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Research paper

Diagnostic accuracy of static CT perfusion for the detection of myocardial ischemia. A systematic review and meta-analysis



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ABSTRACT

Objectives: The aim of this study is to provide a meta-analysis of all published studies assessing the diagnostic accuracy of stress CT myocardial perfusion imaging (CTP) in patients suspected of or with known coronary artery disease. This analysis is limited to static stress CTP.

Methods: Systematic literature review and meta-analysis of studies examining the diagnostic accuracy of static CTP imaging alone or combined with coronary CT angiography (CTA) in comparison to single photon emission computed tomography (SPECT), magnetic resonance perfusion (MRP), and/or invasive coronary angiography with and without fractional flow reserve (FFR).

Results: The search revealed 19 eligible studies including 1188 patients. Pooled results showed that CTP had a good agreement with SPECT and MRP. On a per-patient level, sensitivity, specificity and AUC were 0.85 (95% CI: 0.70–0.93), 0.81 (95% CI: 0.59–0.93), 0.90 (95% CI: 0.87–0.92). On a per-artery level, sensitivity, specificity and AUC were 0.80 (95% CI: 0.67–0.88), 0.81 (95% CI: 0.72–0.88) and 0.87 (95% CI: 0.84–0.90). When invasive coronary angiography was used as reference standard, combined coronary CTA and CTP compared to coronary CTA alone significantly improved the specificity from 0.62 (95% CI: 0.52–0.70) to 0.84 (95% CI: 0.74–0.91) on a per-patient level (p = 0.008) and from 0.72 (95% CI: 0.63 –0.79) to 0.90 (95% CI: 0.85–0.93) on a per-artery level (p = 0.0001) without significant decrease in sensitivity (p = 0.59 and p = 0.23, respectively).

Conclusion: In selected patients, static CT myocardial perfusion has high diagnostic accuracy to detecting myocardial ischemia. Specificity increases significantly when CT myocardial perfusion is combined with coronary CTA.

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Abbreviations: CAD, coronary artery disease; CTA, computed tomography angiography; CT, computed tomography; CTP, computed tomography perfusion; FFR, fractional flow reserve; MRP, magnetic resonance perfusion; NPV, negative predictive value; PPV, positive predictive value; SPECT, single photon emission computed tomography.

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1. Introduction

In current guidelines for the identification and management of patients suspected of stable coronary artery disease (CAD), coronary CT angiography (CTA) is included among recommended diagnostic methods. Coronary CTA has a high diagnostic accuracy for ruling out coronary artery stenoses compared to invasive coronary angiography as clinical reference method. However, the diagnostic specificity and positive predictive value of coronary CTA is only moderate. On one hand, coronary CTA tends to overestimate stenosis degree and on the other, it does not provide

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information about the hemodynamic relevance of coronary artery stenoses, particularly intermediate coronary lesions, where accurate functional assessment is required to determine the indication for revascularization. Accordingly, several studies have investigated the feasibility and the diagnostic accuracy of static stress CT myocardial perfusion imaging (CTP) combined with coronary CTA for the assessment of myocardial ischemia related to stenotic coronary lesions. The published CTP studies up to date comprise a large number of small size single-center studies and one multicenter study and they have used a variety of CT scanners and different reference methods.^{4–8} An summarized appraisal of the results of these studies may hence be useful to determine the overall diagnostic accuracy and to assess a possible clinical role of this novel diagnostic approach.

This systematic review and meta-analysis aimes to summarize all published studies on this subject and pool as much extractable data as possible in order to evaluate the diagnostic accuracy of static CTP both in isolation as well as in combination with coronary CTA, in comparison to clinically established reference methods.

2. Materials and methods

2.1. Search strategy

No industry support was provided for this systematic review and meta-analysis which was conducted according to the PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions (Preferred Reporting Items for systematic review and Meta-analysis). A search through the electronic databases PubMed, EMBASE, and Cochrane library from January 2005 to August 2014 was performed. Published studies that examined the diagnostic accuracy of CTP in patients suspected of or with known CAD compared to SPECT, MRP, invasive coronary angiography and FFR were sought. The following keywords in different combinations were used: computed tomography, angiography, coronary artery and myocardial perfusion. All relevant published systematic reviews and meta-analyses on CTP were identified and their reference lists were screened. Reference lists of the retrieved articles were screened as well.

