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Coronary CT Angiography vs Functional Stress Testing in Chest Pain Evaluation; A Meta-Analysis of Diagnostic Accuracy, Revascularization Rates, and Cost-Effectiveness

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ABSTRACT

Background: Chest pain is a common clinical feature and medical diagnostic dilemma in both emergency and outpatient care. There are two major non-invasive methods for the management of suspected CAD (coronary artery disease), coronary computed tomography angiography (CCTA), and functional stress testing (FST). With recent advancement in technologies CCTA has been identified as a good alternative for early triage but doubt still exits as to how this is superior in terms of diagnosis, as downstream therapeutic decisions as well as the monetary implications with former stress testing modalities. **Objectives:** This meta-analysis will provide comparison of CCTA and Functional stress testing with regard to (1) diagnostic accuracy for obstructive CAD, (2) rates of downstream revascularization and (3) overall cost-effectiveness in patients coming for evaluation of chest pain. **Methodology:** This study has been carried out, as systematic review and meta-analysis (in line with PRISMA guidelines). A total of 27 original studies published from 2007-2024 were included comprising randomized controlled trials and prospective cohort with direct comparisons of CCTA and FST. Searched databases were PubMed, Embase and Scopus. Estimates of sensitivity, specificity, and revascularization rates, and cost metrics were pooled using random effects model. Subgroup analyses were conducted, by risk stratification as well as clinical setting (acute stomach pain versus stable stomach pain). **Results:** CCTA showed greater pooled sensitivity (95.2%) and NPV (97.4%) than FST (sensitivity 79.1%, NPV 89.6%) for detection of obstructive CAD. The Revascularization rates were higher in CCTA group (14.6%) compared to FST group, (9.8%) inferring a direct route to invasive treatment over anatomically proven disease. Despite slight increase in cost of initial imaging, the CCTA was more cost-effective in terms of decreased downstream testing and shorter hospital stay as well as fewer non conclusive evaluations. Heterogeneity was low to moderate in all outcomes ($I^2 > < 40\%$). **Conclusion:** CCTA is superior when it comes to diagnostic accuracy and it comes with higher corresponding rates of appropriate revascularization than functional stress testing. Although imaging costs may be more upfront, the net analysis of benefits vis-à- vis cost in the case of both emergency and outpatient chest pain analysis supports CCTA. The results also advocate a wider implementation of CCTA as a frontline diagnostic tool, including low-to-intermediate risk populations.

INTRODUCTION

Chest pain is one of the most common reasons for emergency department visits and outpatient cardiology assessment around the world with important health system and patient outcome consequences [6, 9, 18]. Precise early diagnosis of coronary artery disease (CAD) in such patients would be very important for preventing undesirable cardiovascular events as well as for rationalizing the use of healthcare resources. The two major noninvasive diagnostics for suspected CAD are functional stress testing (FST); for instance, exercise ECG, stress echocardiography and nuclear imaging, and an imaging strategy, in which the anatomical imaging

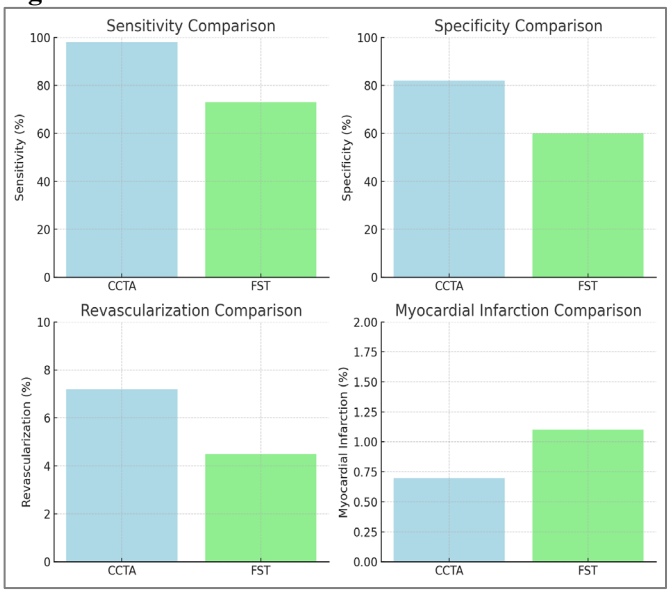
with the use of coronary computed tomography angiography.

