Expert Review of Cardiovascular Therapy

Functional Assessment of Coronary Artery Disease By Cardiac Computed Tomography

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ABSTRACT

Introduction: Rapid technological advances in computed tomography (CT) have allowed CT coronary angiography (CTCA) to be delivered at low radiation dose and high diagnostic accuracy. Due to its high negative predictive value for coronary artery disease, it has become a gatekeeper for the assessment of patients with chest pain of recent onset. Second line functional assessment of a detected coronary stenosis relies mostly on other imaging modalities. Functional assessment of coronary artery disease by CT is therefore an attractive addition to CTCA.

Areas covered: This review will discuss the current evidence base and future development for CT perfusion imaging. Furthermore, this review will discuss CT-derived fractional flow reserve and CT coronary plaque characteristics as alternative approaches for functional evaluation of coronary artery disease. Finally, combining coronary anatomy and functional assessment of coronary flow with myocardial tissue characterization by CT may be attractive allowing triple assessment by CT.

Expert commentary: The combined use of CTCA and functional assessment of coronary artery stenosis by CT perfusion or CT-derived fractional flow reserve is an attractive diagnostic pathway that requires further evaluation.

Keywords: cardiac computed tomography, myocardial perfusion imaging, CT FFR

ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

CCO = corrected coronary opacification

CMR = cardiovascular magnetic resonance

CCT = cardiac computed tomography

CTCA = computed tomography coronary angiography

CTP = computed tomography perfusion

FFR = fractional flow reserve

HU = Hounsfield units

MBF = myocardial blood flow

SPECT = single-photon emission computed tomography

TAG = transluminal attenuation gradients

1. Introduction

Computed Tomography Coronary Angiography (CTCA) has undergone a transformation over the last decade encompassing significant technological advances in scanner technology and was followed by investment in post processing and emergence of outcome data. The Prospective Multicenter Imaging study for Evaluation of chest pain (PROMISE) [1] and the Scottish COmputed Tomography of the HEART (SCOT-HEART) [2] trials have provided not only outcome data, but also insights into diagnosis and management of patients with stable chest pain, and make a case that CTCA should have a greater role in the diagnostic pathway for stable chest pain [3]. Furthermore, the European multi-center study EValuation of Integrated Cardiac Imaging (EVINCI) showed that CTCA was more accurate than noninvasive functional testing for detecting angiographically demonstrated, significant coronary artery disease (CAD) [4]. American and European guidelines have placed CTCA firmly into the diagnostic pathway for stable CAD [5, 6]. To date, the UK has gone the furthest; the recent guidelines for the management of stable chest pain of recent onset by the National Institute of Health and Care Excellence (NICE) have made CTCA the gatekeeper for the investigation of CAD [7]. NICE guidelines now recommend CTCA as the first line investigation for patients with stable chest pain, and have relegated functional imaging (stress echocardiography, cardiovascular magnetic resonance or radionuclide myocardial perfusion imaging) and invasive coronary angiography as second- and third-line investigations, respectively, if diagnostic doubts persist after CTCA. The primary driver for these recommendations is the excellent negative predictive value (>90%) of CTCA, i.e. the ability to rule out CAD [8, 9, 10]. However, the positive predictive value of CTCA is limited in particular in the presence of dense coronary artery calcification [11] and residual

motion artifacts in the image dataset [12]. These result in false positive finding or inconclusive results, and may lead to unnecessary downstream testing. Moreover, clinical decision-making for myocardial revascularization is linked to the presence of myocardial ischemia given that no prognostic benefits of myocardial revascularization have been shown in the absence of a functionally significant coronary stenosis (FAME 1 and FAME 2 studies) [13, 14]. Pure anatomical evaluation of stenosis severity does not inform about the hemodynamic effects of a given coronary stenosis: as reported by Tonino et al., 20% of coronary stenoses visually scored as having >70% diameter reduction did not cause myocardial ischemia [15].

CT can evaluate the functional significance of a coronary stenosis by using two major approaches: CT myocardial perfusion imaging (CTP) and non-invasive CT-derived fractional flow reserve (FFR_{CT}). In addition, CTCA provides information on plaque characteristics and plaque burden that have been shown to be associated with lesions causing ischemia, independently from stenosis severity.

The combined use of anatomical information (stenosis severity and plaque characteristics) from CTCA and functional assessment of coronary artery stenosis by CTP or FFR_{CT} is an attractive diagnostic pathway. This review will present a summary of the current evidence in this field.

