ORIGINAL ARTICLE

CT stress perfusion imaging for detection of haemodynamically relevant coronary stenosis as defined by FFR

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ABSTRACT

Objectives To evaluate the diagnostic accuracy (DA) of CT-myocardial perfusion imaging (CT-MPI) and a combined approach with CT angiography (CTA) for the detection of haemodynamically relevant coronary stenoses in patients with both suspected and known coronary artery disease.

Design Prospective, non-randomised, diagnostic study.

Setting Academic hospital-based study.

Patients 65 patients (42 men age 70.4±9) with typical or atypical chest pain.

Interventions CTA and CT-MPI with adenosine stress using a fast dual-source CT system. At subsequent invasive angiography, FFR measurement was performed in coronary arteries to define haemodynamic relevance of stenosis.

Main outcome measures We tried to correlate haemodynamically relevant stenosis (FFR < 0.80) to a reduced myocardial blood flow (MBF) as assessed by CT-MPI and determined the DA of CT-MPI for the detection of haemodynamically relevant stenosis.

Results Sensitivity and negative predictive value (NPV) of CTA alone were very high (100% respectively) for ruling out haemodynamically significant stenoses, specificity, Positive predictive value (PPV) and DA were low (43.8, 67.3 and 72%, respectively). CT-MPI showed a significant increase in specificity, PPV and DA for the detection of haemodynamically relevant stenoses (65.6, 74.4 and 81.5%, respectively) with persisting high sensitivity and NPV for ruling out haemodynamically relevant stenoses (97% and 95.5% respectively). The combination of CTA and CT-MPI showed no further increase in detection of haemodynamically significant stenosis compared with CT-MPI alone.

Conclusions Our data suggest that CT-MPI permits the detection of haemodynamically relevant coronary artery stenoses with a moderate DA. CT may, therefore, allow the simultaneous assessment of both coronary morphology and function.

INTRODUCTION

Cardiac CT has established itself as a valuable tool for physicians. The coronary artery calcium score is an important and worthwhile parameter for cardiovascular risk stratification. By using CT angiography (CTA) in patients with suspected coronary artery disease (CAD), significant coronary artery stenoses can be ruled out non-invasively and with a high diagnostic accuracy (DA). Coronary artery stenoses can be visualised by CTA, and the grade of stenosis can be determined. However, the haemodynamic significance of any detected stenosis could so far not be evaluated by CT because the acquired information was strictly morphologic in nature. The haemodynamic significance of a coronary artery stenosis had to be assessed by other imaging modalities, such as single-photon emission CT (SPECT), or stress myocardial perfusion MRI. These modalities have been shown to deliver reliable information about myocardial perfusion defects at rest and under stress conditions, however, they do not provide information about the morphology of the coronary vessel and the causal stenosis. So far, morphologic and functional information could only be obtained in the same examination invasively by coronary angiography and fractional flow reserve measurement.

From a clinical point of view, it is crucial to identify the haemodynamically significant stenosis, because only the treatment of the latter results in reduced mortality and myocardial infarction, as shown by the FAME[1] and the COURAGE study.[2]

Over the last few years, a number of initial studies have reported that the detection of myocardial perfusion defects, at rest or even stress-induced defect,[3–6] is feasible if using CT. Two recent small patient series could also show that detection of myocardial perfusion defects at rest or under stress conditions is viable.[7 8] It was the aim of this study to investigate the feasibility of myocardial perfusion imaging (MPI) to detect haemodynamically significant coronary artery stenoses, as defined by FFR, in a larger series of patients.

METHODS

Patients

Sixty-seven patients (43 men; age 70.6±9) presenting at our institution with typical or atypical chest pain (74.3% with known CAD, 49% with a history of stent implantation, 9.4% with a history of bypass surgery) or suspected CAD were included. Patients with unstable angina, prior myocardial infarction, atrial fibrillation, serum creatinine levels greater than 1.5 mg/dl, atrioventricular block greater than type I, or patients younger than 50 years, were excluded. ß-adrenergic blocking agents were discontinued at least 1 day before CT-MPI, no coffee or tea was allowed before the examination.

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All patients signed written informed consent. The study was approved by the institutional review board and the Federal Radiation Safety Council (Bundesamt für Strahlenschutz).

Further patients characteristic are given in table 1.

CT angiography and CT stress myocardial perfusion

Images were generated by using a fast dual-source CT system (Somatom Definition Flash; Siemens Healthcare, Forchheim, Germany) with a collimation of 64×2×0.6 mm and flying focus, resulting in 2×128 sections. Two intravenous lines were placed in both antecubital veins for administration of contrast agent and adenosine. After scout images and administration of a test bolus (injected at 5 ml/s) of contrast agent (Ultravist 370; Bayer Schering Pharma), standard prospective CTA was performed. Because of possible interference with adenosine efficacy, no ß-adrenergic blocking agent was applied. CTA was triggered at 200 ms in the craniocaudal direction. Further standard scan parameters were as follows: 2×100 kVp tube voltage (120 kVp in patients with a BMI >30 kg/m^2), 320 mAs per rotation, and 0.28-s gantry rotation time. Evaluation of images and determination of significant coronary artery stenoses (>50%) was performed by two independent experienced investigators (FS and FvZ) using a modified 17-segment model of the coronary artery tree.[9] Both were blinded to perfusion results as well as coronary angiography results. If a significant stenosis in a segment could not be ruled out, a stenosis of >50% in this segment was assumed.

