Geleijnse chest pain scoring and coll.[2];</li> <li>• without diagnostic ST-alterations of the ECG</li> <li>• without increase of the myocardial biomarkers or slight increment of troponina (troponina I &lt;1ng/ml);</li> <li>• low-medium SCA risk (TIMI score <math>\leq 2</math>)[23].</li> </ul>	

**Table 2.** Demographics and risk factors

Parameters	All	Group 1	Group 2
Male (%)	30(63,8)	16(66,7)	14(60,9)
Female (%)	17(36,2)	8(33,3)	9(39,1)
Age (SD)	61(13,7)	58,2(13,9)	64,0(13,2)
Age < 65yrs (%)	25(53,2)	15(62,5)	10(43,5)
Age > 65yrs (%)	23(48,9)	10(41,7)	13(56,5)
Familiarity (%)	20(42,6)	6(25,0)	14(60,9)
Smoking (%)	14(29,8)	7(29,2)	7(30,4)
Diabetes (%)	10(21,3)	5(20,8)	5(21,7)
Hypertension (%)	30(63,8)	13(54,2)	17(73,9)
BMI >30 (%)	9(19,1)	1(4,2)	8(34,8)
BMI = 25-30 (%)	32(68,1)	17(70,8)	15(65,2)
BMI < 25 (%)	0(0,0)	0(0,0)	0(0,0)
Hypercholesterolemia (%)	7(14,9)	1(4,2)	6(26,1)
CRP (%)	4(8,5)	0(0,0)	4(17,4)

Data are presented as number of patients and percentages on the respective population (in brackets), with the exception of age in which data are presented as mean and standard deviation (in brackets)

Abbreviations: SD = standard deviation; BMI = Body Mass Index; CRP = C Reactive Protein.

**Table 3.** Chest pain clinical features

Parameters	All	Group 1	Group 2
Typical chest pain (%)	9(19.1)	3(12.5)	6(26.1)
Atypical chest pain (%)	37(78.7)	20(83.3)	17(73.9)
Associated symptoms (%)	26(55.3)	13(54.2)	13(56.5)
CRP (%)	4(8,5)	0(0,0)	4(17,4)

Data are presented as number of patients and percentages (between brackets) on the respective population.

the amount of calcification with dedicated software (Calcium Score, Siemens, Forchheim, Germany). Agatston Score, Calcium Mass and Calcium Volume were measured.

### *Coronary Angiography*

A 64-slice clinical CT scanner was used for the study (Sensation 64, Siemens, Forchheim, Germany).

In patients with heart rate  $\geq 65$  bpm, we administered a single intravenous dose of 5 mg of atenolol, repeated according to the clinical history, ejection fraction, ECG alterations, and blood pressure assessment during administration.

CT-CA protocol was performed after an intra-

venous administration of 100-125ml of iodinated contrast agent (Iomeprol, Iomeron® 400 mgI/ml, Bracco, Milan) and 40-50ml of saline with an injection rate of 5ml/s

The image reconstruction was performed according to previously described protocols (11).

### *CT Image Analysis*

Two observer, blind to CT-CA results, performed the evaluation using a modified 16-segment AHA classification (24). All segments were included for the CT-CA evaluation.

Axial CT images were obtained using multiplanar and curved reconstructions.

Diseased segments were assessed. The degree of stenoses was classified as: normal coronary artery( no stenosis), non significant stenoses (<50% lumen reduction), significant stenosis (>50% lumen reduction).

#### *Conventional Coronary Angiography (CAG)*

The standard CAG protocol of the Academic Hospital of Parma (Italy) was used for this study.

One observer, blind to CT-CA results, performed CAG evaluations.

An orthogonal bi-dimension projection was used with a dedicated software (CAAS®, Pie Medical, Maastricht, NL) in order to quantify the degree of coronary stenoses (≥50% lumen reduction = significant).

#### *Data Analysis*

Data are presented using descriptive statistics and expressed as prevalence, mean value and standard deviation. The Calcium Scoring was calculated with Agatston score. Differences in dataset were tested with an unpaired t test (parametric analysis), Chi quadro and McNemar test (non parametric analysis) on per-characteristic data basis. A  $p < 0.05$  was considered as statistically significant.

## **Results**

Only one patient was excluded from the study analysis. Mean heart rate was  $60.5 \pm 13.3$  bpm. Mean Agatstone Scoring was not statistically different between the two groups (Group 1:  $162.7 \pm 222.3$  vs. Group 2:  $283.3 \pm 427.0$ ;  $p > 0.05$ ; Table 4).

The CT-CA results showed normal coronary arteries in 38.3% (18/47) of the patient population, non

significant stenosis (<50% lumen reduction) in 31.9% (15/47), and significant stenosis (≥50% lumen reduction) in 29.8% (14/47).