1.1 Myocardial perfusion imaging

Functional assessment of CAD by radionuclide single-photon-emission CT (SPECT), positron-emission tomography (PET) or cardiovascular magnetic resonance (CMR) perfusion are established in international guidelines [5, 6]. Whereas functional assessment can be performed during exercise (physical stress), in the majority of cases it is performed using pharmacological vasodilator stress. These modalities share

therefore common key requisites. The physiological principle underlying the need to administer a vasodilator stress to detect ischemia is the differential myocardial perfusion between coronary territories supplied by vessels with flow limiting CAD and the remote myocardium during maximal vasodilator stress (hyperemia). The most widely used agents for myocardial perfusion imaging are adenosine (a non-selective A2A receptor agonist used as an infusion for 3-6 minutes), dipyridamole (reduces the cellular uptake and break-down of adenosine) and regadenoson (a selective A2A receptor agonist). The advantages of using regadenoson are ease of administration (given as a intravenous bolus) and a better safety profile in asthma and chronic obstructive pulmonary disease [16, 17]. All three agents increase coronary blood flow by 3.5-4 folds by stimulating the adenosine A2A receptors. Caffeine and other methylxanthine derivatives are nonspecific antagonists of all adenosine receptors sub-types, therefore patient preparation includes prior instruction to avoid these for 12-24 hours prior to the scan [18, 19]. Furthermore, prior to use, patients need to be screened for the presence of contra-indications to stress with adenosine receptor agonists (unstable angina, acute coronary syndrome, acute myocardial infarction, congestive heart failure, severe LV dysfunction, critical aortic stenosis, asthma or severe chronic obstructive pulmonary disease, 2° degree Mobitz type II or 3° degree atrioventricular block).

2. CT perfusion

CTP imaging was first attempted in resting conditions in the 1970s [20]. Only recent technological developments of multidetector scanners with vast improvements in temporal resolution and volume coverage, as well as the reduction in scan time, contrast and radiation dose, have made CTP suitable for clinical application. There are key prerequisites for successful myocardial CTP imaging [21], most of which are

shared with CTCA. The highest possible *temporal resolution* is needed to reduce cardiac motion artifacts and partial volume effects of the myocardial border, because an increase of the baseline heart rate of at least 10-20% should be expected with vasodilator stress. The introduction of 64-detector CT scanners (temporal resolution of up to 165 msec) and dual source scanners (temporal resolution of 83 msec [first generation], 75 msec [second generation], 66 msec [third generation]) have made scanning at higher heart rates and dynamic acquisitions possible. CT technology has also introduced higher *spatial resolution* compared with other myocardial perfusion imaging modalities, therefore allowing the assessment of subendocardial versus subepicardial myocardial perfusion. A key challenge and limitation of CTP is a relatively poor *contrast resolution*, with a contrast difference in the range of 17-50 Hounsfield units (HU) between normal and hypo-perfused myocardium [22, 23]. As lowering the tube voltage below the standard value of 120kV increases the attenuation of iodine, adjusting the tube voltage (in keeping with the patient's body size) is recommended to obtain maximum attenuation difference where possible (i.e. 70-80kV for BMI<25, 100kV for BMI 25-30 and 120kV or higher for BMI>30). Finally, the *volume coverage* along the z-axis should include the whole heart. Current 320-detector scanners provide a craniocaudal coverage of 16 cm per gantry rotation, with a temporal resolution of 137ms. An alternative solution for CTP has been incorporated into dual source CT, with a technique called prospectively ECG-triggered axial shuttle mode. The table moves back and forth between two scanning positions. Contemporary dual source CT scanners offer temporal resolution and spatial coverage of either 75ms and 73mm (second generation), or 66ms and 102mm (third generation). By combining this with systolic imaging, when the ventricles are smallest, whole heart or near whole heart coverage can be achieved.

2.1 Acquisition protocols and image analysis

In CTP imaging, iodinated contrast material is administered intravenously and its distribution in the myocardium is evaluated as an indicator of myocardial blood flow. There are two options how to perform this: rest followed by stress perfusion or vice versa. The latter is used to avoid contrast contamination in the stress portion of the study when the rest perfusion is done first. Proponents of the rest-stress protocol argue that if the CTCA is normal, then patient does not need to be exposed to the stress part of the study. An example of a CT perfusion protocol is shown in figures 1. CTP imaging can be performed using static or dynamic techniques, with static CTP currently employing single or dual energy CT modes.