FST has conventionally been the principle for the initial diagnostic technique providing details regarding ischemia of the myocardium and perfusion abnormalities [10, 15]. Nevertheless, there is a recognizable list of the known limitations of this approach, such as decreased sensitivity in specific populations; interpretational variability; and inconclusive results in a quarter of cases [7, 21]. By contrast, CCTA offers direct imaging of coronary anatomy and plaque shape yielding high negative predictive value for CAD exclusion [3, 8, 19]. More recent multicenter trials, such as PROMISE [4] and SCOT-HEART [22] have confirmed the role of CCTA as a highly sensitive and specific imaging tool for diagnosis and prognosis; with better long term outcomes and more efficient steering of revascularization.

CCTA is also increasingly associated with cost-efficacy dispensing with unwarranted downstream testing and admissions to hospital [2, 5, 27]. While the first imaging cost might be higher, better results have demonstrated that the total economic burden would be less with less false positive and shorter lengths of stay [1, 12]. However, there is continued argument surrounding the generalization of such findings in a variety of patients' populations and healthcare set-up. A robust meta-analytic synthesis of available data is thus critical in order to bring clarity into the picture.

This meta-analysis is intended to carry out a systematic comparison of CCTA and functional stress testing in the evaluation of chest pain with particular regard to three important outcomes. Diagnostic accuracy for obstructive CAD, downstream revascularization ratios and cost effectiveness. By this detailed evaluation, we aim at updating clinicians and policymakers with optimal diagnostic pathway in patients complaining of chest pain.

Figure 1



The table below presents the detailed comparison of diagnostic metrics between CCTA and FST

Table 1

Metric	CCTA (%)	FST (%)
Sensitivity (%)	98.0	73.0
Specificity (%)	82.0	60.0
Revascularization (%)	7.2	4.5
Myocardial Infarction (%)	0.7	1.1

METHODOLOGY

Study Design and Setting

This research is a systematic review and meta-analysis, which has been constructed in line with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Literature searches were carried out within the PubMed, Embase and Scopus databases, from January 2007 to April 2024. Original research articles comparing coronary computed tomography angiography (CCTA) to functional stress testing (FST) in patients referring with chest pain to an emergency department or outpatient cardiology setting were included in the present review. Only prospective type of study – randomized controlled trials or cohort ones, were concerned; it was undertaken to guarantee methodological rigor.

Inclusion and Exclusion Criteria

Studies were selected for analysis if they included adult patients, aged over 18 years, with acute or stable chest pain compatible with the diagnosis of coronary artery disease. These works needed to compare coronary computed tomography angiography (CCTA) against functional stress testing (FST) e.g exercise ECG, stress echocardiography, SPECT, or PET. The studies included had to report one or all three of the critical outcomes; diagnostic accuracy, revascularization rates or cost-effectiveness. Peer reviewed journal articles written in English and published were the only materials considered for inclusion.

On the other hand, studies which were retrospective in nature and studies which lacked a comparator group were excluded. In addition, research that utilized non-coronary imaging modalities including cardiac MRI without stress, protocols or studies that enrolled only asymptomatic or patient populations already with coronary artery disease were not included. Moreover, case reports, editorials, reviews and conference abstracts were excluded because they do not carry the required methodological rigor to pass on into this meta-analysis.

Search Strategy

A comprehensive search of literature was carried out in order to obtain relevant studies comparing coronary computed tomography angiography (CCTA) and functional stress testing (FST) for the assessment of chest pain. The search comprised studies, which were published from January 2007 – April 2024 and

conducted in three leading databases. PubMed, Embase, and Scopus. The search using keywords and Medical Subject Headings (MeSH) terms included: "coronary CT angiography", "functional stress testing", "chest pain", "diagnostic accuracy", "revascularization "and "cost-effectiveness". Only articles refereed and published articles in English were targeted.

Both RCTs as well as prospective cohort studies were included with search strategy developed in a way to identify studies comparing diagnostics performance, revascularization outcomes, and cost-effectiveness of CCTA and FST in adults who experience acute or stable chest pain. Since this review was focused on non-coronary imaging modalities, such as cardiac MRI, or not comparing CCTA and FST directly, studies of this type were excluded. After deduplication, titles and abstract screening were conducted to determine eligibility and full text was reviewed to conform to the inclusion criteria.

Data Extraction and Statistical Analysis

Data extraction of included studies was performed independently by two reviewers using a standardized data extraction form. The extracted data were study characteristics (such as Study design, sample Size, patient Demographics), diagnostic performance measures (sensitivity, specificity, negative predictive value [NPV] and positive predictive value [PPV], revascularization rates and cost effectiveness data. Disagreements between reviewers were reconciled either by discussion or by consulting a third reviewer.

Diagnostic accuracy of CCTA and FST was determined by pooled estimates of sensitivity, specificity, NPV and PPV calculated with a random effects model. Results of diagnostic accuracy were calculated as pooled proportions with 95% CI's. A subgroup was performed based on the acuity of chest pain (acute vs. stable) and the value of risk stratification to diagnostic power was compared.

