Non-invasive assessment of low risk acute chest pain in the emergency department: A comparative meta-analysis of prospective studies

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ABSTRACT

Background: The aim of this meta-analysis was to compare the diagnostic accuracy of cardiac computed tomographic angiography (CCTA), stress echocardiography (SE) and radionuclide single photon emission computed tomography (SPECT) for the assessment of chest pain in emergency department (ED) setting.
Methods: A systematic review of Medline, Cochrane and Embase was undertaken for prospective clinical studies assessing the diagnostic efficacy of CCTA, SE or SPECT, as compared to intracoronary angiography (ICA) or the later presence of major adverse clinical outcomes (MACE), in patients presenting to the ED with chest pain. Standard approach and bivariate analysis were performed.
Results: Thirty-seven studies (15 CCTA, 9 SE, 13 SPECT) comprising a total of 7800 patients fulfilled inclusion criteria. The respective weighted mean sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and total diagnostic accuracy for CCTA were: 95%, 99%, 84%, 100% and 99%, for SE were: 84%, 94%, 73%, 96% and 96%, and for SPECT were: 85%, 86%, 57%, 95% and 88%. There was no significant difference between modalities in terms of NPV. Bivariate analysis revealed that CCTA had statistically greater sensitivity, specificity, PPV and overall diagnostic accuracy when compared to SE and SPECT.
Conclusions: All three modalities, when employed by an experienced clinician, are highly accurate. Each has its own strengths and limitations making each well suited for different patient groups. CCTA has higher accuracy than SE and SPECT, but it has many drawbacks, most importantly its lack of physiologic data.

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1. Introduction

The prevalence of chest pain as a presenting complaint among American adults has been estimated to be 7.8 million cases per year or 5.4% of all emergency department (ED) visits annually nationwide [1,2]. In the United States, about 595,000 of those patients will experience a myocardial infarction [1,3,4].

In a multicenter, prospective clinical trial of more than 10,000 patients presenting with chest pain to the ED, only 17% met criteria for myocardial infarction (MI) or unstable angina; of which 2.1% and 2.3%, respectively, were mistakenly discharged [5]. Missed diagnoses and failure to admit patients with MI, have a high social and legal impact due to increased mortality and significant liability. Conversely, admitting the vast majority of these patients who do not require hospitalization represents a major burden to the U.S. health system.

Accepted clinical practice is based on the premise that non-invasive cardiac imaging can accurately stratify the risk level of chest pain patients. The most common imaging modalities used for evaluation of obstructive coronary artery disease (CAD) in the ED include coronary computed tomographic angiography (CCTA), stress echocardiography (SE) and radionuclide single photon emission computed tomography (SPECT). These modalities are remarkably different because CCTA detects anatomic coronary stenosis, SE detects physiologic stress induced wall motion abnormality and SPECT detects relative myocardial perfusion defects. Even so, they are all used to triage chest pain patients and frequently lead to hospital discharge (when negative) or cardiac catheterization (when positive). The use of a specific modality is usually

clinical site/requesting physician dependent rather than based on strict evidence since there have been relatively few head-to-head comparisons [6–8]. Therefore, the objective of this meta-analysis was to evaluate the available studies in which CCTA, SE or SPECT was compared to coronary angiography or clinical outcomes in the assessment of patients presenting to the ED with acute chest pain (ACP) suspicious for acute coronary syndrome (ACS).

2. Methods

2.1. Search strategy

A study protocol is not published but available upon request. A comprehensive search of PubMed, Embase and Cochrane Library and Clinical Trial Registry was performed from 1966 to September, 2013, without language filters, using the following terms:

For CCTA: (coronary computed tomography OR coronary computed tomography angiography OR CCT) AND (coronary artery disease OR CAD OR acute coronary syndrome OR ACS OR emergency department OR ER OR ED OR chest pain OR angina);

For SE: (dobutamine stress echocardiography OR dobutamine stress test OR stress echocardiography OR SE OR exercise stress echocardiography OR exercise stress) AND (coronary artery disease OR CAD OR acute coronary syndrome OR ACS OR emergency department OR ER OR ED OR chest pain OR angina);

For SPECT: (SPECT OR single photon emission computed tomography OR nuclear stress testing OR nuclear stress) AND (coronary artery disease OR CAD OR acute coronary syndrome OR ACS OR emergency department OR ER OR ED OR chest pain OR angina).

2.2. Inclusion criteria

To be included in the meta-analysis, a study had to fulfill all the criteria found in Fig. 1.

2.3. Data extraction

Three authors (J.R., S.A.H., P.C.) identified the studies and extracted the data independently and in duplicate. Data to calculate diagnostic accuracy was extracted using standardized protocol and reporting forms. Disagreements were resolved by arbitration (M.G.). We also extracted baseline patient demographics, characteristics of each trial, and CCTA, SE and SPECT methodology for our analysis.

2.4. Quality assessment

To assess the quality and reporting of studies, we evaluated 14 items that were considered relevant to the review topic, based on the Quality Assessment of Diagnostic Accuracy Studies instrument-2 (QUADAS-2) [9]. Three reviewers (J.R., S.A.H., A.A.H.) independently assessed the quality items and disagreements were resolved by arbitration (M.G.).

2.5. Statistical analysis

Sensitivities, specificities, PPV and NPV were calculated for every testing modality. We estimated summary sensitivity and specificity using both a random effects model and a bivariate random effects model [10,11]. The summary ROC curve was obtained by transforming the regression line of logit sensitivity and specificity into ROC space [10].

Publication bias was assessed for each analysis using Peters' method. We assessed inter-study heterogeneity visually by plotting sensitivity and specificity in the ROC curves. We also drew summary ROC curves and confidence regions for summary sensitivity and specificity [11,12]. A heterogeneity analysis was independently performed for each imaging modality.

We further evaluated whether the performance of each technique depends on features of the technique and patient characteristics. A logistic regression for each modality was used to model the sensitivity on these factors. Analyses were conducted using STATA 12 (Metandi Syntax) and the figures were generated using STATA graph editor. All continuous variables are reported as mean ± standard deviation.

3. Results

3.1. Study selection

We identified 19,034 abstracts, of which 111 were retrieved and reviewed in detail for possible inclusion (Fig. 2). Thirty-seven studies with a total of 7800 patients fulfilled the inclusion criteria and were included in the meta-analysis.

3.2. Baseline characteristics

Of the 37 studies, 15 studies enrolling 2697 patients [mean age 55 ± 7 years; male: 58%] using CCTA for the evaluation of acute chest pain were included, represented in Table 1. Of these, 13 studies (87%) used 64-slide multi-detector computed tomography (MDCT); ten (66%) defined significant coronary artery stenosis as >50%; three studies (20%) used >70% as a cutoff. The prevalence of CAD among included subjects

Inclusion Criteria
1) Prospective design
2) Enrolled patients who presented with chest pain suspected to be cardiac in origin- with no ECG changes diagnostic of myocardial infarction or acute ischemia and negative cardiac biomarkers
3) Patient underwent any of the following tests: CCTA, SE or SPECT
4) Intracoronary angiography was used as the gold standard reference test when performed; when not performed, Major Adverse Cardiovascular Events was considered the gold standard reference test.
5) The study was carried out in the ED setting
6) The study allowed for sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) calculations.

Fig. 1. Title: Inclusion criteria. Legend: CCTA: cardiac computed tomographic angiography; MACE: major adverse cardiac events; SE: stress echocardiography; SPECT: single photon emission computed tomography.