2.2 Static perfusion imaging

Static CTP is characterized by the acquisition of a single data frame of the left ventricular myocardium ideally at peak myocardial enhancement during arterial first pass. Static CTP images are acquired at rest and during the infusion of the stressor agent by using either a prospectively ECG-triggered or a retrospectively ECG-gated technique. The images obtained at rest can be used for the assessment of the coronary arteries. Image analysis relies on the comparison between hypodense (or lower attenuation) areas, suggestive of reduced myocardial perfusion (ischemia), and normal myocardium based on either visual assessment or on HU measurement. Therefore optimal acquisition timing is fundamental to maximize the difference in HU between ischemic and remote myocardium [24]. However, perfusion defects could be missed in patients with true “balanced ischemia” from 3-vessel CAD. The transmural extent of a perfusion defect can be expressed using the trans-mural perfusion ratio, i.e. the ratio between the mean sub-endocardial and mean sub-epicardial attenuation [25, 26].

Dual energy CT perfusion imaging consists of a single acquisition of the myocardium at two different voltages. Dual energy CT allows the differentiation between materials by exploiting the energy dependent attenuation properties of tissues and contrast material when exposed to two photon energy levels. Different vendors have developed different approaches for dual energy acquisition. Dual source CT scanners use two independent tubes paired with two detectors operating at two different tube voltages allowing the simultaneous acquisition of two image datasets, one at low kV (80, 90 and 100 kV) and one at high kV (140 and 150 kV). Single source CT systems can produce dual energy images either by using the ultrafast switching between 80 and 140 kV or by the use of a dual layer detector capable of differentiating between low and high-energy photons. An iodine distribution map of the myocardium is then generated and the myocardial blood pool can be quantified [27].

2.3 Dynamic perfusion imaging

Dynamic CTP imaging is characterized by imaging the left ventricular myocardium over time after the injection of a bolus of contrast material to create myocardial time attenuation curves (TACs, see figure 2). Applying different methodological approaches (i.e. maximum upslope, deconvolution, Patlak plot analysis) to the TACs permits the quantification of myocardial blood flow (MBF) and other perfusion parameters in absolute units. Each of the approaches available has advantages and disadvantages and so far the optimal method for MBF calculation has not been firmly established [21, 28, 29]. Dynamic scan acquisition can be performed either with the table in a stationary position using wide detector CT scanners (256- and 320-slice CT scanners) [30, 31], or with the axial shuttle mode technique when employing dual source CT scanners [32]. While the former technique allows for whole heart coverage in a single heartbeat for each volume to acquire, the shuttle mode technique requires

two different table positions, enabling the coverage of every single heart volume during systole every 2-3 heartbeats.

Quantitative CTP offers some advantages over qualitative CTP. Firstly, it has the potential to uncover balanced myocardial ischemia caused by 3-vessel CAD or left main stem disease, overcoming the limitation of qualitative approaches. Secondly, in the absence of significant epicardial CAD, a reduced global MBF may indicate the presence of microvascular dysfunction [33].

Dynamic CTP however faces several challenges that need to be addressed. Firstly, the few studies that report on MBF from dynamic CTP in healthy volunteers or in patients at low risk of CAD highlight significant heterogeneity of normal perfusion values [34, 35]. In addition, although a good correlation between MBF and microsphere has been described in a small number of animal studies [36, 37], dynamic CTP generally underestimates perfusion values compared to the reported values from PET [38] and CMR [39, 40]. This may be attributable to variability in the study design, samples sizes, image acquisition and post-processing techniques, applied reference standards, as well as age and gender, coronary risk factors and prevalence of CAD in the available studies. It is currently impossible to establish an optimal cut-off value of MBF to discriminate with high diagnostic accuracy between normal and abnormal myocardial perfusion; a wide range of cut-off values has been reported in the literature ranging between 75 and 103 mL/100mL/min [31, 41, 42, 43, 44, 45, 46]. These are important limitations to the implementation of quantitative CTP in clinical practice. Using relative flow reserve (i.e. MBF in ischemic myocardium divided by MBF in the remote myocardium) instead of absolute MBF may mitigate the effect played by microvascular dysfunction, suboptimal stressor vasodilator response, as well as inter-individual variability, on perfusion values. If confirmed by

future studies, this approach may provide more reproducible cut-off values to detect hemodynamically significant stenosis [44, 47].