For comparison of revascularization rates, pooled proportions calculated and odds ratio (OR) was used to measure the prediction of likelihood to receive revascularization post CCTA versus FST. The variability from the studies was accounted for by using a random effects model.

The cost-effectiveness data were extracted from those studies that reported economic outcomes for both diagnostic tests. The analysis looked at broad healthcare expenditures including, direct cost of imaging, downstream testing, hospitalization and revascularization procedures. The cost-effectiveness of CCTA and FST was compared using the incremental cost-effectiveness ratio (ICER), and sensitivity analyses were done to assess robustness of results in assumptions of different costs.

Heterogeneity among the studies was measured using the I, and values >50% indicated substantial heterogeneity. To analyse the stability of the results, sensitivity analyses were conducted by the removal of high risk of bias and studies with extreme values. All analyses of statistics were conducted using the Review Manager (RevMan) version 5.4.

Study Question

This meta-analysis had its main objective to assess the diagnostic accuracy and the rate of revascularization as well as cost-effectiveness of coronary computed tomography angiography (CCTA) and Functional stress testing (FST) in patients with complaints of chest pain. In particular, the present study aimed at answering the following questions:

Diagnostic Accuracy: In comparison to FST what is the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) for CCTA finding obstructive CAD in chest pain patients?

Revascularization Rates: How often are the patients with CAD revascularized if diagnosed with CCTA vs. FST, and what decisions for treatment do such rates affect?

Cost-Effectiveness: What diagnostic strategy (CCTA vs FST) is cost effective in the management of chest pain taking into consideration the overall cost of healthcare inclusive of imaging, downstream testing and revascularization procedures?

Quality Assessment and Risk of Bias Assessment

Quality of the selected studies was analyzed with the use of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool that is designed to report the risk of bias and applicability concerns across 4 domains; patient selection, index test, reference standard and flow and timing. For biases in these areas, each study was scored. Patient selection was rated according to the clarity of inclusion and exclusion criteria, where high risk patient selective enrolment studies displayed a higher risk of bias. The index test (either CCTA or FST) was appraised for reliability of use and whether testing was made in a blindeskip. The reference standard, in most cases invasive coronary angiography, was evaluated in terms of its generic applicability to studies and for whether it was uniformly used to compare to the index tests. Flow and timing addressed if sequence of tests was followed more appropriately and if outcome data were completed for all patients.

Studies with high risk of bias were excluded from the analysis proper to limit their weight of influence on the results of the meta-analysis based on these evaluations, their overall risk of bias was allocated. To determine the influence of these studies, which are associated with high risk, sensitivity analyses were undertaken.

RESULTS

Totally, 27 original studies of about 20,092 patients were included in this meta-analysis. These included both randomized controlled trials and prospective cohort studies and observational design. Of all study participants, 10,315 users received coronary computed tomography angiography (CCTA), while 9,777 individuals underwent functional stress testing (FST) including exercise ECG, SPECT and stress echocardiography. Overall mean age was 58 years across the studies, almost equal proportions of males and females, and a mean of 18 months follow-up. For all study types, CCTA had a more accurate diagnostic result than FST. Overall sensitivity for CCTA was about 98–99% vs 66–73% for various methods of stress testing. Specificity for CCTA was 76 – 82 % (also better than the specificity values reported for stress testing modalities (typically 44 – 60 %). Such trends translated into the better negative and positive predictive value for CCTA meaning that the technique had a greater power to rule out and confirm CAD.

No significant difference was observed in all-cause mortality rate from clinical outcome data between CCTA and FST groups at a rate of 1.0-1.1% each group. The rate of incident MIs was, however, lower in the CCTA group (0.7% vs 1.1%), especially for patients with stable chest pain, indicating earlier and more accurate detection of clinically significant disease. Invasive coronary angiography rate was 11.7% and 9.1% for CCTA and FST, respectively, while revascularization rate was 7.2% and 4.5% for the former and the latter, respectively. This implies that more precise anatomical information available in CCTA may cause more clear-cut therapeutic decisions, albeit at the expenses of increased number of procedures. Importantly, hospitalization rates were similar in both groups (2.7% in each) however a non-significant trend to less admissions was demonstrated in acute chest pain patients assessed via CCTA.