After 3 min of continuous adenosine administration (Adrekar; Sanofi, Munich, Germany) at an infusion rate of 0.14 mg/kg/min, MPI was started.

Data acquisition was performed for 30 s with both tubes set at 100 kV, a gantry rotation time of 0.28 s, and a total tube current of 300 mAs per rotation. In the electrocardiographically triggered mode the table was shifting between two positions ('shuttle mode,' table acceleration time 300 mm/s²). With a defined detector width of 38 mm, and a 10% overlap between both imaging positions, the coverage of the acquisition was 73 mm. A total of 14–15 datasets were acquired. Overall, 50 ml of iodinated contrast agent (Ultravist 370; Bayer Scherimg Pharma; flow rate 5 ml/s.) was needed to generate the images. Two independent experienced readers (FB and AB) performed image analysis using a dedicated software tool on our workstation (Leonardo; Siemens Medical Solutions, Erlangen, Germany). These readers were blinded to CT angiography results.

Perfusion images were reconstructed with a 3 mm section width every 2 mm by using a smooth convolution kernel (B30), and then processed on a standard workstation (Syngo VPN; Siemens Healthcare, Forchheim, Germany). Myocardial blood flow (MBF) and mean attenuation in Hounsfield units were determined for each of the 16 myocardial segments, excluding the apical segment. A 1 mm subendocardial zone directly adjacent to the contrast material-filled left ventricle, and a 1 mm subepicardial zone were excluded from analysis. A region of interest of 2.5 cm^2 was manually placed in a representative area of each myocardial segment. To estimate MBF, a dedicated parametric deconvolution technique, which was based on a two-compartment model of intravascular and extravascular space, was used to fit the time-attenuation curves.[10] The precision of the fit is increased significantly by double sampling of the arterial input function (AIF). The input function is sampled from regions of interest (ROIs) placed in the descending aorta with every table position and combined into one AIF that has twice the sampling rate of the tissue time-attenuation curve (TAC). The algorithm then determines the maximum slope from the fit model curve for every voxel, and calculates MBF according to the following relationship: MBF=(MaxSlope(TissueTAC))/(Maximum(AIF)).[11]

The intraclass correlation coefficient was used to determine the agreement of measurement of MBF between two observers. A paired t test and repeated-measures analysis of variance was used to compare MBF between segments, which were and were not associated with a haemodynamically significant coronary artery stenosis and according to CT stenosis category.

To determine whether the observed difference between territories was independent of heart rate during the scan, age, sex and body mass index, we fitted linear regression models by using the MBF as the predictor of interest. The MBF cut point was derived by maximisation of the C statistic by using logistic regression modelling.[12] The asymptomatic 95% CIs for the C statistic were estimated by using a non-parametric approach, which is closely related to the jack-knife technique proposed by DeLong *et al*.[13]

Table 1 Baseline characteristics

	All
N	65
Age	70.4±9
Male	42
Known CAD	74.3
History of stent implantation%	49.0
History of CABG%	9.4
Hypercholesterolemia%	47.6
Hypertension%	67.3
Smoking%	25.4
Family history of CAD	33.4
Diabetes %	17.9

CAD, coronary artery disease.

Conventional coronary angiography

All patients underwent coronary angiography 1–3 days after CT-MPI. Coronary angiography was performed as a standard procedure via femoral access using a 6F guiding catheter in our catheter laboratory (Siemens Medical Solutions, Forchheim, Germany). Each coronary segment was visually assessed for degree of luminal stenosis by two independent experienced invasive cardiologists (JT and MG) who were blinded to the CT findings. If a 50–85% luminal stenosis was detected, a fractional flow reserve measurement was performed.

FFR measuring

Using a sensor tipped 0.014-inch guidewire (Prime Wire Prestige; Volcano, Japan) coronary artery stenosis suspected to be haemodynamically relevant (lumen narrowing between 50% and 85%), were evaluated as follows. After placement of the pressure wire distal to the target lesion, a continuous intravenous infusion of adenosine at an infusion rate of 0.14 mg per kilogram of body weight per minute, similar to infusion rate for MPI-CT, was started. FFR was calculated by dividing the mean coronary pressure, measured by the pressure wire distal to the stenosis by the mean proximal pressure measured by the guiding catheter. If within 3 min, the FFR was 0.80 or less, the stenosis was considered haemodynamically relevant. Stenosis greater than 90% clearly heamodynamically significant or totally occluded vessels were considered functionally significant without performing FFR measurement. This procedure was

repeated for all coronary arteries having a stenosis of 50–85% by angiographic evaluation.