2.2. Study eligibility

Only original research papers using static CTP on patients suspected of or with known CAD and comparing it with SPECT, MRP, FFR alone or SPECT/MRP/FFR combined with invasive coronary angiography, or invasive coronary angiography alone, were included. Only studies, using newer CT generations with at least 64 detectors, that compared coronary CTA/CTP diagnostic accuracy with the above mentioned methods as standard references, were included. Eligible studies had to provide diagnostic accuracy measurements and absolute numbers of diagnostic accuracy tests using 2×2 tables for each comparison. In studies where a combined index test of coronary CTA and CTP was used the adjudication criteria for a positive test needed to be defined as a coronary CTA with a luminal stenosis of \geq 50% and a corresponding perfusion defect by CTP. This should also be the case for studies using a combined reference standard of invasive coronary angiography in combination with either FFR, SPECT or MRP where a positive reference standard needed to be defined as \geq 50% reduction in diameter using quantitative or visual estimation and invasive FFR with the threshold value of 0.80 or a corresponding perfusion defect by SPECT and MRP. This was also the case in studies including patients with coronary stents. Studies comparing CTP with either SPECT or MRP needed to use reversible perfusion defects of at least 10% as positive test results, and the perfusion defect by the index test had to be located in the same myocardial segments. Studies not providing relevant data on diagnostic accuracy, using older CT generations (16–40 slice) or including less than 20 patients were excluded. Reviews and meta-analyses on CTP were used to screen for eligible studies, no data from these publications were used in this study.

2.3. Data extraction

Demographic, methodological, image acquisition data, numbers of patients and arterial territories, numbers of true positive, false positive, true negative and false negative values were all extracted from each study wherever available. The angiographic results reported either as per-patient or per-artery categories were extracted. Authors of studies with insufficient published data were contacted to provide the missing data. Two authors (MS and JA) conducted the search process, systematic literature review and data extraction. Any conflict was resolved by consensus.

2.4. Study quality assessment

Methodological quality of the selected studies was assessed by Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2). Two authors (MS and JA) independently reviewed all selected studies for fulfillment of the criteria and any disagreement was solved by consensus.

2.5. Statistical analysis

The main analyses were performed using the standard metaanalytic methods for combining data for diagnostic accuracy tests. Analyses were performed to compare the accuracy of coronary CTA/CTP versus SPECT, MRP, FFR and invasive coronary angiography as reference methods. The following accuracy tests were performed: sensitivity, specificity, PPV, NPV, likelihood ratios, diagnostic odds ratio (DOR) and finally summarizing data in summary receiver operating characteristic (SROC) curves with the AUC.¹¹

The homogeneity among studies was tested by chi² test and a pvalue <0.05 indicated significant heterogeneity. We also used inconsistency (I²%) to test inter-study variation attributed to heterogeneity whereas an I² value > 20% indicated significant variation. The data assessing coronary CTA alone compared with combined coronary CTA and CTP were pooled together regardless of the type of reference methods, in order to detect any changes in sensitivity and specificity after addition of CTP. Results of these analyses provided the odds ratios (OR) and theirs p-values for any improvement or worsening in sensitivity and specificity. Unreported standard deviations were calculated and the estimated difference in effective radiation dose between coronary CTA + CTP vs. SPECT was meta-analyzed using weighted mean difference method. Sensitivity analyses were performed by step-wise exclusion of large-size studies. All p-values <0.05 were considered significant. All diagnostic accuracy meta-analyses, meta-regression and plots were performed using midas module for meta-analytical integration of diagnostic accuracy tests in STATA version 13 MP (STATA Corporation, Lakeway Drive, College Station, Texas, USA).

3. Results

3.1. Search results

The search strategy and results are shown in Fig. 1. Authors of six studies^{4,5,7,8,12,13} provided supplementary unpublished data for the completeness of the analyses.

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