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Diagnostic performance and cost of CT angiography versus stress ECG — A randomized prospective study of suspected acute coronary syndrome chest pain in the emergency department (CT-COMPARE)☆,☆☆

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ABSTRACT

Background: Coronary CT angiography (CCTA) has high sensitivity, with 3 recent randomized trials favorably comparing CCTA to standard-of-care. Comparison to exercise stress ECG (ExECG), the most available and least expensive standard-of-care worldwide, has not been systematically tested.
Methods: CT-COMPARE was a randomized, single-center trial of low–intermediate risk chest pain subjects undergoing CCTA or ExECG after the first negative troponin. From March 2010 to April 2011, 562 patients randomized to either dual-source CCTA (n = 322) or ExECG (n = 240). Primary endpoints were diagnostic performance for ACS, and hospital cost at 30 days. Secondary endpoints were time-to-discharge, admission rates, and downstream resource utilization.
Results: ACS occurred in 24 (4%) patients. ExECG had 213 negative studies and 27 (26%) positive studies for ACS with sensitivity of 83% [95% CI: 36, 99.6%], specificity of 91% [CI: 86, 94%], and ROC AUC of 0.87 [CI: 0.70, 1]. CCTA (>50% stenosis considered positive) had 288 negative studies and 18/35 (51%) positive studies with a sensitivity of 100% [CI: 81.5, 100], specificity of 94% [CI: 91.2, 96.7%], and ROC of 0.97 [CI: 0.92, 1.0; p = 0.2]. Despite CCTA having higher odds of downstream testing (OR 2.0), 30 day per-patient cost was significantly lower for CCTA ($2193 vs $2704, p < 0.001). Length of stay for CCTA was significantly reduced (13.5 h [95% CI: 11.2–15.7], ExECG 19.7 h [95% CI: 17.4–22.1], p < 0.0005), which drove the reduction in cost. No patient had post-discharge cardiovascular events at 30 days.
Conclusions: CCTA had improved diagnostic performance compared to ExECG, combined with 35% relative reduction in length-of-stay, and 20% reduction in hospital costs. These data lend further evidence that CCTA is useful as a first line assessment in emergency department chest pain.

1. Introduction

Chest pain is a common cause for presentations to hospital emergency departments (EDs). The clinical investigation of undifferentiated chest pain must include the expeditious assessment for acute coronary syndrome (ACS). Many chest pain assessment pathways include serial electrocardiography and biomarkers followed by a provocative stress test to rule out myocardial ischemia [1,2]. In many institutions, treadmill exercise stress ECG (ExECG) is used to stratify intermediate risk patients due to the widespread availability and low cost, and is a Class IB indication in the AHA/ACC guidelines [3]. However, ExECG has relatively limited diagnostic performance with low sensitivity and specificity in unselected populations [4]. More recently, coronary computed tomographic angiography (CCTA) has been investigated as a rapid,

Abbreviations: ACS, acute coronary syndrome; CCTA, coronary computed tomographic angiography; CPAS, chest pain assessment service; ED, emergency department; ExECG, exercise treadmill electrocardiography; MACE, major adverse cardiovascular events.

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noninvasive test with a high negative predictive value and reduced length of stay in low to intermediate risk patients with possible ACS [5–7]. These studies have suggested that CCTA-based care is also less expensive compared to provocative stress testing when coupled with imaging. However, cost analyses suggest that CCTA may be more expensive compared to ExECG-based care [8]. To date, there have been no large-scale clinical trials comparing CCTA-based care to ExECG-based care in possible ACS patients.

The CT Coronary Angiography Compared to Exercise ECG (CT-COMPARE) study was a prospective randomized trial that compared dual source CCTA with ExECG as part of the standard of care in low–intermediate risk possible ACS patients presenting to the ED. The primary endpoints were the diagnostic performance measures and the hospital-based costs of CCTA-based care as compared to ECG-based care.

2. Methods

2.1. Study design

CT-COMPARE was a randomized, prospective, non-blinded single-center study conducted in a large tertiary academic Australian hospital. Enrolled subjects were randomized to either CCTA or ExECG performed as part of an established chest pain assessment service [1,9]. The local Human Research and Ethics Committee approved the study (HREC/09/QPCH/89) and all subjects were required to give informed consent prior to randomization. The study was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12614000630617).

2.2. Study subjects

Males ≥30 and females ≥40 years of age presenting to the ED with acute undifferentiated chest pain were eligible for inclusion in the trial. Inclusion criteria included intermediate probability of coronary artery disease according to the Cardiac Society of Australia and New Zealand guidelines [10], initial 12-lead ECG without evidence of acute ischemia, TIMI (Thrombolysis in Myocardial Infarction) risk score <4 and a negative first serum sensitive troponin-I with a 99th centile at <0.04 ng/ml (Access 2 immunoassay, Beckman-Coulter) (Fig. 1). Exclusion criteria were previous diagnosis of coronary artery disease; confirmed pregnancy or lactating female; history of severe reactive airway disease or current exacerbation; allergy or contraindication to iodinated contrast or beta-blockade medications; current atrial fibrillation; and renal impairment (eGFR < 50 ml/min using the MDRD equation). To be eligible for randomization, subjects needed to be pain-free and potentially able to exercise on a treadmill. Using a computer-generated random sequence, randomization occurred after the first negative serum troponin result. Randomization was available 24 h a day, and the subsequent testing (whether ExECG or CTCA) was performed as soon as available (described below). All subjects received 300 mg oral aspirin (unless contraindicated) and underwent continuous ST-segment ECG monitoring as part of the standard-of-care. Appendix 1 shows flow diagrams for patient recruitment in the ExECG and CCTA arms. Patients were randomized 24 h a day.

