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Cardiac Computed Tomographic Angiography in Patients with Acute Chest Pain and Moderately-increased Troponin

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Abstract. *Aim: The aim of the study was to investigate patients with undefined chest pain and moderately increased troponin based on the results of cardiac computed tomographic (CT) angiography (CCTA). Patients and Methods: We analysed the cases of 43 patients with acute chest pain and moderately increased troponin in whom CCTA was performed. Patients with suspected stenosis on CCTA underwent percutaneous coronary angiography (PCA). Results: CCTA ruled-out significant coronary stenosis in 32 patients. Eleven patients had suspected significant coronary stenosis on CCTA. Ten patients underwent PCA, which verified significant coronary lesions in nine. Out of these, four patients were treated by percutaneous coronary intervention (PCI). One patient had to undergo coronary artery bypass grafting. A triple-rule-out CT protocol was performed in 18 patients, demonstrating pulmonary embolism in three and pericardial effusion of unknown origin in two. Conclusion: CCTA accurately identifies or rules out patients with undefined chest pain and moderately elevated troponin, which require PCA and allows detection of other significant clinical findings.*

Troponin is considered as the most sensitive marker of myocardial cell damage and is of special importance for risk stratification of acute coronary syndromes (ACS) (1-5). In accordance with current guidelines for ACS, pathologically elevated troponin levels define myocardial infarction and represent, in addition to electrocardiography and clinical parameters, an important criterion for high-risk status (6, 7). The significance of moderately-elevated troponin levels is less clear. In current guidelines, troponin levels which are increased but do not exceed the threshold defining myocardial infraction are interpreted as an intermediate-risk criterion (6). This assessment, however, is not universally-accepted. On the other hand, many patients with non-coronary conditions exhibit moderate troponin elevations indicative of involvement of myocardial tissue (8-13). Thus, for risk assessment of patients with acute chest pain and moderately elevated troponin levels, the probability of ACS, as well as differential diagnoses must be considered. The assessment of patients with acute chest pain and moderately elevated troponin levels is controversial.

The aim of our study was to provide a more accurate assessment of patients with acute chest pain and moderately elevated troponin levels, with regard to the diagnosis of coronary heart disease (CHD) or relevant differential diagnoses by cardiac computed-tomographic angiography (CCTA).

Patients and Methods

Study population. Data regarding patients presenting with acute chest pain to the Emergency Department (ED) of the Mannheim University Hospital who had moderately-elevated troponin I levels and underwent CCTA from September 2007 to July 2009 were retrospectively analysed.

Due to the retrospective nature of the study protocol, the institutional Ethical Review Board waived the need for informed consent. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki

Diagnostic algorithm and laboratory measurements. The ED standard protocol for the assessment of patients with chest pain included a focused medical history and physical examination, a 12-lead ECG within 10 min after presentation to the ED and routine blood tests including troponin I and D-dimer. CCTA was carried out according to standard inclusion and exclusion criteria (6, 7) (Table I).

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Table I. *Inclusion and exclusion criteria for cardiac computed tomographic angiography (CCTA).*

Inclusion criteria:
Undefined chest pain
Age >40 years
Exclusion criteria:
Cardiac high-risk criteria (ST elevation, instability)
Age <40 years
Pregnancy
Hyperthyroidism
Metformin treatment
Serum creatinine >1.5 mg/dl
Known contrast agent allergy

Table II. *Patient baseline characteristics (n=43).*

Age (years)+	62±16 (range=40-95)
Gender (n)	
Female	18 (42%)
Male	25 (58%)
Risk factors (n)	
Diabetes	11 (26%)
Hypertension	30 (70%)
Hyperlipidemia	13 (30%)
Current smoker	22 (51%)
Family history of CAD	5 (12%)
Obesity	23 (53%)
Heart rate (beats/min)+	82±20 (range=54-142)
Blood pressure (mmHg)+	
Systolic	147±28 (range=107-233)
Diastolic	80±13 (range=60-120)

CAD: Coronary artery disease. +Mean±Standard Deviation.

All patients with verified or suspected coronary stenosis by CCTA were hospitalized and underwent invasive coronary angiography. In patients who had elevated D-dimer levels, CCTA was performed using a triple-rule-out protocol.

