



## Research paper

## CT myocardial perfusion and coronary CT angiography: Influence of coronary calcium on a stress–rest protocol



Ricardo Ladeiras-Lopes <sup>a, b, \*, 1</sup>, Nuno Bettencourt <sup>a, b, 1</sup>, Nuno Ferreira <sup>a, b</sup>,  
Francisco Sampaio <sup>a, b</sup>, Gustavo Pires-Morais <sup>a</sup>, Lino Santos <sup>a</sup>, Bruno Melica <sup>a</sup>,  
Alberto Rodrigues <sup>a</sup>, Pedro Braga <sup>a</sup>, Adelino Leite-Moreira <sup>b</sup>, José Silva-Cardoso <sup>b</sup>,  
Vasco Gama <sup>a, b</sup>

<sup>a</sup> Department of Cardiology, Gaia Hospital Centre, Vila Nova de Gaia, Portugal

<sup>b</sup> Cardiovascular Research and Development Centre, Faculty of Medicine of the University of Porto, Porto, Portugal

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## ABSTRACT

**Background:** High amounts of coronary artery calcium limit image quality and diagnostic accuracy of multidetector computed tomography (MDCT) angiography (CTA) regarding the assessment of obstructive coronary artery disease (CAD). CT myocardial perfusion imaging may represent an opportunity to overcome this limitation.

**Objective:** To explore the additive value of CT myocardial perfusion to CTA depending on the patient's calcium score and in comparison to the reference standard of invasive coronary angiography plus fractional flow reserve (FFR) measurement.

**Methods:** Symptomatic patients with intermediate pretest probability of CAD were prospectively recruited and underwent both cardiac MDCT (64-slice scanner, retrospectively-gated stress–rest protocol) and invasive coronary angiography including FFR assessment. We defined hemodynamically significant CAD by the presence of occlusive or subocclusive (99%) stenosis, >50% stenosis in left main or  $FFR \leq 0.80$ . Stress CT myocardial perfusion imaging was performed in all patients in addition to CTA. The additive value of CT myocardial perfusion to rule in or rule out the presence of hemodynamically relevant stenosis on a per-patient basis was assessed and analyzed relative to the patient's calcium score.

**Results:** 95 patients were included in the analysis ( $62 \pm 8.2$  years, 68% males). Hemodynamically significant CAD was present in 42 patients. Sixty-four patients had a fully evaluable CTA examination. Per-patient, CTA alone had a sensitivity, specificity and AUC of 100%, 59% and 0.79 respectively (77% patients correctly classified). Adding CT myocardial perfusion to evaluate uninterpretable vessel territories in CTA in 66 patients with a calcium score >100 yielded a sensitivity of 88%, a specificity of 74% and an AUC of 0.81 (81% patients correctly classified), and in 52 patients with a calcium score >400 sensitivity was 91%, specificity 70%, and AUC 0.80 (82% patients correctly classified,  $p = 0.733$  versus using perfusion imaging in all patients).

**Conclusions:** From a pragmatic standpoint, limiting the use of CT perfusion to individuals with a calcium score above 400 might be a feasible strategy to optimize the diagnostic accuracy of CT imaging for diagnosis of obstructive CAD.

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**Abbreviations:** AUC, area under the curve; CAC, coronary artery calcium; CAD, coronary artery disease; CTA, computed tomography angiography; CTP, myocardial CT perfusion angiography; hsCAD, hemodynamically significant coronary artery disease; MDCT, multidetector computed tomography; FFR, myocardial fractional flow reserve.

\* Corresponding author. Department of Cardiology, Gaia Hospital Centre Rua Conceição Fernandes, 4434-502, Vila Nova de Gaia, Portugal.

E-mail address: [ricardoladeiraslopes@gmail.com](mailto:ricardoladeiraslopes@gmail.com) (R. Ladeiras-Lopes).

<sup>1</sup> These authors equally contributed to this work.

## 1. Introduction

Coronary CTA is a robust non-invasive imaging method to exclude obstructive CAD in symptomatic patients with low to intermediate pre-test probability.<sup>1</sup> However, the presence of coronary artery calcium impairs the diagnostic accuracy of CTA, especially in older patients with multiple cardiovascular risk factors and high calcium scores.<sup>2</sup> In these patients, stress-rest CTP protocols

improve the diagnostic accuracy of CT to detect hemodynamically significant CAD (hsCAD).<sup>3</sup> Therefore, adaptation of the CT protocol according to the calcium score may provide a way of decreasing non-diagnostic exams and collecting more information on functional significance of the coronary lesions.

This study aims to explore the additive value of CT myocardial perfusion to CTA depending on the patient's calcium score and in comparison to the reference standard of invasive coronary angiography plus fractional flow reserve (FFR) measurement.

## 2. Technical methods

### 2.1. Population

Patients referred to our cardiology outpatient clinic for assessment of CAD during a 2-year period were prospectively screened. To be included, patients would need to be more than 40 years old, have a history of symptoms suggestive of CAD, have at least 2 cardiovascular risk factors or a positive/inconclusive treadmill test and an intermediate pretest probability of CAD, according to the modified Diamond-Forrester model. Using this updated model for calculation of pretest probability of CAD, dyspnea was classified as atypical chest pain.

