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Research paper

Rationale and design of the PERFECTION (comparison between stress cardiac computed tomography PERfusion versus Fractional flow rEserve measured by Computed Tomography angiography In the evaluation of suspected cOroNary artery disease) prospective study

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ABSTRACT

Background: Non-invasive stress tests are commonly used as gatekeepers to invasive coronary angiography (ICA) in patients with suspected coronary artery disease (CAD). New computed tomography angiography (CTA) techniques such as fractional flow reserve calculated by CTA (FFR_{CT}) and stress myocardial computed tomography perfusion (CTP) have emerged as potential strategies to combine anatomical and functional evaluation of CAD in one technique. The aim of this study is to compare per-vessel diagnostic accuracy of FFR_{CT} versus stress myocardial CTP for the detection of functionally significant coronary artery disease (CAD), using invasive FFR as the reference standard.

Methods: Subjects with suspected CAD due to chest pain who have no contra-indications to FFR_{CT} or stress myocardial CTP and who are referred for non-emergent, clinically indicated invasive coronary angiography (ICA), will be enrolled. A total of 300 subjects will be enrolled within 24 months.

Results: The primary study endpoint will be the comparison of per-vessel diagnostic accuracy of CTA versus FFR_{CT} versus stress myocardial CTP for the diagnosis of hemodynamically significant stenosis as defined by invasive FFR $\leq$0.80.

Conclusions: In the PERFECTION study, the comparison between FFR_{CT} and stress myocardial CTP will provide understanding about which technology is more accurate for the diagnosis of functionally significant CAD.

1. Introduction

Non-invasive stress tests are used as gatekeepers to invasive coronary angiography (ICA) in patients with suspected coronary artery disease (CAD). New computed tomography angiography (CTA) techniques such as fractional flow reserve measured by CTA (FFR_{CT})[1–4] and stress myocardial computed tomography perfusion (CTP)[5–7] have recently emerged as potential strategies to combine anatomical and functional evaluation in one technique.[8] The aim of this study is to compare the diagnostic accuracy of FFR_{CT} versus stress myocardial CTP for the detection of functionally significant CAD, using invasive FFR as the reference standard.

Abbreviations list: BPM, beat per minute; CAD, coronary artery disease; CTA, computed tomography angiography; CTP, computed tomography perfusion; ED, effective dose; FFR, fractional flow reserve; FFR_{CT}, fractional flow reserve measured by computed tomography angiography; HR, heart rate; MBF, myocardial blood flow; QCA, quantitative coronary angiography; TPR, transmural perfusion ratio.

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2. Technical methods

Symptomatic subjects with suspected CAD and no contra-indications to FFR_{CT} or stress myocardial CTP and who are referred for non-emergent and clinically indicated ICA will be enrolled. Fig. 1 and Table 1 shows the study design and exclusion criteria, respectively.

All 300 subjects will receive a rest CTA and stress myocardial CTP. The rest CTA will be used to compute FFR_{CT}. The first 150 subjects will receive a static CTP scan, and the second 150 subjects will receive a dynamic CTP scan. The study protocol has received ethics committee approval and the study has been registered with the number R250/15-CCM 262. Written informed consent will be obtained from all subjects.

Subjects will be asked to refrain from smoking and caffeine for 24 hours and to maintain fasting for 6 hours before the scan. In subjects with a resting HR > 65 bpm before the scan, metoprolol will be administered intravenously with a titration dose up to 15 mg to achieve a target HR $\leq$ 65 bpm. However, no subjects will be excluded based on maximum HR. Before the rest scan, all subjects will receive sublingual nitrates to ensure coronary vasodilatation.

2.1. Rest CTA performance and interpretation

We will perform rest CTA on a 256 detector row scanner capable of whole heart coverage in one beat (Revolution CT, GE Healthcare, Milwaukee, WI). This scan will be completed according to the recommendations of the Society of Cardiovascular Computed Tomography (SCCT).[9] All subjects will receive a 50 ml bolus of Iodixanol 320 (Visipaque 320 mg/ml, GE Healthcare, Oslo, Norway) at an infusion rate of 6.2 ml/s followed by 50 ml of saline solution with a tube voltage and tube current based on BMI of the patient and with a scan window based on heart rate. Data sets of each CTA examination will be transferred to an image-processing workstation (Advantage Workstation Version 4.7, GE Healthcare, Milwaukee, WI) and analyzed. According to SCCT guidelines for reporting,[9] image quality, plaque characteristics and severity of coronary lesions will be evaluated. A stenosis >50% will be considered significant when assessing anatomy in the rest CTA.