Plasma samples were collected immediately after the initial presentation to the ED and at least 6 hours after the onset of chest pain for additional measurement of troponin I. Plasma troponin I concentrations were detected using a commercially-available and fully-automated assay (AccuTnI; Beckman Coulter, Krefeld, Germany). Troponin I values of >0.5 μg/l were regarded as significant. Troponin I values from 0.03 to 0.5 μg/l were considered as moderately-increased, and values <0.03 μg/l were regarded as normal. D-Dimer values were determined with the TINA-quant D-dimer assay from Roche Diagnostics (Mannheim, Germany).

CCTA. All CCTA and triple-rule-out studies were performed using a dual-source CT (DSCT) system (Somatom Definition; Siemens Healthcare Sector, Forchheim, Germany). The CCTA scanning technique was chosen individually for each patient, depending on heart rate/rhythm and body mass index (BMI), with the goal of minimizing radiation exposure. Scan techniques included traditional retrospective ECG-gating with default use of ECG-dependent tube current modulation and prospective ECG-triggering. Acquisition parameters were 2×32×0.6 mm detector collimation, 330 ms gantry rotation time, and 320 reference mAs per rotation tube current time product. In patients with a BMI >25 kg/m^2, 120 kV tube potential was used whereas in patients with a BMI <25 kg/m^2, the tube potential was reduced to 100 kV. In patients who required a tripe-rule-out CT angiography protocol, a biphasic ECG-gated spiral protocol of the whole chest was performed. In this protocol, the level of the carina was defined as the trigger point where the second tube of the DSCT system is switched on additionally and the retrospectively ECG-gated spiral dual-source CT angiography of the heart region starts.

Percutaneous coronary angiography (PCA) and coronary intervention. PCA was performed using standard techniques. After gaining femoral or radial access a diagnostic procedure was performed using 5-French catheters. Stenosis >50% of any major epicardial coronary artery was defined as significant. Percutaneous coronary intervention (PCI) was carried out immediately, after indication was provided by the cardiologist performing the procedure.

Statistical analysis. All statistical calculations were carried out by the statistical software package SPSS (SPSS Inc., IL, USA) and InStat (GraphPad Software, La Jolla, USA). Continuous variables are expressed as means, standard deviation (SD) and range. For non-continuous variables, numbers and percentages were used.

Results

Patients' characteristics are shown in Table II. The mean age of the study cohort was 62 (range=40-95) years.

ECG recording showed sinus rhythm in 41 patients (95%). In two patients (5%) atrial fibrillation was recorded. An ST-segment depression >0.1 mV was found in three patients (7.0%) and a negative T-wave >0.2 mV in four patients (9.3%) (Table III).

In all patients moderately-elevated troponin I concentrations were measured within the defined (intermediate) range of 0.03-0.5 μg/l. In 39 patients (90.7%) troponin I levels were already elevated within the intermediate range upon admission to the ED and did not increase above 0.5 μg/l during follow-up. Four patients (9.3%) had troponin I values of <0.03 μg/l upon admission to the ED, but 6 h after the onset of chest pain, elevated troponin concentrations were measured within the intermediate range in these patients.

Coronary stenosis was reliably ruled-out in 32 patients (74%) using CCTA. In five patients (11%), possible- and in six (14%) definite coronary stenosis ≥50% was diagnosed. PCA was performed in 10 (23%) out of these 11 patients. One patient refused further invasive examination. In nine patients (21%) significant coronary stenosis of >50% was found by PCA. The results of PCA are shown in Table III. In one patient (2.3%), the dominant intraluminal stenosis was borderline (about 50%) by PCA. In this patient, the coronary lesion was found to be possibly relevant by CCTA.

Table III. *Results of electrocardiography (ECG), cardiac computed tomographic angiography (CCTA), percutaneous coronary angiography (PCA), and final therapy (n=43).*

ECG (n)	
Sinus rhythm	41 (95%)
Atrial fibrillation	2 (4.7%)
AV block I°	2 (4.7%)
Left anterior hemiblock	2 (4.7%)
Left bundle branch block	1 (2.3%)
Right bundle branch block	1 (2.3%)
ST-segment depression >0.1 mV	3 (7.0%)
T inv. >0.2 mV	4 (9.3%)
Supraventricular extrasystole	1 (2.3%)
Ventricular extrasystole	1 (2.3%)
CCTA (n)	43 (100%)
Normal	32 (74%)
Suspected obstruction ≥50%	5 (12%)*
Reliable obstruction ≥50%	6 (14%)
PCA confirmed stenosis >50% (n)	10 (23%)
1- Vessel disease	4 (9.3%)
2- Vessel disease	2 (4.7%)
3- Vessel disease	4 (9.3%)
Final therapy (n)	9 (21%)
Stent	4 (9.3%)
CABG	1 (2.3%)
Conservative	4 (9.3%)

CABG: Coronary artery bypass graft. *PCA not accepted by one patient.

