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ORIGINAL PAPER

Low-dose CT and cardiac MR for the diagnosis of coronary artery disease: accuracy of single and combined approaches

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Abstract To prospectively compare the diagnostic performance of low-dose computed tomography coronary angiography (CTCA) and cardiac magnetic resonance imaging (CMR) and combinations thereof for the diagnosis of significant coronary stenoses. Forty-three consecutive patients with known or suspected coronary artery disease underwent catheter coronary angiography (CA), dual-source CTCA with prospective electrocardiography-gating, and cardiac CMR (1.5 Tesla). The following tests were analyzed: (1) low-dose CTCA, (2) adenosine stress-rest perfusion-CMR, (3) late gadolinium enhancement (LGE), (4) perfusion-CMR and LGE, (5) low-dose CTCA combined with perfusion-CMR, (5) low-dose CTCA combined with late gadolinium-enhancement, (6) low-dose CTCA combined with perfusion-CMR and LGE. CA served as the standard of reference. CA revealed >50% diameter stenoses in 68/129 (57.7%) coronary arteries in 29/43 (70%) patients. In the patient-based analysis, sensitivity, specificity, NPV and PPV of low-dose CTCA for the detection of significant stenoses were 100, 92.9, 100 and 96.7%, respectively. For perfusion-CMR and LGE, sensitivity, specificity, NPV, PPV, and accuracy were 89.7, 100, 82.4, and 100%, respectively. In the artery-based analysis, sensitivity and NPV of low-dose CTCA was significantly ($P < 0.05$) higher than that of perfusion-CMR and LGE. All combinations of low-dose CTCA and perfusion-CMR and/or LGE did not improve the diagnostic performance when compared to low-dose CTCA alone. Taking CA as standard of reference, low-dose CTCA outperforms CMR with regard to sensitivity and NPV, whereas CMR is more specific and has a higher PPV than low-dose CTCA.

Keywords Computed tomography · Magnetic resonance imaging · Catheter coronary angiography · Myocardial perfusion imaging · Coronary artery disease

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Introduction

Conventional coronary angiography (CA) represents the clinical standard of reference for the diagnosis and management of patients with known or suspected coronary artery disease (CAD). Nevertheless, non-

invasive imaging modalities including nuclear tests [1], cardiac magnetic resonance imaging (CMR) [2], and computed tomography coronary angiography (CTCA) [3, 4] have challenged the role of the invasive standard.

CTCA using single-source or dual-source 64-slice CT scanners has emerged as a robust and accurate tool for the non-invasive diagnosis of significant coronary stenoses. On the other hand, concerns regarding the radiation exposure of patients undergoing CTCA have been raised, which prompted various dose reducing algorithms. One of the most efficient techniques for radiation dose reduction in CTCA is prospective electrocardiography (ECG)-gating, where radiation is only delivered at selected time points of the cardiac cycle [5]. First studies have shown that the low-dose technique for CTCA is accurate for the diagnosis of significant coronary stenoses as compared with CA [6]. Due to maintained diagnostic accuracy combined with the reduction of applied radiation dose, CTCA with prospective ECG-gating has become the standard method for CTCA in many centers [7].

CMR represents an important modality for the indirect detection of CAD through demonstration of myocardial perfusion defects. Stress- and rest adenosine first pass perfusion-CMR with late gadolinium-enhancement (LGE) allows for the detection of both ischemic and infarcted myocardium, both indicating the hemodynamic relevance of a coronary stenosis. Various studies have demonstrated a high diagnostic performance of CMR in comparison with CA [2, 8, 9]. Nevertheless, no study has—to the best of our knowledge—directly compared these two non-invasive imaging modalities, i.e., low-dose CTCA and CMR, with regard to their diagnostic performance in the same patient population.

The purpose of this study was to compare the diagnostic performance of low-dose CTCA and perfusion-CMR with LGE as well as combinations thereof for the diagnosis of significant CAD in one patient population taking CA as the standard of reference.