Statistical analysis

Statistical analyses were performed using the SPSS software package (V.18.0, SPSS, Chicago, Illinois). All values are expressed as mean score±SD exceptions were indicated. Values were compared between groups with a two-tailed unpaired Student t test for continuous data, whereas, categorical data were compared using an ×2 or Fisher exact test. A $p<0.05$ was considered as significant. DA was compared using the McNemar Test. All values illustrated in the figures are given as mean±SD.

RESULTS

Of 67 enrolled patients, 65 completed the CT scan. Two patients had to be excluded from further analysis due to technical failure. The two technical failures occurred in the first 20 patients, following which no more technical failures occurred. Thus, 65 patients formed our study cohort.

Average scan duration was 34.7±6.3 min. Mean effective radiation exposure was 2.9±0.9 mSv for CTA, and 9.7±2.2 mSv for CT myocardial perfusion. 80 ml of contrast agent were used for CTA and 50 ml of contrast agent for CT -MPI. Heart rate at baseline was 67±23 bpm. This showed a significant increase after adenosine administration up to 81±14 bpm ($p<0.001$). Complete coverage of the myocardium could be achieved in 49 patients (77.7%). In 11 patients (17.4%) the inferior territories and in three patients (4.7%) the anterior territories of the myocardium were only partially covered. Seven studies (11.1%) showed reduced image quality, mainly to motion artefacts, and required secondary postprocessing; 31 not evaluable segments were rated as segments without perfusion defects. In case of haemodynamically relevant stenosis in FFR, these patients would have been considered as false negative. No examination was completely excluded from analysis.

MBF cut-off

Myocardial segments pertaining to haemodynamically significant coronary artery lesions had significantly lower mean MBF (78.7 ml/100 ml/min±26.1 vs 122.7±34 ml/100 ml/min), ($p<0.001$ for both). The predicted difference in MBF between ischaemic and non-ischaemic myocardial segments persisted after adjusting for age, sex, body mass index and difference in heart rate (ß, 36.2 ml/100 ml/min; 95% CI: 26.8,43.1; $p<0.001$). The best cut-off of MBF for the differentiation between haemodynamically significant and non-significant coronary artery stenosis was 75 ml/100 ml/min (c statistic, 0.712; $p<0.001$).

Conventional angiography

All 65 patients included in the study underwent conventional angiography. In 10 patients, no coronary stenosis ≥50% was found; 55 patients showed at least one stenosis ≥50%; 33 of these patients had a haemodynamically relevant stenosis detected by FFR, and underwent stent implantation or coronary artery bypass surgery.

CTA for the detection of haemodynamically relevant coronary stenoses

All 65 patients underwent CTA. CTA detected all haemodynamically relevant coronary stenoses resulting in a sensitivity of 100%. The specificity of CTA for the detection of a haemodynamically significant coronary stenosis was low, with 43.8%. A positive predictive value (PPV) of 67.3% was calculated. Even though CTA had many false positive findings, the negative predictive value (NPV) was 100%. All seven patients with exclusion of a significant coronary artery stenosis in CTA had no haemodynamically relevant stenosis revealed by coronary angiography.

In 58 patients, CTA revealed at least one stenosis ≥50%, in one of their coronary artery vessels. Of these 58 patients, only 33 patients had a haemodynamically significant stenosis detected by FFR, 25 had no haemodynamically significant stenosis. Overall sensitivity, specificity, negative and PPV and DA of CTA for the presence of a haemodynamically significant stenosis were 100, 43.8, 100, 67.3, and 72%, respectively. These findings remained unaffected with a high sensitivity, a high NPV, a low specificity, and a low PPV in a vessel-based analysis. There was no significant difference in DA between the single coronary arteries (see table 2).

CT-MPI for the detection of haemodynamically relevant coronary stenosis

CT-MPI revealed a territorial perfusion defect under adenosine stress (defined as a MBF under 75 ml/100 ml/min) in 45 of 65 patients (69.2%), whereas 20 patients had no territorial perfusion defect under adenosine stress (30.7%); 33 (73.3%) of the 45 patients having a territorial perfusion defect under adenosine stress, demonstrated a haemodynamically relevant coronary stenosis on FFR. Of the remaining 20 patients without any perfusion defect, 19 patients had no haemodynamically relevant coronary stenosis on FFR, one patient of these 20 without a perfusion defect under adenosine stress revealed a haemodynamically relevant coronary stenosis on FFR. Overall sensitivity, specificity, negative and PPV and DA of CT-MPI for the detection of a haemodynamically significant stenosis were 97, 65.6, 95.5, 74.4 and 81.5%, respectively. As for CTA, these results persisted in a vessel-based analysis, and there was no difference in DA between the single coronary arteries (see table 2).

Combination of a ≥50% stenosis on CTA and perfusion defect on CT-MPI for the detection of haemodynamically relevant coronary stenoses

In this analysis, only patients with a stenosis ≥50% on CTA and a perfusion defect in the perfusion images were rated as having a haemodynamically significant stenosis. This means that patients with a stenosis ≥50% on CTA but without a perfusion defect on perfusion imaging, or inversely, with a perfusion defect on perfusion imaging but without stenosis ≥50% on CTA, were rated as having no haemodynamically significant stenoses.