A triple-rule-out CT angiography protocol was carried out in 18 patients. In these patients, pulmonary embolism was present in three patients (7.0%) and pericardial effusion of unknown aetiology was present in two patients (4.7%). No cases of aortic dissection were discovered.

Re-vascularisation therapy was carried out in five out of nine patients with significant coronary stenoses. Four patients (9.3%) were treated with coronary stent implantation; three of these patients (7.0%) had one-vessel disease and one patient (2.3%) had two-vessel disease. One (2.3%) out of the nine patients with significant coronary stenosis had to undergo urgent coronary by-pass surgery due to two-vessel disease with involvement of the left main coronary artery. Four patients (12%) with three-vessel disease were treated conservatively (Table III). No patient died during hospitalization. After treatment in the ED, 21 (49%) out of the 43 study patients were discharged and 22 patients (51%) were admitted to hospital.

Discussion

The significance of moderately elevated troponin levels in patients with acute chest pain is still not completely elucidated. There is a considerable degree of uncertainty in the management of these patients in the ED. It has been shown that troponin levels which are elevated yet below the threshold defining myocardial infarction, are indicative of adverse short- and long-term prognosis including increased mortality in patients with acute chest pain (14, 15). The aim of our study was to determine the incidence of relevant CHD in patients presenting with chest pain who have moderately elevated troponin levels. In this group of patients, the role of non-invasive coronary imaging by cardiac multi-detector CT has become increasingly important in recent years (16-18). In addition to quantification of coronary calcifications using the Agatston score, contrast-enhanced 64-slice CT angiography of the coronary arteries is suitable. The special significance of this method lies in the reliable exclusion of CHD with high negative predictive values. CCTA is not suitable for the quantification of manifest coronary stenoses and thus not for high-risk cardiac patients (19-23). In clinical practice, CCTA is being increasingly used in the risk stratification of patients with acute chest pain and low- or moderate-cardiac pre-test probability (24). Relevant differential diagnoses of ACS, such as pulmonary embolism or aortic dissection, can be excluded or verified, given the presence of appropriate clinical indicators, in an extended process step, in the sense of a triple rule-out (25-27).

According to our diagnostic algorithm, CCTA has been routinely used in patients with acute chest pain and moderately elevated troponin levels, unless there were pre-specified contraindications present. Out of the 43 patients presenting with acute chest pain and moderately-elevated troponin I concentrations studied in the present investigation, relevant CHD was definitively excluded by CCTA in 32 (74%) patients. In all but one case with suspected or definite coronary stenosis using CCTA, invasive coronary angiography was performed and demonstrated CHD with significant coronary stenosis in nine out of ten patients. More than half of these patients with significant CHD required PCI or coronary artery by-pass graft. Thus, our data demonstrate that even moderately-elevated troponin levels in patients with acute chest pain seem to be associated with ACS in more than 20% of cases. Furthermore, there is a substantial risk of relevant differential diagnosis which can be found using DSCT. In 12% of the patients studied, other pathological results were found. The triple rule-out protocol revealed three cases of pulmonary embolism and two of pericardial effusion. On the other hand, due to exclusion of CHD and other relevant differential diagnoses using CCTA, half of the patients were able to receive outpatient treatment.

The issue is further aggravated by the recent introduction of highly sensitive troponin assays, as these tests have higher sensitivity but lower specificity (28-31). Troponin can even be measured in >80% of healthy people, with a coefficient of variation <10% at the recommended cut-off. Using highly-sensitive troponin assays enables the troponin cut-off value to be lowered, resulting in a 160% increase of chest pain patients

being diagnosed with acute myocardial infarction and a 200% increase of troponin-positive patients with non-coronary cardiac chest pain (14). The evaluation of moderately-elevated troponin levels in patients with acute chest pain will thus become even more important in the future. For emergency facilities, this means an increasing importance of standardized algorithms that take account of this development. The high diagnostic reliability of non-invasive coronary imaging argues for the inclusion of CCTA in such standards. About half of the patients in our study with chest pain and moderately-elevated troponin were discharged from the ED after exclusion of CHD and other relevant differential diagnoses. Moreover, one should not fail to appreciate the early information gained by the triple rule-out protocol.

Conclusion

CCTA accurately identifies or rules-out patients with undefined chest pain and moderately-elevated troponin whom require PCA and allows for detection of other significant clinical findings.

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