Materials and methods

Study population

We prospectively screened 55 consecutive patients with known or suspected CAD undergoing elective CA. Data for 39 of the patients are from an earlier study [10]. The clinical decision to perform CA was based on the history and the symptoms of the patient as well as on the results from exercise stress tests. The patients were asked to participate in this study and written informed consent was obtained. Patients were excluded if they had previous coronary artery bypass graft ($n = 3$), impaired renal function ($n = 2$), known hypersensitivity to contrast medium used in CMR or CTCA ($n = 0$), heart rate >70 bpm being not feasible for prospective ECG-gating [11] ($n = 2$), contraindications for adenosine (second or third AV-block, sick sinus syndrome, symptomatic bradycardia, severe asthma or obstructive pulmonary disease; $n = 1$) or to MR (implanted electronic devices, metallic foreign bodies in the eye, claustrophobia, and others according to local regulations and manufacturer's recommendations; $n = 4$). Thus, a total of 43 patients (9 female, mean age 63 ± 9 years, range 41–76 years) could be enrolled in this study (Fig. 1). Patient characteristics are summarized in Table 1. Of the 36/43 (84%) patients who had stress-ECG testing before CA, 21/36 (58%) had signs of ischemia, 11/36 (31%) had no signs of ischemia and in 4/36 (11%) patients, results of stress-ECG testing remained inconclusive. Twenty-seven of the 43 patients (63%) were receiving oral β blockers as part of their baseline treatment.

All low-dose CTCA and CMR examinations were performed within 1 day. The median time interval between low-dose CTCA/CMR and CA was 20 days (range 1–47 days).

The study protocol was approved by the local institutional review board, all patients gave written informed consent.

Low-dose CTCA

All CT examinations were performed on a dual-source CT machine (Somatom Definition, Siemens Healthcare, Forchheim, Germany) using prospective ECG-gating. All patients received a single 2.5-mg dose of sublingual isosorbide dinitrate (Isoket, Schwarz Pharma). No additional beta-blockers were given prior to CT. Eighty to 100 ml of contrast medium (iopromidum, Ultravist 370, Bayer Schering Pharma, Berlin, Germany) were administered at a flow rate of 5–6 ml s^{-1}, followed by 50 ml of a 20% contrast agent/80% saline solution mixture. Contrast agent was applied using a dual-head power injector