2.3. Exercise ECG procedure

Treadmill ExECG was performed as part of an established 24-hour, 7 day per week chest pain assessment service, with testing available during and outside standard hours [1]. Subjects with a second negative 6-hour troponin for myocardial infarction (troponin I < 0.04 mg/dl) underwent the standard Bruce treadmill ExECG protocol (Marquette, GE Healthcare). A cardiology registrar/fellow performed continuous ECG and vital sign monitoring during ExECG testing. A cardiologist independently adjudicated the ExECG result using standard criteria for myocardial ischemia [11]. Subjects without ExECG evidence of myocardial ischemia were discharged. Subjects with positive or equivocal ExECG results were managed at the discretion of the treating cardiologist.

2.4. CCTA procedure

CCTA was performed after the first negative troponin, available daily from 0800–2200 h including weekends [9]. Subjects received 50–200 mg oral metoprolol tartrate, with a goal heart rate of <60 bpm. Further IV metoprolol, in 5 mg aliquots up to a total of 20 mg, was provided in CT if heart rate remained >60 bpm. Sublingual nitroglycerin 300 mg spray was administered 5 min prior to scanning (Somaton Definition 64 detector, or Definition Flash 128-detector; Siemens, Erlangen, Germany). 80 ml of non-ionic iso-osmolar contrast (Iomeron 350, Bracco, Italy) was injected via an 18-gauge cubital fossa cannula at 6.0–7.0 ml/min augmented with a 50 ml normal saline flush at 6.0 ml/min. Radiation exposure was minimized by using prospective ECG triggered imaging for patients with a stable heart rate of <60 bpm ("adaptive sequential" mode), or dose-modulated retrospective ECG gating with automated pulse width ("min-dose auto", Siemens, Erlangen, Germany), for patients with HR > 60 or >10% heart rate variability. Tube voltage was reduced to 100 kVp for subjects weighing <80 kg [12]. Calcium scoring was not performed in these symptomatic subjects. CCTA images were interpreted independently using a dedicated workstation (Leonardo, Siemens, Erlangen, Germany; or Brilliance, Philips, Best, Netherlands) by an expert radiologist and cardiologist (>5 years of CCTA experience each), blinded to subject history and clinical course. Discrepancies were resolved by consensus. Coronary artery lesions were categorized in an ordinal scale as normal (no disease), mild (1–49% diameter stenosis), moderate (50–69% stenosis) or severe stenosis (>70% stenosis), and analyzed on a per-patient and per-vessel basis. Negative (normal CCTA) subjects were discharged without repeat troponin (Appendix 1). Patients with mild CCTA disease had a 6-hour troponin before being discharged with a letter to their family physician. Moderate disease (50–70%) was admitted for a second troponin, and managed at the discretion of the treating cardiologist. Severe disease (>70%) subjects were admitted to the coronary care unit, treated as ACS according to current guidelines, and managed by the treating cardiologist with open access to CCTA data.

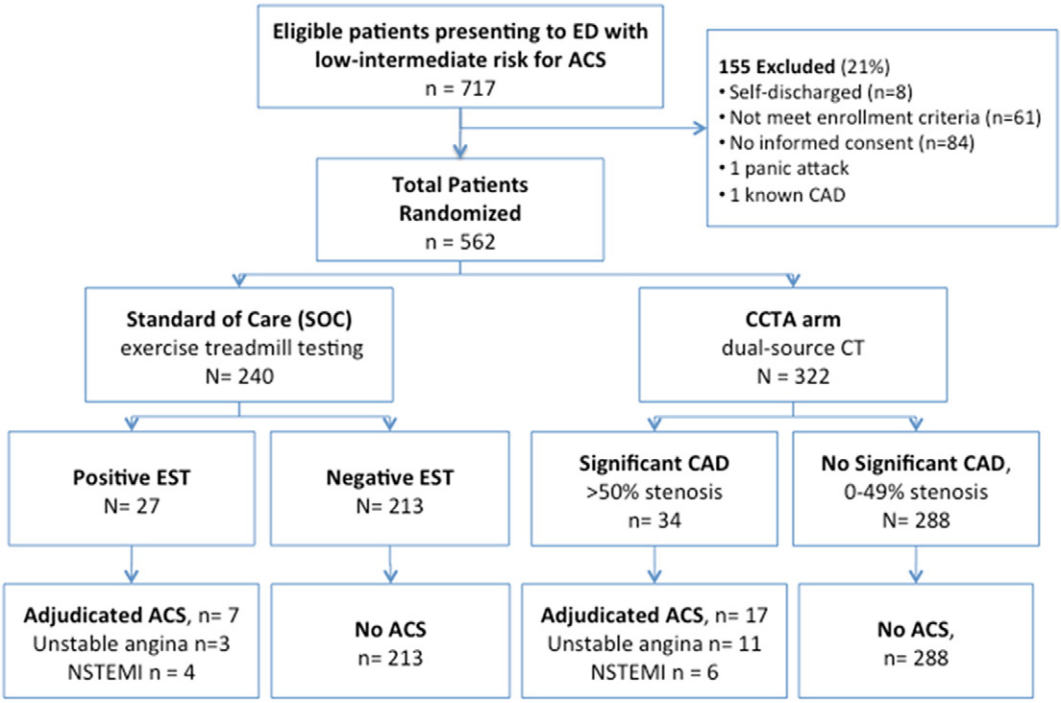

Fig. 1. CONSORT schematic diagram of study design and enrollment.