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Research paper

Triple rule-out computed tomography for risk stratification of patients with acute chest pain

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ABSTRACT

Aims: Clinical evidence supporting triple rule-out computed tomography (TRO-CT) for rapid screening of cardiovascular disease is limited. We investigated the clinical value of TRO-CT in patients with acute chest pain.

Methods: We retrospectively enrolled 1024 patients who visited the emergency department (ED) with acute chest pain and underwent TRO-CT using a 128-slice CT system. TRO-CT was classified as "positive" if it revealed clinically significant cardiovascular disease including obstructive coronary artery disease, pulmonary thromboembolism, or acute aortic syndrome. The clinical endpoint was occurrence of a major adverse cardiovascular event (MACE) within 30 days, defined by a composite of all cause death, myocardial infarction, revascularization, major cardiovascular surgery, or thrombolytic therapy. Clinical risk scores for acute chest pain including TIMI, GRACE, Diamond-Forrester, and HEART were determined and compared to the TRO-CT findings.

Results: TRO-CT revealed clinically significant cardiovascular disease in 239 patients (23.3%). MACE occurred in 119 patients (49.8%) with positive TRO-CT and in 7 patients (0.9%) with negative TRO-CT ($p < 0.001$). Sensitivity, specificity, positive predictive value, and negative predictive value of TRO-CT was 95%, 88%, 54%, and 99%, respectively. TRO-CT was a better discriminator between patients with vs. without events as compared to clinical risk scores (c-statistics = 0.91 versus 0.64 to 0.71; integrated discrimination improvement = 0.31 to 0.37; $p < 0.001$ for all comparisons). Patients with a negative TRO-CT showed shorter ED stay times and admission rates compared to patients with positive TRO-CT, irrespective of clinical risk scores ($p < 0.001$ for all comparisons).

Conclusion: Triple rule-out CT has high predictive performance for 30-day MACE and permits rapid triage and low admission rates irrespective of clinical risk scores.

1. Introduction

Acute chest pain is a major diagnostic challenge in the emergency department (ED).[1–4] Diagnosis can be easily made in most patients with typical symptoms accompanied by significant electrocardiographic (ECG) changes or elevated cardiac biomarkers. However, symptoms alone are not sufficiently reliable[5–7] and absence of an abnormal ECG or cardiac biomarkers does not rule out acute cardiovascular disease. Therefore, means to obtain rapid and accurate diagnosis is necessary to decrease mortality and to maximize the clinical benefit of early treatment.[8,9]

Coronary computed tomography (CT) angiography enables

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evaluation of cardiovascular disease with a high negative predictive value, resulting in rapid and safe triage of acute chest pain at the ED.[10–12] Triple rule-out CT (TRO-CT) describes a modified coronary CT angiography protocol with extended thoracic coverage and may have advantages in the detection of life-threatening causes of chest pain beyond coronary artery disease (CAD) such as pulmonary thromboembolism or acute aortic syndromes.[13–17] However, the current clinical evidence supporting TRO-CT for screening of acute chest pain is still insufficient to justify its implementation in the ED.[18–22] We investigated the 30-day clinical outcome of patients who underwent TRO-CT in the ED, and compared it with clinical risk scores for acute chest pain.

2. Methods

2.1. Patients

From October 2009 to March 2012, we enrolled 1024 patients who underwent TRO-CT as part of their clinical evaluation for acute chest pain. This retrospective analysis was limited to the handling of anonymized imaging datasets an obtained approval with waiver of informed consent by the institutional review board of Samsung Medical Center.

ED physicians ordered TRO-CT to identify the cause of unidentified acute chest pain that developed within the last 24 h, when a clinical benefit of TRO-CT imaging was expected. Patients with prior history of myocardial infarction (MI) or revascularization were not included. Patients with ST-elevation on ECG, shock, renal failure, contraindication to beta-blockade or nitroglycerin did not undergo TRO-CT.[21] Women of childbearing potential were excluded unless a negative pregnancy test was available.

TRO-CT data sets were reconstructed by a dedicated workstation (iNtuition, Terarecon) available 24 h a day 7 days a week, and immediately interpreted by attending radiologists. The time from image acquisition to reading was typically 30 min in the daytime and 30 min to 1 h at night or on holidays. ED physicians reviewed the results of TRO-CT and decided on the further treatment strategy. All patients were followed at the outpatient clinic 30 days later unless they were admitted or had expired.