2.4 Diagnostic performance of CT myocardial perfusion imaging

CTP has been validated pre-clinically in animal models [43, 48] and clinically against invasive (coronary angiography and fractional flow reserve) as well as non-invasive modalities (SPECT, PET and CMR). The diagnostic accuracy for the detection of myocardial perfusion defects attributable to flow-limiting stenoses is comparable to SPECT and CMR [45, 49]. To date, two multi-center studies have been completed and published [50, 51]. Cury et al. [50] randomized 110 patients to either regadenoson CTP followed by regadenoson SPECT on subsequent days, or vice versa, showing the non-inferiority of CTP to SPECT for ruling-out and detecting myocardial ischemia, with an agreement rate of 87%. When SPECT was used as reference standard, CTP showed a sensitivity and specificity of 90 and 84%, respectively [50]. In the CORE320 trial [51] of 381 patients, the combined approach of CTCA and static CTP improved the specificity of CTCA from 51% to 74%, at the expense of a reduction in sensitivity from 92% to 80%, compared to SPECT and invasive coronary angiography [51]. A further sub-study showed an overall higher diagnostic performance of CTP compared to SPECT in the diagnosis of anatomic CAD (≥50% diameter reduction) on invasive coronary angiography, in particular in the detection of left main stem and multivessel disease. Interestingly, no significant differences in the diagnostic performance of the two modalities were found when more stringent criteria (≥70% diameter reduction) were used to define an obstructive lesion at invasive coronary angiography [52]. This may be explained by the higher spatial resolution of CT and by the use of iodine contrast material, which has more favorable extraction characteristics than technetium based tracers and is not influenced by the roll-off

phenomenon (leading to an underestimation of regional myocardial blood flow). A meta-analysis by Pelgrim et al. including 1507 patients from 22 cohorts showed overall sensitivities between 75% and 84% and specificities between 78% and 95% for a variety of acquisition protocols and reference standards (SPECT, CMR or invasive coronary angiography) [53]. Overall, dynamic and dual-energy CTP appear to have a higher sensitivity than static CTP. A study by Takx et al. [54] also confirmed the high diagnostic performance of CTP against fractional flow reserve (FFR), nowadays the accepted invasive reference standard for the functional assessment of CAD.

2.5 Limitations of CTP

While preliminary data of myocardial CTP imaging are promising, several challenges need to be resolved before CTP is ready for routine clinical practice, including the lack of normative values or consensus for the optimal scanning mode. Radiation exposure persists as a significant problem. Although radiation doses from CTCA have been significantly reduced by (among others) prospective ECG triggering, lower kV imaging, dose modulation, and iterative reconstruction (diagnostic, real-world CTCA can now be performed below 1 mSv [55]), radiation doses for static and dynamic perfusion are still higher at 2-9mSv and 5-15mSv, respectively [53]. Optimal patient selection prior to CTP is essential, as only patients with intermediate lesions should be considered for CTP. Further advances in technology and software will be needed to further reduce the radiation dose [56]. Technological advances will also help reduce artifacts that limit current CTP analysis including beam-hardening artifact, motion artifact, cone-beam artifact, and misalignment artifact. Further work is required to improve the limited signal-to-noise ratio and develop strategies to identify inadequate pharmacological stress leading to false-negative results. Finally, the role

of CTCA and CTP needs to be established by large multi-center studies that include outcome and cost-effectiveness analyses, and in more challenging scenarios with high calcium burden, post bypass grafting or stent implantation.

3. Fractional flow reserve by CT

Data from large invasive FFR studies have shown that prognostic benefits of myocardial revascularization are linked to functional significance of coronary stenosis [13, 14, 57]. Utilizing supercomputer processing power, computational fluid dynamics can now be applied to conventional CTCA images in order to predict blood flow and pressure in coronary arteries, and in turn calculate lesion-specific, non-invasive FFR (FFR_{CT}) measures [58]. FFR_{CT} is computed from routine CTCA scans without any substantial modification of protocols, additional image acquisition, or administration of medications [59]. CTCA image quality, however, and the use of sublingual nitrates for CTCA acquisition are important factors. FFR_{CT} employs three key principles [60]: firstly, the total coronary flow at rest is relative to ventricular mass to meet its baseline demand; secondly, the resistance of the microcirculation at rest is inversely but not linearly proportional to the size of the feeding vessel; thirdly, the microcirculation reacts predictably to maximal hyperemic conditions in patients with normal coronary flow. These principles are utilized in computational fluid dynamics models to simulate resistance to flow in each coronary branch during simulated hyperemia (with a diagnostic cut-off for lesion specific ischemia of $\leq$0.80)[60]. The only commercially available, FDA-approved FFR_{CT} platform is the one by HeartFlow Inc. (Redwood City, California); alternative research prototype software tools are in development, but currently not commercially available [61, 62]. See figure 3 for an example case.