Fig. 1 shows the selection of participants for inclusion in the study, as well as the exclusion criteria. The final population consisted of 95 individuals. This study protocol was approved by the Local Ethics' Committee. Written informed consent was obtained from all participants.

### 2.2. MDCT stress–rest protocol

All patients included in the study underwent stress–rest CT

coronary angiography as previously described, using a Somatom Sensation 64 scanner (Siemens Medical Solutions, Forchheim, Germany).<sup>3</sup> No pre-test medication was administered.

After scout images, patients underwent a low-dose prospective scan (tube voltage 120 kV; tube current 190 mAs) to assess coronary calcium using established protocols.<sup>4</sup> A retrospectively gated scan during the first passage of contrast medium (iopromide, 80 ml, at 4.5 ml/s) under adenosine infusion ( $140 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  for 3 to 6 min) was obtained (tube voltage: 100 kV; tube current modulation with full tube current [600 mAs] applied at 60% to 65% of the RR interval; collimation,  $64 \times 0.6 \text{ mm}$ ). After an interval of 10 minutes, a rest scan was acquired, using prospective triggering (65% of R-R interval; 100 kV; 110 mAs). For the latter, intravenous beta-blockade was used as needed (2.5 to 20 mg metoprolol, targeting a heart rate  $\leq 60$  beats/min) and all patients received 0.5 mg of sublingual nitroglycerine.

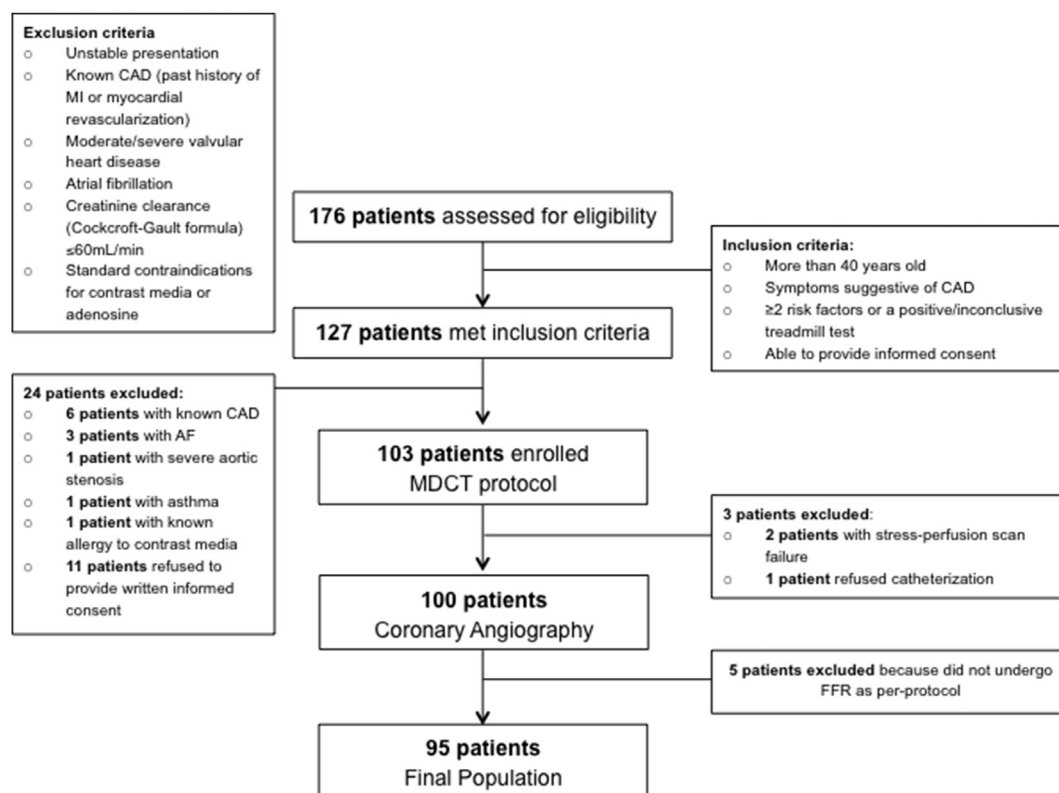
### 2.3. MDCT image analysis

#### 2.3.1. Coronary artery calcium quantification

Image reconstruction of the calcium score acquisition was performed using an effective slice thickness of 3 mm. Coronary calcification was quantified using the Agatston score with a detection threshold of 130 HU.<sup>4</sup>

#### 2.3.2. CT angiography

For CTA analysis, both stress and rest contrasted acquisitions were used. From the stress acquisition, a set of 10 (5% to 95%) plus 1 (60%) phases was reconstructed using a standard soft frequency cardiac filter (Siemens-B25f), with a slice-thickness of 0.6 mm. From rest, a single-phase (65%) reconstruction was obtained using the same slice thickness and filter. Resulting datasets were



**Fig. 1.** Study flow chart. From the 176 patients assessed for eligibility, the final population of patients that underwent MDCT and invasive coronary angiography included 95 patients. AF – atrial fibrillation; CAD – coronary artery disease; FFR – fractional flow reserve; MDCT – multidetector CT; MI – myocardial infarction.

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