Of the 65 patients investigated, 44 (67.9%) had a stenosis ≥50% on CTA, and a territorial perfusion defect under adenosine stress, 21 patients (32.1%) did not. Of the 44 patients having a stenosis ≥50% on CTA and a perfusion defect on CT-MPI, 33 (75%) also had a haemodynamically relevant coronary stenosis on FFR while 11 (25%) did not. From the 21 patients with a negative finding on CTA, 20 had no haemodynamically relevant coronary stenoses on FFR, while one patient showed a positive FFR measuring. Overall sensitivity, specificity, negative and PPV and DA of the combination of a ≥50% stenosis on CTA and perfusion defect on CT-MPI for the detection of a haemodynamically significant stenosis were 97, 68.8, 95.7, 76.1 and 83.1%, respectively. Again, these results persisted without significant discord in a patient-based and vessel-based analysis. Again, no difference in DA between the single vessels was found (see table 2).

The combination of CTA and CT-MPI showed a very high sensitivity for the detection of a stenosis ≥50% as well as a very high NPV for the exclusion of a stenosis. While specificity, PPV

Table 2 Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV) and diagnostic accuracy (DA) with 95% CI for CT angiography (CTA), CT-myocardial perfusion, and the combination of both for detecting haemodynamically relevant coronary artery stenoses defined by FFR

	Sensitivity	Specificity	NPV	PPV	DA
Overall n=65					
CTA (%) (95% CI)	100 (0.84 to 1.0)	43.8 (0.18 to 0.65)	100 (0.82 to 1.0)	67.3 (0.5 to 0.9)	72 (0.54 to 0.86)
Perfusion (%) (95% CI)	97 (0.76 to 0.99)	65.6 (0.51 to 0.84)	95.5 (0.84 to 0.98)	74.4 (0.49 to 0.9)	81.5 (0.65 to 0.97)
CTA+perfusion (%) (95% CI)	97 (0.79 to 1.0)	68.8 (0.47 to 0.79)	95.7 (0.76 to 0.99)	76.1 (0.56 to 0.92)	83.1 (0.7 to 0.96)
Vessel n=195					
CTA (%) (95% CI)	97.5 (0.78 to 1)	53.9 (0.26 to 0.74)	98.8 (0.71 to 1.0)	36.6 (0.13 to 0.61)	63.1 (0.38 to 0.85)
Perfusion (%) (95% CI)	95.1 (0.83 to 0.98)	74.0 (0.5 to 0.86)	98.3 (0.82 to 1.0)	49.3 (0.17 to 0.69)	78.2 (0.52 to 0.93)
CTA+perfusion (%) (95% CI)	95.1 (0.79 to 0.99)	74.7 (0.47 to 0.89)	98.2 (0.84 to 1.0)	50.0 (0.26 to 0.65)	79.0 (0.63 to 0.93)
LAD					
CTA (%) (95% CI)	93.8 (0.79 to 0.98)	55.1 (0.28 to 0.76)	96.4 (0.78 to 0.99)	40.5 (0.14 to 0.63)	64.6 (0.49 to 0.81)
Perfusion (%) (95% CI)	93.7 (0.81 to 0.99)	81.6 (0.74 to 0.97)	97.6 (0.84 to 1.0)	62.5 (0.32 to 0.79)	84.5 (0.68 to 0.97)
CTA+perfusion (%) (95% CI)	93.8 (0.82 to 0.98)	79.6 (0.68 to 0.95)	97.5 (0.83 to 1.0)	60.0 (0.3 to 0.77)	83.1 (0.72 to 0.97)
RCX					
CTA (%) (95% CI)	100 (0.82 to 1.0)	52.8 (0.24 to 0.71)	100 (0.79 to 1.0)	32.4 (0.11 to 0.56)	61.5 (0.29 to 0.8)
Perfusion (%) (95% CI)	91.7 (0.84 to 0.98)	69.8 (0.46 to 0.82)	97.3 (0.84 to 1.0)	40.7 (0.14 to 0.65)	73.8 (0.48 to 0.9)
CTA+perfusion (%) (95% CI)	91.7 (0.84 to 1.0)	71.7 (0.55 to 0.87)	97.4 (0.76 to 1.0)	42.3 (0.17 to 0.63)	75.4 (0.55 to 0.91)
RCA					
CTA (%)	100 (0.83 to 1.0)	53.8 (0.28 to 0.7)	100 (0.79 to 1.0)	35.1 (0.12 to 0.58)	63.1 (0.47 to 0.83)
Perfusion (%)	100 (0.82 to 1.0)	71.2 (0.53 to 0.84)	100 (0.83 to 1.0)	46.4 (0.17 to 0.62)	76.9 (0.58 to 0.91)
CTA+perfusion (%)	100 (0.83 to 1.0)	73.1 (0.46 to 0.87)	100 (0.84 to 1.0)	48.1 (0.17 to 0.7)	78.4 (0.58 to 0.91)

and DA for the detection of a haemodynamically significant stenosis by CTA alone, were very low, there was a significant increase in specificity, PPV and DA, for both CT-MPI alone and the combination of CTA and CT-MPI, for the detection of a heamodynamically relevant stenosis (p=0.023).