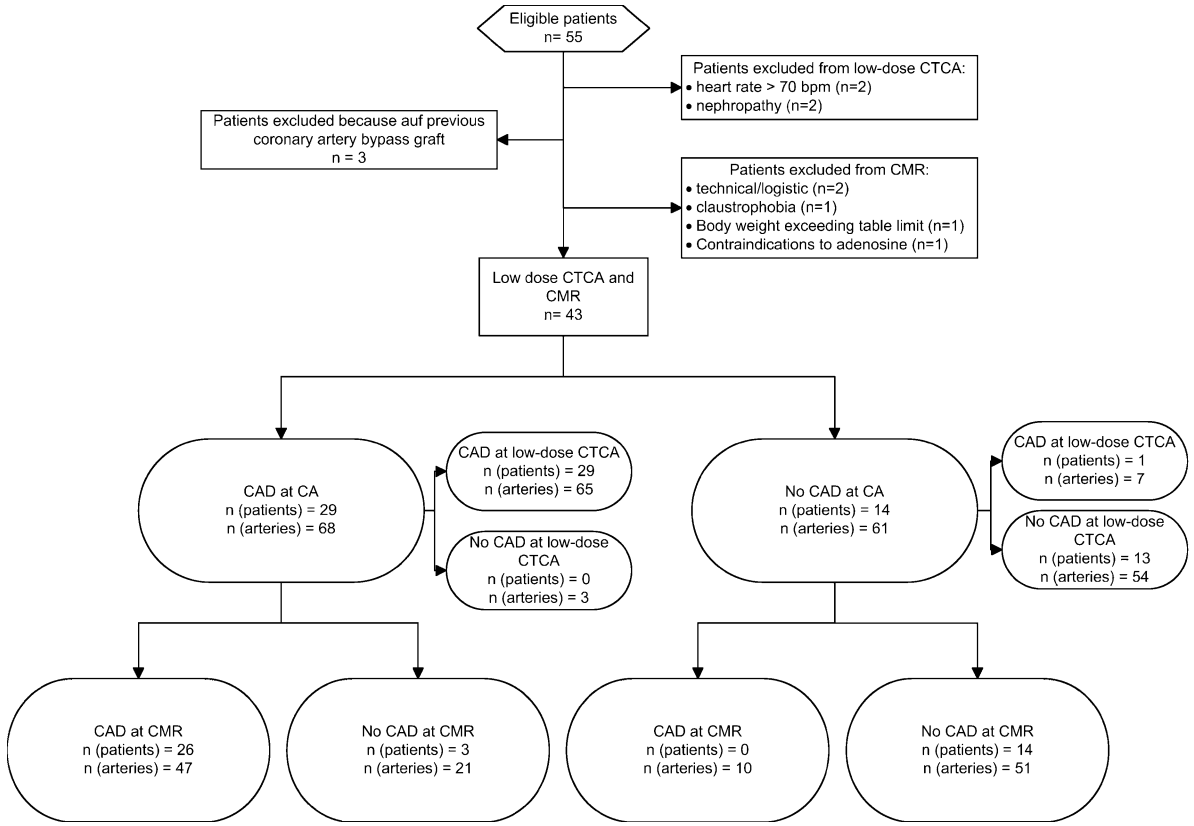

Fig. 1 Study workflow

Table 1 Patient demographics

Males	34 (79%)
Females	9 (21%)
Age (years)	64 ± 9
Body mass index (kg m^{-2})	28 ± 4
Cardiovascular risk factors	
Hypertension	31 (72%)
Smoker	13 (30%)
Hyperlipidemia	30 (70%)
Family history	10 (23%)
Diabetes	8 (19%)
Symptoms	
Dyspnea	23 (54%)
Atypical chest pain	5 (12%)
Typical chest pain	22 (51%)
History of myocardial infarction	9 (21%)
Previous percutaneous coronary intervention	7 (16%)
Oral β blockers part of baseline treatment	27 (63%)

(Stellant, Medrad, Inianola, USA) and was controlled by bolus-tracking using a region-of-interest in the ascending aorta (attenuation threshold 120HU). Data were acquired in the cranio-caudal direction during mid-inspiration using the parameters: detector collimation, $2 \times 32 \times 0.6$ mm; slice acquisition, $2 \times 64 \times 0.6$ mm by means of a z-flying spot; gantry rotation time, 0.33 s. Attenuation-based tube current modulation was used with a reference tube current–time product set at 190 mAs per rotation. The data acquisition window was set at 70% of the R–R interval; the temporal resolution was 83 ms. Patients with a body mass index (BMI) $\geq$25 kg m^{-2} ($n = 30$) were examined with a tube voltage of 120 kV; patients with a BMI <25 kg m^{-2} ($n = 13$) with 100 kV [11]. Low-dose CTCA images were reconstructed with a slice thickness of 0.6 mm, using a medium smooth-tissue convolution kernel (B30f). If the artery segment was calcified, additional reconstructions were

performed using a sharp-tissue convolution kernel (B45f) to compensate for blooming artifacts. All images were anonymized and transferred to an external workstation (Multi-Modality Workplace, Siemens Healthcare) for data analysis.

Low-dose CTCA data analysis

Low-dose CTCA data analysis was performed by two independent radiologists who were both blinded to the clinical history and to the results from any other test (including CA and CMR). All images were evaluated using transverse source images and multi-planar reformations. All segments with a diameter $\geq$1 mm at their origin were included. Vessel segments distal to occlusions were excluded from analysis.

Coronary segments were defined according to a scheme proposed by the American Heart Association [12]. The intermediate artery was designated as segment 16, if present, and together with the left main artery was considered to belong to the left anterior descending coronary artery (LAD).

First, both readers independently rated the image quality of each coronary segment as being diagnostic or non-diagnostic. Reasons for non-diagnostic image quality were assigned to motion or stair step artifacts, image noise, severe vessel wall calcifications, or insufficient contrast attenuation.

Then, both readers independently evaluated all coronary segments for the presence or absence of significant stenoses, defined as luminal diameter narrowing >50 and >70% respectively. Segments containing stents were rated as either patent or non-patent. In case of disagreement, a consensus reading was appended 1 week after the initial read-out.