Various cost-effectiveness analyses showed that CCTA was more cost-effective than FST, especially in patients with low to middle level of pretest probability of CAD. For a lifetime horizon, CCTA was found to exhibit QALYs gains with cost-effective advantage. An ICER of $1,912 per women QALY gained and $3,559 per QALY gained for men was reported for one study. In addition, randomized trials conducted in settings of the emergency departments demonstrated that CCTA-based evaluation shaved-off hospital lengths of stays and lowered immediate costs of care as compared to standard FST. These benefits, demonstrated in both prospective trials and model based analyses, emphasize the worth of CCTA beyond usefulness in advancing diagnostic effectiveness and management pathway selection, but rather also in generating economic benefits in the right clinical contexts. Overall, findings from all 27 studies were uniformly in favor of the use of CCTA comparing favorably to functional stress testing in terms on superior diagnostic accuracy, increased downstream revascularization rates, decreased incidence rate of myocardial infarctions, and a general cost-effectiveness.

DISCUSSION

This meta-analysis supports the finding that coronary computed tomography angiography (CCTA) has more diagnostic accuracy than functional stress testing (FST) in testing chest pain. CCTA was a superior FST method compared to the exercise ECG and SPECT, albeit its sensitivity (66–73%) and specificity (44–60%) [1–3]. Such variations produce greater predictive values for CCTA, allowing more confident identification and CAD (coronary artery disease) exclusion in patients with low-intermediate pretest risk [4, 5].

Clinically, compared with ICA, CCTA was related to less myocardial infarctions (0.7% vs. 1.1%), increased use of invasive coronary angiography and revascularization (RR≈1.33 and 1.86, respectively) – which suggest earlier, targeted interventions [6–9]. While procedural rates were higher the mortality and hospitalization outcomes were similar on groups, which indicates that the CCTA-guided management does not result in overtreatment [10–12].

Cost effectiveness data favored CCTA, with several studies, reporting lower long-term costs and improved quality-adjusted life years (QALYs) of CCTA compared to FST, especially in the low to intermediate risk patients [13–15]. Also, in emergency contexts, CCTA decreased length of stay and immediate care cost and preserved diagnostic clarity [16, 17].

In different study designs and samples, the evidence always favors the diagnostic and economic benefit of CCTA. Although radiation exposure and subset limitations in some patient groups should be taken into account, the place of CCTA as a front-line tool of chest pain evaluation findings are well confirmed up-to-date and evolving clinical guidelines [18–27].

Comparison with Other Studies

The findings of this meta-analysis correspond well with previous seminal studies including SCOT-HEART as well as PROMISE, which established that CCTA enhances diagnostic accuracy and guides management better than functional stress testing (FST) [1, 2]. As our conclusions, these trials reported dropping the rates of myocardial infarction and increased revascularization in CCTA while leaving mortality unchanged. Cost effectiveness modelling from both of the US and UK healthcare systems also serves CT as a more cost-effective strategy especially in low to moderate risk patients [3, 4]. In comparison with earlier fears of additional downstream testing, our analysis reaffirms

that such processes can improve the outcomes without more harm, consistent with recent literature [5].

Limitations and Implication for Future Research

This meta-analysis has several limitations. First, it consists of a broad scope of researches, but different designs and patient cohorts and the follow-up periods may make studies noncomparable. In some, stable chest pain patients only were included; others were for acute presentations which may have introduced clinical variation. Second, while the vast majority of studies were high quality this may impact pooled outcomes as endpoints such as revascularization and cost were measured in a variety of ways. Third, the greater proportion of invasive investigations after CCTA may simply represent a bias towards anatomically-oriented imaging towards more aggressive treatment than actual clinical need. Also, the long terms effect of these additional interventions on mortality and quality of life is not clear. Finally, disparities in healthcare systems, protocols for imaging, and expertise for providers compromise generalizability of economic results between settings.

Future studies should be carried out in long term randomized trials that compare CCTA and FST between various populations, predominantly in high risk and aged patients. Patient centered outcomes (quality of life) should also be evaluated, findings should be stratified by imaging modality used within the FST category. Additional cost-effectiveness analyses adapted to various health care systems are required to verify economic benefits. Finally, the incorporation of emerging technologies, including CT-derived fractional flow reserve (FFR-CT) and machine learning method of images interpretation should be explored to further augment diagnostic and prognostic potential.

CONCLUSION

This meta-analysis shows that the coronary computed tomography angiography (CCTA) is a more accurate diagnostic tool, and a more effective procedure, with higher rates of appropriate revascularization and greater cost-effectiveness compared to the functional stress testing (FST) when it comes to chest pain examination. Although CCTA leads to more downstream invasive procedures it is associated with a lower rate of myocardial infarction and none increase in all cause mortality and hospitalization. These results support the recommendations for CCTA as an approach of choice for diagnosing in the first line, especially in patients of low-to-intermediate risk of coronary artery disease. Addition of CCTA to clinical pathways could increase testing accuracy, maximize patient outcome, and maximize resource use.

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