DISCUSSION

CT has been demonstrated to be a very effective tool for the exclusion of significant coronary artery stenosis in patients without known CAD.[14 15] On the other hand, in patients with known CAD, or in a cohort with a high prevalence of CAD, due to its low specificity and PPV, CT is not recommended. In patients with known CAD, as shown by the FAME-study[1] and the COURAGE-study,[2] it is crucial for the patient's survival to treat stenoses which are haemodynamically relevant. Therefore, an imaging modality providing information about the haemodynamic significance of coronary artery stenoses, in addition to the morphologic information, is required.

As previously reported by our group, we used a dynamic adenosine-stress myocardial perfusion protocol to perform myocardial perfusion scanning.[7] This dynamic protocol permits derivation of a quantitative measure of myocardial perfusion similar to the established CT-based perfusion in brain imaging.[16] Presently, it is not clear whether this added value of 'dynamic' imaging with MBF quantification, provides further clinical information over 'static' imaging (ie, a single set of images obtained during early myocardial perfusion). So far, reported data in the literature demonstrated similar findings regarding radiation exposure and contrast agent use. Also, the DA of these two different approaches is comparable.[7 8]

Our protocol included a first step CTA, with an average effective radiation exposure of 2.9±0.9 mSv, and in a second step, CT myocardial perfusion with a mean effective radiation exposure of 9.7±2.2 mSv. This also included the application of contrast agent twice.

By comparison with other modalities, such as SPECT- MPI and SP- MRI, CT-MPI achieved results in the diagnostic range of SPECT-MPI and SP-MRI. Still, it has to be taken into account that SPECT-MPI and SP-MRI evidence is based on thousands of published patients in numerous clinical trials. Further, the accuracy could deteriorate after distributing the method into different clinical populations and multicentre use.

Ho *et al*,[17] comparing CT-MPI with SPECT-MPI, described a sensitivity of 95% and a specificity of 83% for the detection of haemodynamically relevant senosis using a 128-slice scanner. George *et al*,[18] investigating a patient collective similar to ours with suspected or known CAD, found a sensitivity of 100% and a specificity of 81% using a 320-slice scanner.

Similar results where reported by Feuchtner *et al*[19] comparing SP-MPI to CT-MPI with a sensitivity of 96% and a specificity of 95% also in a collective of patients with suspected or known CAD and by Weininger *et al*[20] with a sensitivity of 93% and a specificity of 99% in patients with acute chest pain.

The aim of this study was to evaluate the diagnostic benefit of CT-MPI in combination with CTA against CT-MPI alone in a larger study population with known (74.3%) and suspected CAD (25.7%). Invasive angiography revealed a stenosis above 50% in 55 (84.6%) and a haemodynamically relevant stenosis in 33 (50.8%) patients. Thus, a reasonable patient selection representing a population scheduled for invasive angiography can be assumed.

As described previously, we defined the cut-off point for MBF on the basis of maximisation of the area under the curve. We calculated a MBF of 75 ml/100 ml/min as an ideal cut-off point. However, this parameter may need further validation. Patients with an average MBF higher than this threshold level could be incorrectly diagnosed as having a non-haemodynamically significant stenosis.

CTA has proven to be a very sensitive tool in ruling out coronary artery stenosis in patients with a low to intermediate

pretest likelihood for coronary artery stenosis.[14 15 21] In this context, CTA has a very high sensitivity and NPV for ruling out significant coronary artery stenoses. These findings have also been consistently demonstrated in our series with a sensitivity of 100% and a NPV of 100% in ruling out haemodynamically relevant stenosis. There was no patient with an exclusion of coronary artery stenosis in CTA, who had a high-grade stenosis in coronary angiography or a stenosis defined as haemodynamically significant by FFR. If CTA already ruled out significant coronary artery stenoses, CT-MPI did not further improve DA. Therefore, we could have refrained from performing CT-MPI in seven patients in our study with no loss of information required for adequate clinical treatment, and with a consequent reduction of radiation exposure and contrast agent use. (figure 1)

In patients with CAD in CTA, Meijboom *et al*[22] described a significant correlation between the quantitative assessment of coronary artery stenosis in CTA and angiographic findings. Still, the correlation with haemodynamic parameters determined by FFR was poor and had a sensitivity of approximately 50%. Again, these findings were consistent in our series with a specificity of 43.8% and a PPV of 67.3%, resulting in a DA of 72% for CTA alone in detecting haemodynamically relevant stenoses.

By contrast, CT-MPI had a significantly higher specificity (65.6%) with a PPV of 74.4%, resulting in a significant increase of DA up to 81.5% for the detection of a haemodynamically significant stenosis as defined by FFR. A comparable DA has been described in SPECT studies. Additionally, the mean effective radiation dose of 9.7±2.2 mSv was comparable with nuclear techniques with the use of SPECT.[23 24]

The combination of CTA and CT-MPI demonstrated no significant further improvement in specificity (68.8%), PPV (76.1%) and DA (83.1%) for the detection of haemodynamically significant coronary artery stenoses as defined by FFR in comparison to CT-MPI alone.