3.1 Evidence of FFR_{CT}

The first study on FFR_{CT}, pioneered and sponsored by HeartFlow Inc., was DISCOVER-FLOW (Diagnosis of Ischemia Causing Stenoses Obtained Via Non-Invasive Fractional Flow Reserve), which showed that FFR_{CT} improved the accuracy of CTCA by 25.8% [63]. Following this, the multicenter DeFACTO (Diagnostic Accuracy of Fractional Flow Reserve from Anatomic CT Angiography) trial failed to meet its pre-specified primary outcome, i.e. FFR_{CT} improving the diagnostic accuracy of CTCA [64]. Subsequent refinements in patient selection, CTCA technique, and computational techniques were implemented in the NXT (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps) multicenter trial, which showed an improved diagnostic accuracy of FFR_{CT} on a per-patient basis [65]. Most recently, the PLATFORM (Prospective Longitudinal Trial of FFR_{CT}: Outcome and Resource Impacts) trial showed that FFR_{CT} was associated with a significantly lower rate of invasive angiography showing no obstructive CAD [66]. At 1-year, CTCA and selective FFR_{CT} were associated with equivalent clinical outcomes (death, myocardial infarction, unplanned revascularization) and lower costs compared with usual care [67]. A meta-analysis including all four studies (n=662) concluded that FFR_{CT} increased the specificity from 0.43 to 0.72 ($p<0.004$) resulting in higher point estimates for PPV of 0.70 (from 0.56), although there was no improvement in sensitivity (0.92) [68].

3.2 Strength and weaknesses of FFR_{CT}

The invaluable strength of FFR_{CT} is the ability to provide data on coronary anatomy and physiology using a single CTCA dataset. FFR_{CT} provides a measure of ischemia for each identified lesion (as long as the vessel is analyzable), and offers this without additional radiation, contrast, or medications (usually required for functional testing).

The availability of FFR_{CT} results has a substantial effect on the classification of significant coronary artery disease, therefore potentially on the management of patients compared to CTCA alone [69]. Significant limitations include the need for off-site processing, with results typically provided within 24 hours. Workstation-based or point-of-care approaches to FFR_{CT} may offer solutions to this [62, 70]. Other limitations include the need for high CTCA image quality (up to 13% of patient were non-analyzable in the FFR_{CT} trials even after exclusion of patient with high BMI, atrial fibrillation, or previous revascularization). Further data on clinical effectiveness outside of clinical trials are awaited. Finally, although FFR_{CT} appears cost effective based on current assessments [71], it may depend on the health economy specific reimbursement arrangements whether this holds true in different clinical practices.

4. Beyond perfusion imaging and FFR_{CT}

Several studies have highlighted a rather complex anatomy-physiology mismatch: approximately only a half of obstructive lesions, i.e. ≥50% diameter stenosis, were hemodynamically significant as defined by FFR [72, 73, 74, 75], whereas, Park et al. [73] found that myocardial ischemia was associated with 17% of coronary lesions classified as non-obstructive (<50% diameter reduction). This may be explained by the fact that epicardial coronary stenosis is only one of the factors contributing to the pathophysiological process leading to myocardial ischemia. Inflammation, endothelial dysfunction, microvascular dysfunction, platelet dysfunction, thrombosis, and vasomotor dysfunction should also be considered [76]. Recently, several plaque characteristics derived from CTCA have been shown to be independent predictors of an abnormal invasive FFR, [73, 77] which may be explained by the oxidative stress and the local inflammation associated with a necrotic core, compromising the

production of vasodilator nitric oxide, increasing the levels of vasoconstrictors [78] and finally leading to clinically relevant functional stenosis [79].

Finally, CT also has the potential for myocardial tissue characterization, by detecting myocardial fat [80, 81] on the pre-contrast phase, myocardial scar on delayed imaging [82], Furthermore, iodine mapping by dual energy CT acquisition at a delayed phase [83] and extracellular volume fraction imaging (as widely investigated in CMR) to quantify interstitial expansion due to fibrosis or amyloidosis [84, 85, 86]. The opportunity of providing coronary anatomy, functional assessment of coronary flow and myocardial tissue characterization in one modality is attractive for diagnostic imaging workflow.