2.2. FFR_{CT} performance and interpretation

We will submit all rest CTA datasets to HeartFlow (HeartFlow Inc., Redwood City, CA) for FFR_{CT} analysis.[3,4] A lesion with FFR_{CT} $\leq$0.80 will be considered significant. Fig. 2 shows the details of the FFR_{CT} methodology.

2.3. Stress myocardial static CTP

Fig. 3 shows the stress myocardial CTP acquisition protocol. Vasodilatation will be induced with i.v. adenosine injection (0.14 mg/Kg/min over 4 min). Using the same technique as described for rest CTA, a single stress CTP scan will be acquired during first-pass enhancement. The myocardium will be evaluated on short axis (apical, medium and basal slices) and long-axis views (2-, 3- and 4-chamber projections) with 8-mm thick average multi-planar reformatted images. A narrow window width and level (350 W and 150 L) will be used for perfusion defect evaluation. Each myocardial segment will be correlated to the specific coronary territory as described by Cerci et al.[10] True perfusion defects will be qualitatively defined as subendocardial hypoenhancement encompassing $\geq$25% of transmural myocardial thickness within a specific coronary territory. Additionally, quantitative analysis of the transmural perfusion ratio (TPR) will be performed as previously described.[6] A subject will be defined as positive for myocardial ischemia when the TPR will be <0.99 on stress myocardial static CTP showing worsening as compared with rest CTP in more than one myocardial segment.[6]

2.4. Stress myocardial dynamic CTP

Vasodilatation will be induced with the same protocol described for stress myocardial static CTP. At the end of the third minute of adenosine infusion, multiple sequential scans of myocardial attenuation (one scan every three seconds for a total breath hold of 30 s) will be acquired with the same scan parameters as described for rest CTA. Evaluation of the myocardium will be performed as described for stress myocardial static CTP. In addition, the myocardial blood flow (MBF) will be calculated.[7] A value below 75 ml/100 ml/min will be used to identify hemodynamically

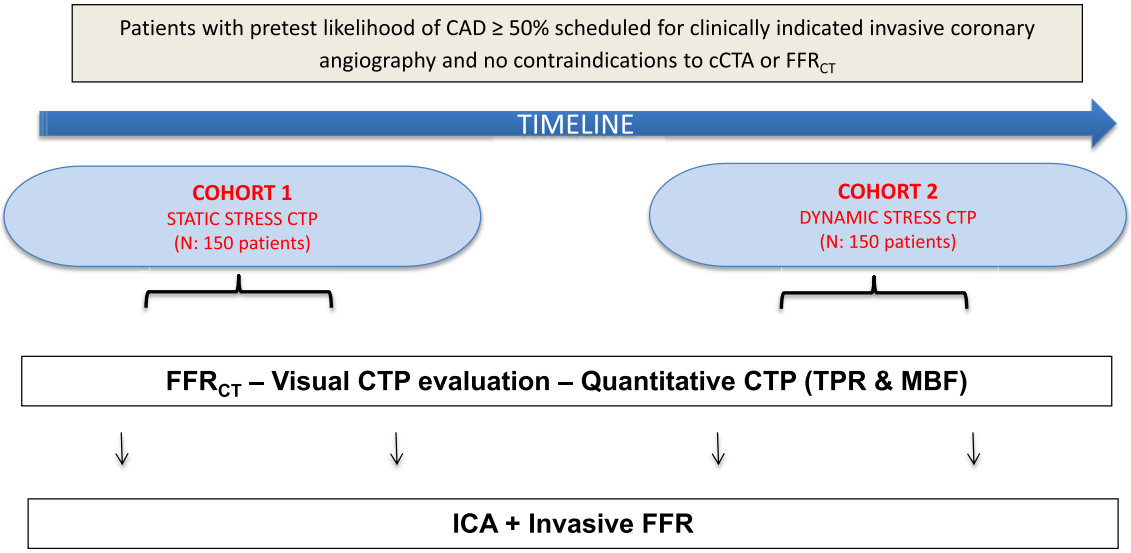

Fig. 1. PERFECTION study workflow. CTP: computed tomography perfusion; FFR: fractional flow reserve; FFR_{CT}: fractional flow reserve measured by computed tomography angiography; ICA: invasive coronary angiography; MBF: myocardial blood flow, TPR: transmural perfusion ratio.