2.2. Triple rule-out CT

A 128-slice dual-source scanner (SOMATOM Definition Flash, Siemens Medical Solution) was used. Oral beta-blockers were used when heart rate was more than 65/min. Sublingual nitroglycerin was given 1 min before scanning. A biphasic injection technique was employed to achieve optimal contrast in both coronary and pulmonary arteries: a bolus of 70 ml of iomeprol 350 (Iomeron 350 mg/ml; Bracco) was injected at 3.5 ml/s, followed by 10 ml of the same contrast material at 2.0 ml/s and 30 ml of saline flush at 3.0 ml/s. X-ray data acquisition was initiated with a delay of 10 s after the trigger of contrast monitoring using an automated bolus tracking system. The region of interest was located at the ascending aorta. Image data were acquired in caudo-cranial direction from the diaphragm to the lung apices. A retrospectively ECG-triggered helical data acquisition technique was used with the full radiation dose window set at 68–78% of the R-R interval in patients with heart rates <65 bpm, and 200–400 msec after the R peak in patients with a heart rate of ≥65 bpm. A reduced dose with 4% of full radiation dose during acquisition window was adapted for the rest of the R-R interval to minimize the radiation dose. Radiation was modified by 50% outside the cardiac area in z-direction. The following scan parameters were used: tube voltage = 120 kV, tube current = 320 mA, gantry rotation time = 280 msec, pitch = 0.22–0.24, and 2 × 64 × 0.6 mm detector collimation resulting in 2 × 128 × 0.6 mm sections by means of the z-axis flying focal spot technique.

Transaxial images were reconstructed from the level of the carina to the cardiac apex with 0.6 mm section thickness and 0.4 mm intervals. The data sets were reconstructed using a standard soft kernel (B26f). A sharp kernel (B46f) was also used for cases with significantly calcified plaques. A further reconstruction of transaxial images with 2 mm section thickness and 2 mm intervals was performed for the entire scan range. Effective radiation exposure (mSv) was calculated from the total dose-length product using a conversion factor of 0.017 mSv/mGy·cm.[23]

2.3. Clinical definitions

Research nurses who were blinded to the imaging results performed a structured review of electronic medical records. Angina-equivalent symptoms were categorized into typical anginal chest pain or atypical chest pain. Typical chest pain was defined when the chest pain was (1) substernal in location, (2) provoked by exertional or emotional stress, and (3) relieved by rest and/or nitroglycerine. Chest pain that did not fulfill all of the above criteria was defined as atypical chest pain. The ED stay time and the time from TRO-CT to discharge were calculated from the timestamp of electronic medical records.

Acute MI was defined according to the 3rd universal definition of MI.[24] The results of TRO-CT were reviewed and organized by cardiovascular radiologists who were blinded to all clinical data. TRO-CT was defined as “positive” if previously unknown cardiovascular disease deemed clinically significant, including coronary artery disease (CAD), pulmonary thromboembolism and acute aortic syndrome, was identified. CAD was diagnosed by the presence of >50% diameter stenosis in proximal to mid segments of the major epicardial coronary arteries. The extent of CAD was assessed using the modified Duke score, segment involvement score, and segment stenosis score.[25,26] Diagnosis of an acute aortic syndrome or pulmonary thromboembolism was based on the respective radiological findings. Significant aggravation of a pre-existing cardiovascular disease, such as newly developed tight coronary artery stenosis unprotected by bypass grafts or aortic dissection of patients with prior history of revascularization, was also regarded as positive TRO-CT. The clinical endpoint was occurrence of a major cardiovascular adverse event (MACE) including all cause death, myocardial infarction (MI), revascularization, major cardiovascular surgery, or thrombolytic therapy within 30 days.

2.4. Clinical risk scores

We used scoring systems that stratify the clinical risk of acute chest pain at the ED and have been validated in previous studies.[27] The TIMI (Thrombolysis in Myocardial Infarction) risk score was developed from patients with confirmed ACS enrolled in the TIMI-11B trial,[1] and was validated in the ESSENCE trial and other studies.[28–30] The TIMI risk score comprises age > 65 years, ≥3 classical risk factors for CAD, use of aspirin in the past 7 days, severe angina in the past 24 h, elevated cardiac markers and ST-segment deviation ≥ 0.5 mm. The TIMI score ranges from 0 to 7 which correspond to event risk of 4.7%–40.9%, and showed c-statistics of 0.63–0.65.

The GRACE (Global Registry of Acute Coronary Events) score was developed from a registry of ACS patients and has been validated in the GUSTO-IIb trial.[31,32] The GRACE score is based on the Killip class, systolic blood pressure, heart rate, age, and creatinine. The presence of cardiac arrest, ST-segment deviation, and abnormal cardiac biomarker is added to the score. The GRACE score ranges from 1 to 372 with corresponding event risks of 0.2%–90%, and shows c-