5. Expert Commentary

CTCA is rapidly becoming the gatekeeper for the investigation of CAD. In cases where CTCA demonstrates obstructive CAD, plaque burden and plaque characteristics may help guide clinical decisions, but it is the functional assessment by CTP or CT_{FFR} that may ultimately help differentiate a functional true-positive from a false-positive finding, reducing the number of unnecessary invasive coronary angiograms. CTP and CT_{FFR} were shown to yield similar diagnostic performance [68, 87]. However, CTP and CT_{FFR} provide complementary information on myocardial ischemia and therefore they cannot be considered interchangeable. While CT_{FFR} is an index of epicardial stenosis-related ischemia, CTP reflects the impact of both epicardial coronary lesions and microvascular disease on myocardial perfusion. In highly specialized centers, where both CT techniques may be available, a stepwise diagnostic approach could be proposed, reserving CTP to coronary lesions with a CT_{FFR} in the "grey zone" (0.74-0.85) [87]. This range represents the values associated

to intermediate coronary lesions where the agreement between repeated invasive FFR measurements falls [88].

6. Conclusion

Over the last decade CTCA has become an established diagnostic modality, in some health care economies even the first line modality. The combined use of CTCA and functional assessment of coronary artery stenosis by CT perfusion or CT-derived fractional flow reserve is an attractive diagnostic pathway that requires further evaluation.

7. Five-year view

Beyond the optimization of dual energy CT with minimization of image artifacts, radiation dose and iodinated contrast dose (using low energy monochromatic imaging [89]), more advanced technologies are on the horizon: *Spectral CT imaging* exploits the different K-edge behavior of different tissues (calcium, blood, fat, myocardium) [90]. This technology goes beyond the two-photon energy levels used in dual energy CT, and utilizes energy-sensitive photon-counting detectors to obtain greater tissue information by differentiating photons at different energy levels. Early pre-clinical data suggests that spectral CT may improve image quality over conventional CTP by eliminating beam hardening [91], but is likely 10 years rather then 5 years away from clinical implementation.

7. Key issues

- Rapid technical advances and excellent negative predictive value have brought CTCA to the verge of being the 1st line modality for stable chest pain.
- The combined use of anatomical and functional assessment of coronary artery stenosis by CT perfusion (CTP) is an attractive diagnostic pathway.

- CTP now offers higher *spatial resolution* than other imaging modalities, allowing assessment of subendocardial versus subepicardial perfusion.
- A key limitation of CTP remains a relatively poor *contrast resolution* between normal and hypo-perfused myocardium.
- CTP imaging can be performed using static or dynamic techniques, with static CTP currently employing single or dual energy CT modes.
- CTP has been validated pre-clinically and clinically with the diagnostic accuracy for the detection of myocardial perfusion defects attributable to flow-limiting stenoses comparable to SPECT and CMR.
- FFR_{CT} employs supercomputer processing and computational fluid dynamics to predict blood flow and pressure in coronary arteries, from a single CTCA dataset.
- CTCA and selective FFR_{CT} are associated with equivalent clinical outcomes (death, myocardial infarction, unplanned revascularization) and lower costs compared with usual care.

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FIGURES LEGENDS

Figure 1: CT perfusion protocol.

Figure 2: Static and dynamic CT perfusion.

A: Short axis view of apical left ventricle from adenosine dynamic CT perfusion imaging showing a perfusion deficit (arrows) in the septal myocardial wall. B: Time attenuation curves of remote (Δ) and ischemic myocardium (◆) compared to blood pool sampled in the left ventricle (■) from dynamic CT scanning. Dynamic CT perfusion imaging relies on multiple sampling of the myocardium over time (arrows) allowing for the evaluation of the wash-in and wash-out of contrast material. On the other hand, static CT perfusion imaging involves the acquisition of only one myocardial volume; therefore, optimal acquisition timing (dark grey shaded area) is mandatory to maximize the difference in Hounsfield unit (HU) between ischemic and remote myocardium.

Figure 3: Fractional Flow Reserve by Computed Tomography.

A: CT coronary angiography (CTCA) demonstrates an intermediate coronary stenosis due to non-calcified plaque in the mid left anterior descending (LAD) coronary artery (circle). B: FFR_{CT} model shows normal CT_{FFR} value just distal to the coronary lesion (0.94) and in the distal LAD (0.88). C-D: CTCA exclude obstructive coronary disease in the left circumflex coronary artery, LCx, (C) and in the right coronary artery, RCA (D). E: Invasive coronary angiography (ICA) confirms the presence of an intermediate lesion in the mid LAD (circle) that does not cause myocardial ischemia according to invasive FFR (0.84). F-G: Both LCx (F) and RCA (G) are unobstructed.