CT-CA was positive (presence of at least one significant stenosis) and Stress-Test was negative or doubt in 8.5% (4/47) of the patients. In 2 patients non cardiac pathology was detected by CT-CA.

Among the entire population 12.8% (6/47) underwent CAG based on the CT-CA indication of significant stenosis. Of those lesion, 50% (3/6) were judged non significant stenosis (<70%; inclusion criteria for revascularization) by CAG, the remaining 3 patients underwent PCI. No patients reported major adverse cardiovascular events at 6 months follow-up (Table 5).

#### *Diagnostic Accuracy Data*

Diagnostic accuracy of CT-CA was: sensitivity 80%, specificity 76% (32/42), positive predictive value 29% (4/14), negative predictive value 97% (32/33). The calculation was performed using quantitative CAG (Figure 1, 2) as the gold standard in 6 patients and using follow-up data in the remaining ones (41/47).

#### *Negative CT-CA (without CAG)*

In Group 1, all patient with negative CT-CA (<50% lumen reduction) did not reported any cardiovascular events at 6 months follow-up (high negative predictive value).

In Group 2, two patients without significant stenosis at CT-CA, referred recurrence of chest pain at follow-up. The first one, was a chronic pericarditis (diagnosed with Cardiac MRI), while the second one was diagnosed of gastro-esophageal reflux.

**Table 4.** Coronary Calcium score.

Parameters	All	Group 1	Group 2
Agatston (SD)	221.7 (340.0)	162.7(222.3)	283.3(427.0)
Volume (SD)	194.6(294.7)	145.3(197.3)	246.0(368.2)
Mass (SD)	25.6(30.8)	20.9(24.6)	30.6(36.0)

Data are presented as number of patients and percentages (in brackets) on the respective population.

Abbreviations: SD = standard deviation

**Table 5.** Clinical follow-up.

Parameters	All	Group 1	Group 2
Death (%)	0(0.0)	0(0.0)	0(0.0)
Re-hospitalization (%)	0(0.0)	0(0.0)	0(0.0)
Recurrence of Angina (%)	6(8.6)	1(4.0)	5(21.7)
CAG (%)	0(0.0)	0(0.0)	0(0.0)
PCI (%)	1(1.4)	1(4.0)	0(0.0)
CABG (%)	0(0.0)	0(0.0)	0(0.0)
Stress-SPECT (%)	0(0.0)	0(0.0)	0(0.0)
Stress-ECG (%)	1(1.4)	1(4.0)	0(0.0)
Pharmacological (%)	10(14.3)	3(12.0)	7(30.4)
Echocardiography (%)	3(4.3)	2(8.0)	1(4.3)

Data are presented as number of patients and percentages (in brackets) on the respective population.

Abbreviations: PCI = Percutaneous Coronary Intervention; Pharmacological = Pharmacological treatment.

#### *Positive CT-CA (without CAG)*

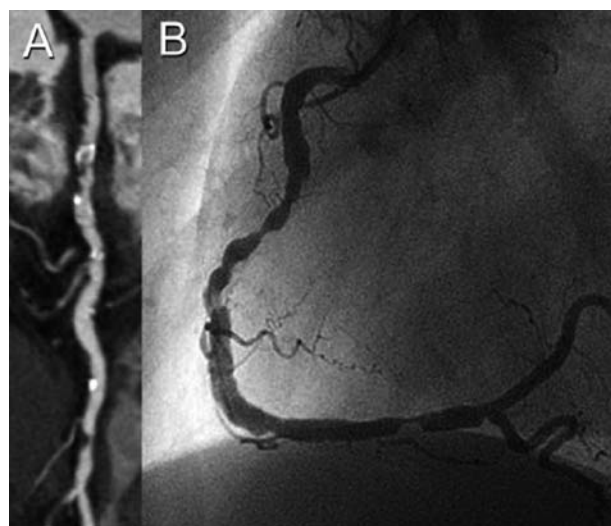
Overall, 9 patients with significant lesions at CT-CA did not undergo CAG: 3 patients showed pulmonary embolism, 2 patients did not give their consent for CAG, and 4 underwent stress ECG/SPECT that was judged as negative.

In Group 1 (5/24; 20.1%), all patients with positive CA-CT did not refer symptoms. In Group 2

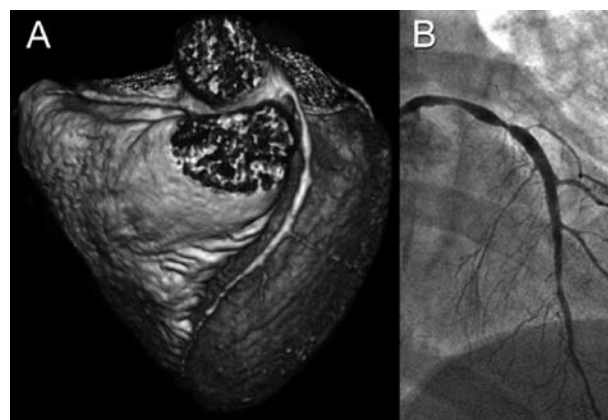
(4/22; 18,2%), one patient with positive CA-TC referred chest pain at follow-up.