Based on these results, in patients with known CAD, or after stent implantation, CT-MPI alone might be sufficient, as the exclusion of haemodynamically relevant stenosis would not lead to a change in the treatment regime. Nevertheless, it might be reasonable to combine CTA and CT-MPI in patients without known CAD, but with an intermediate likelihood for CAD. Should CT-MPI reveal a perfusion defect under adenosine-stress, the patient might be suitable for coronary angiography and revascularisation. (figure 2) If there is no myocardial perfusion defect under adenosine-stress, but CTA reveals

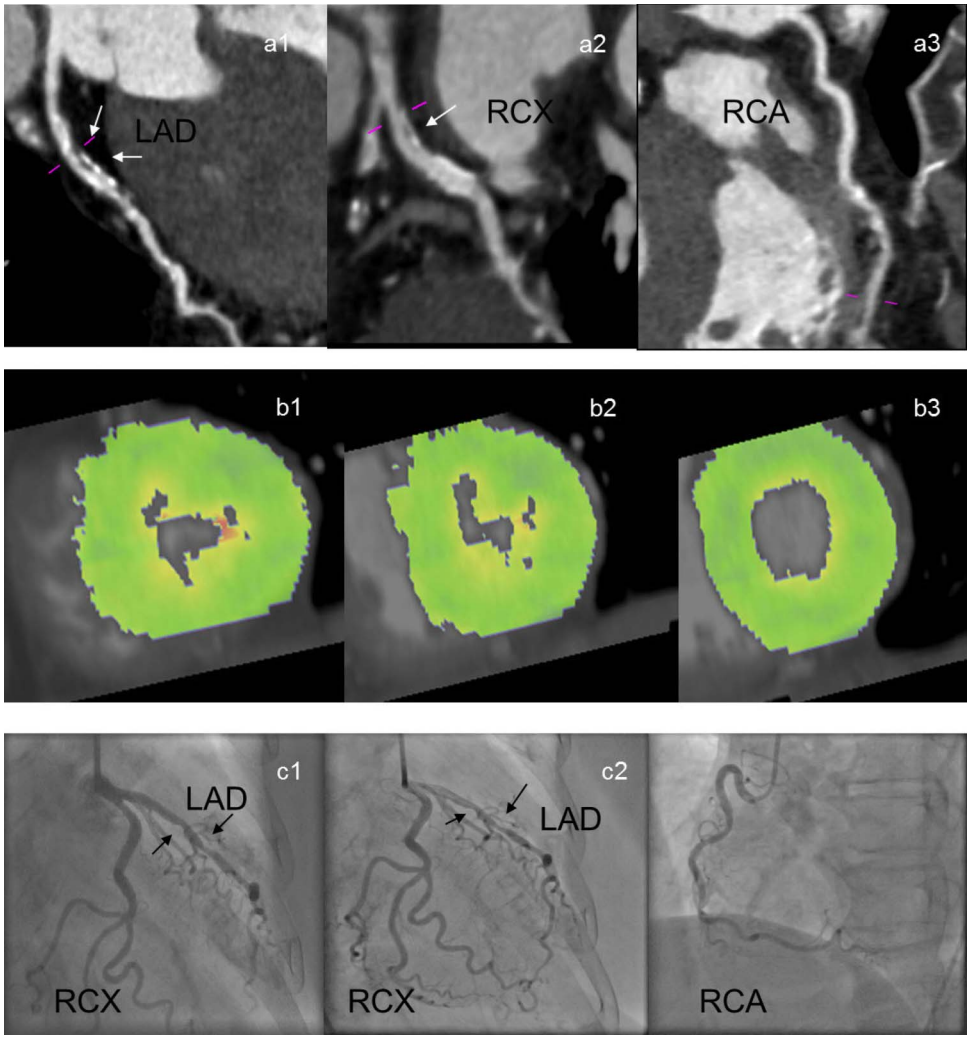

Figure 1 CTA reveals a mixed plaque in the proximal LAD with suspected stenosis (a1). The LCX shows a stent with a smaller mixed plaque proximal to the stent (a2). The RCA shows no plaque formation (a3). CT-MPI reveals no perfusion defect in the myocardium after adenosine stress (apical b1, mid b2, basal b3). MBF >75 ml/100 ml/min (marked in green and yellow)) Coronary angiography reveals a tandem stenosis in the LAD (c1 and c2). FFR measurement after adenosine stress reveals a haemodynamically not relevant tandem stenosis in the LAD with a FFR value of 0.83.

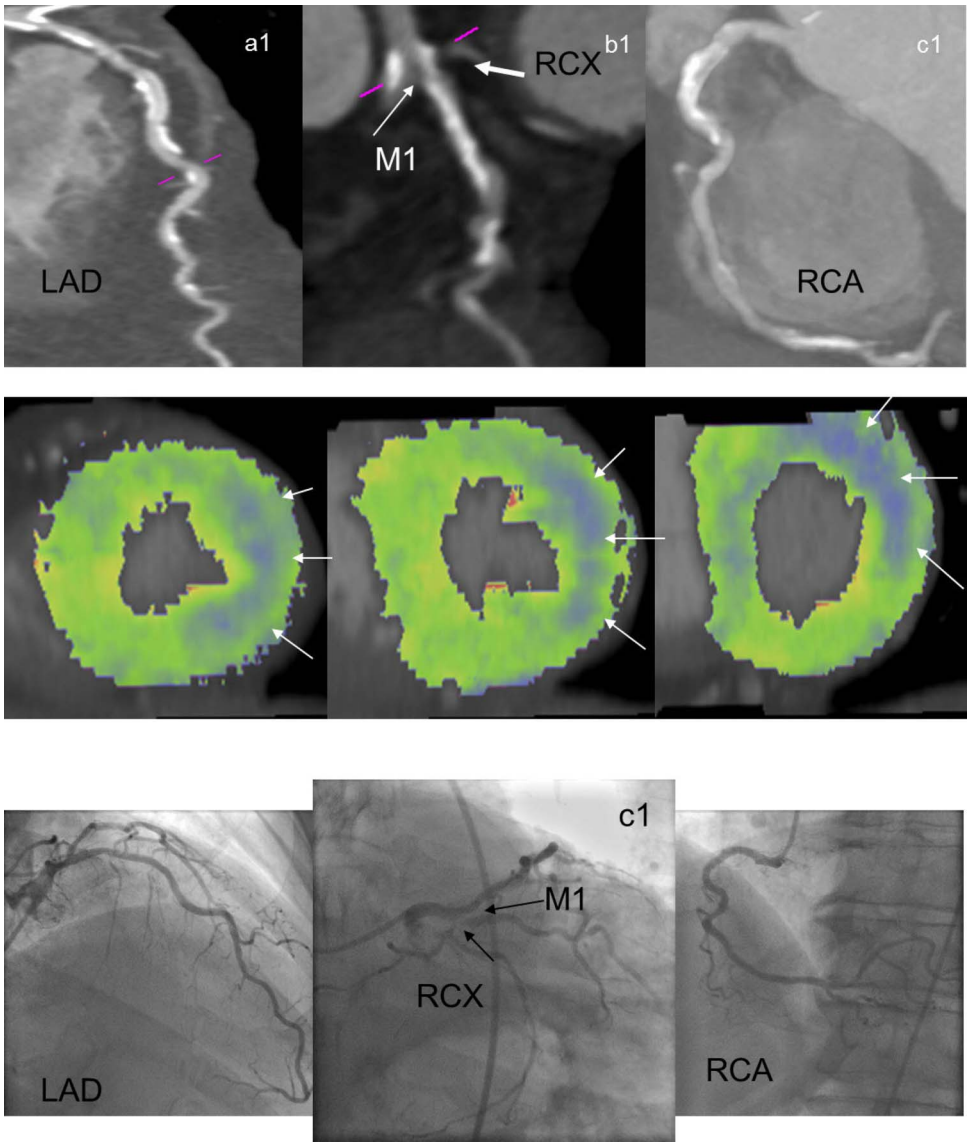

Figure 2 CTA shows many calcified plaques in the LAD (a1). The origin of the big first marginal branch (M1), as well as the origin of the smaller LCX, show a significant stenosis (a2). The RCA shows a calcified plaque in the proximal part (a3). CT-MPI reveals a significant perfusion defect under adenosine stress (MBF <75 ml/100 ml/min) marked blue/grey in the LCX territories. Of note, as the LCX is a large vessel with two branches running towards the RCA territories. Thus, a part of the basal septal segment coloured in blue/grey indicates a perfusion defect in the borderline segments (apical, mid, basal). Coronary angiography shows a high-grade stenosis on the origin of the first marginal branch (M1) as well as of the origin of the LCX with a FFR of 0.69 and 0.72, respectively. (c1) There was no coronary artery stenosis in the LAD or RCA.

coronary artery plaque formation, or a haemodynamically non-significant coronary artery stenosis, a preventive medical treatment (eg, aspirin, statins) might be favourable (figure 3). In this context, CT is currently the sole available imaging tool which offers the unique possibility to anatomically visualise the coronary arteries and their pathological changes, and also enables the determination the haemodynamic significance of any detected stenosis.

Limitations

Our study has several limitations. First, selection bias may be present because patients included presented with typical or atypical chest pain, and had an intermediate to high risk for the presence of coronary artery stenosis. Further, the PPV and NPV are dependent on the prevalence of disease. Thus, our results are limited to populations with the same prevalence as in our series. Nevertheless, this is the typical patient population to be referred for a stress test. Still, patients with previous myocardial infarction were excluded.

Second, to achieve optimal results, the patients need adequate preparation and should be able to hold their breath for almost 30 s, otherwise, breathing artefacts or suboptimal vasodilatory stress influence image quality and results. This limits the perfusion study to a patient population in a relatively good clinical condition.