#### **Discussion**

The aim of this study was to assess the predictive value of CT coronary angiography (CT-CA) in the stratification of patients with acute chest pain. We have to consider that our results were obtained in a highly selected patients' population with chest pain and a low-medium likelihood of disease (ACS - non



**Figure 1.** Example of significant stenosis of the right coronary artery from diffused mixed atherosclerosis with Computed Tomography Coronary Angiography (CT-CA (A) and CAG (B). Abbreviations: CT-CA = Computed Tomography Coronary Angiography; CAG = Conventional Coronary Angiography



**Figure 2.** Example of significant stenosis of the left anterior descending coronary artery from focal non calcific atherosclerosis with CT-CA(A) and CAG (B). Abbreviations: CT-CA = Computed Tomography Coronary Angiography; CAG = Conventional Coronary Angiography.



diagnostic alteration of the ECG and negative Troponine). The number of patients presenting with this features is very high in the clinical practice, however this population carries a low prevalence of significant disease. Therefore, in this population CAG may result in several invasive investigations not followed by revascularization (25). Haberl et al. showed that 32% of CAG performed in patients with chest pain may be avoided introducing CT-CA (26).

Guidelines for patients with chest pain are not recommending yet CT-CA as a method for patients with acute chest pain of suspected coronary origin (27).

White et al. reported CT-CA as an excellent tool for the assessment of chest pain of non cardiac origin. In their series 75% of the patients was diagnosed as negative with CT-CA, 19% were positive (10 cardiac and 3 non cardiac findings) (28).

Gallagher et al. showed CT-CA as useful tool for the exclusion of ACS in patients with chest pain and low likelihood of disease, comparable to SPECT (19).

A randomized study from Goldstein et al. showed the excellent diagnostic accuracy of CT-CA for the assessment of chest pain; in this study CT-CA was faster and less expensive as compared to the standard of care of their Institution based on SPECT imaging (18).

Hoffmann et al. reported a 100% negative predictive value of CT-CA for the exclusion of ACS with optimal short-term prognosis (16).

In our study CT-CA showed a high negative predictive value for the exclusion of significant coronary artery disease in a population with acute chest pain and low-intermediate pre-test likelihood of ACS.

At present, this patient population undergoes stress-ECG. When stress-ECG is negative patients are sent home (27).

A study performed on patients with non acute chest pain confirmed the high negative predictive value CA-CT for the population without major cardiovascular events (22).

Moreover the assessment of coronary lumen, the incremental value of CT-CA with respect to CAG relies on the capability of CT-CA to measure the attenuation values of atherosclerotic lesions. This may be helpful in diagnostic and prognostic terms. CT-CA may be a reliable alternative to CAG in situations in which Cath-lab and revascularization are not immediately required (12, 14).

In low risk patients, CT-CA may be a useful diagnostic tool to exclude the coronary origin of acute chest pain, in particular in patients with only slight increase of troponine. In fact, troponine levels may be altered in conditions such as ACS with non thrombotic etiology. Troponine levels are very sensitive but not very specific, and in patients with acute chest pain and low risk this may be misleading. Also in conditions such as pulmonary embolism a slight increase of troponine levels may "divert the attention" towards a cardiological issue, exposing the patient to unnecessary non-invasive and invasive tests. In this group of patients, CT-CA may be a useful, robust and quick gate-keeper for CAG. In low risk patients stress/exercise ECG is not effective both because of the high prevalence of co-morbidities and for the poor diagnostic accuracy. CT-CA does not require stress and can reduce time and costs (18).

Finally, CT-CA is also able to exclude/diagnose several other thoracic conditions that may cause chest pain (e.g. pulmonary embolism, aortic dissection, pneumothorax, pulmonary infiltration, pleural/pericardial effusion, and so forth) (28).

## Limitations

This study is a preliminary experience with low number of patients and low prevalence of disease. For this reason it is difficult to extrapolate results in larger populations.

No diagnostic gold standard was present (only few patients were referred for CAG), however, this was not a major endpoint of our study. We studied the prognostic value of CT-CA at 6 months.

Estimated radiation dose was three-fold in CT-CA (15-21mSv) as compared to CAG, and equal to stress-SPECT (29).

## Conclusions

CT-CA showed high sensitivity for the detection of significant coronary artery disease and a high negative predictive value at 6-month follow-up.

Larger studies are necessary to confirm the potential of CA-CT in this field.

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