Third, it is important to point out, that the MBF calculated in CT MPI cannot be considered to be the absolute blood flow. At its best, it is a semiquantitative analysis, which allows to compare different myocardial regions. This might explain the values beyond the physiological range.

Fourth, further work is needed to improve our scanning protocol to reduce radiation exposure. Finally, this is a single-centre study, and further research is needed to confirm our findings.

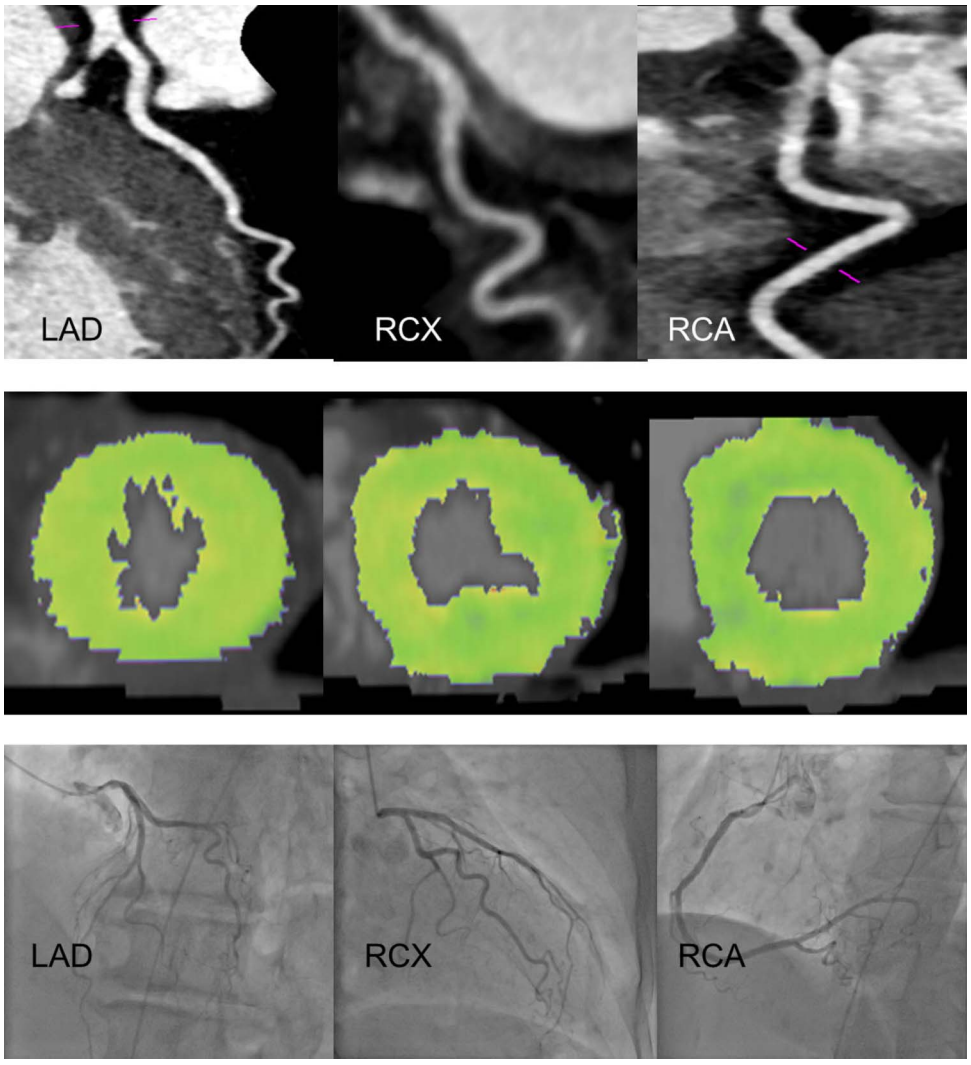

Figure 3 CTA shows no plaque formation in the coronary vessels. CT-MPI shows no perfusion defect under adenosine stress. MBF >75 ml/100 ml/min (marked with green/yellow) (apical, mid, basal). Coronary angiography shows no coronary stenosis.

CONCLUSION

Our data suggest that CT-MPI permits detection of haemodynamic relevant coronary artery stenoses with a moderate DA. CT may, therefore, allow the simultaneous assessment of both coronary morphology and function.

Contributors MG: initiation of the study (concept), data collection and analysis, manuscript writing. FB: concept of the study, CT image analysis. FvZ: patient recruitment, CT image analysis. JT: patient recruitment, coronary angiography analysis. FS and RPM: CT image analysis. MD: manuscript review, language correction.JS: patient recruitment. CB: manuscript review. KN: concept of the study, CT image analysis. AB: concept of the study, CT image analysis, manuscript writing and review.

Competing interests None.

Patient consent Obtained.

Ethics approval The study was approved by the institutional review board and the Federal Radiation Safety Council (Bundesamt für Strahlenschutz).

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Heart

CT stress perfusion imaging for detection of haemodynamically relevant coronary stenosis as defined by FFR

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