CMR

All CMR studies were performed on a 1.5-T clinical MR system (Achieva, Philips Medical Systems, Best, the Netherlands). Dedicated cardiac phased-array receiver coils were used for signal reception (five elements). All data were acquired during breath hold in end-inspiration. The true short-axis of the left ventricle was determined from a series of scout images. Three representative short-axis sections were obtained, one each in the basal, mid-ventricular, and apical region of the left ventricle according to the standardized 17-segment model of the American Heart Association [13]. Pharmacological stress was applied using adenosine which was administered intravenously at 140 μg per kilogram of body weight over 2.5 min under ECG, oxygen-saturation and blood pressure monitoring. Acquisition of perfusion-CMR images was started immediately after the injection of gadobutrolum (Gadovist® 1,0; Bayer AG, Zurich, Switzerland). Contrast media was dosed at 0.1 mmol per kilogram of body weight using a power injector (MR Spectris; Medrad, Pittsburgh, Pa) at an injection rate of 5 ml s^{-1}, followed by a 40-ml saline flush. Ten minutes after stress perfusion imaging, a second bolus of 0.1 mmol gadobutrolum was injected and rest perfusion images were obtained with the same orientation and position as in stress-perfusion imaging. A delay of 10 min after the stress-perfusion examination allowed residual gadobutrolum to be washed out from the myocardium. k–t sensitivity encoding (SENSE) perfusion-CMR imaging was used in combination with a saturation recovery gradient-echo pulse sequence for both of these sequences (repetition time/echo time, 3.1/1.1 ms; flip angle, 20°; saturation pre-pulse delay, 110 ms; partial Fourier sampling; acquisition window, 120 ms; section thickness, 10 mm; k–t factor of five with 11 k–t interleaved training profiles; effective acceleration, 3.7; three sections acquired sequentially during a single R–R interval), as previously shown [14–16]. High-spatial resolution perfusion-CMR was performed with an in-plane resolution of 1.25 × 1.25 mm.

Ten minutes after rest perfusion, late gadolinium enhancement (LGE) images were acquired in continuous short-axis view using an inversion-recovery gradient-recalled echo MR sequence with the following parameters: field of view, 350–400 mm; repetition time/echo time, 7.4/4.3 ms; inversion time, 200–350 ms; flip angle, 20°; matrix, 240 × 240; slice thickness, 10 mm. The inversion time was optimized individually to null the signal from normal myocardium.

CMR Data analysis

CMR data analysis was performed on the commercially available ViewForum (Philips, Best, Netherlands) by two different, independent radiologists who were both blinded to the clinical history and to the results from any other test (including CA and low-dose CTCA). In case of disagreement between the

readers, a consensus reading was appended after 1 week.

Perfusion-CMR as well as LGE images were evaluated by visual analysis in each segment of a 16-segment model (17-segment American Heart Association model [13] minus the apical segment) and graded using a scale from 0 to 3 (0: normal, 1: probably normal, 2: probably abnormal, 3: definitely abnormal), as previously shown [16]. Myocardial territories were assigned to the three major coronary arteries according to standard definitions [13] and were analyzed for the presence of hemodynamically relevant CAD using three different approaches:

1) perfusion-CMR alone (PERF),
2) LGE alone, and
3) Perfusion-CMR combined with LGE according to the following scheme: Segments were considered to have a perfusion defect if (a) late gadolinium enhancement was present and/or (b) a perfusion deficit was found in stress-perfusion but not in rest-perfusion [17] (COMB).

Catheter coronary angiography

Biplane conventional CA was performed according to standard techniques. The angiograms were evaluated by an experienced observer who was blinded to the results from both low-dose CTCA and CMR. The coronary arteries were subdivided according to the same scheme used for CTCA [12] and were quantitatively assessed with the use of an automated edge-detection system (Xcelera 1.2, Philips Medical Systems, Best, The Netherlands). Vessel diameter measurements were performed on two different image planes and included the diameter of the reference vessel (proximal and distal to the stenosis), the minimal luminal diameter and the extent of stenosis (defined as the diameter of the reference vessel minus the minimal luminal diameter, divided by the reference diameter and multiplied by 100). A significant stenosis was defined as a diameter reduction of >50%.

Statistical analysis

Quantitative data are expressed as means ± standard deviations and categorical data are given in proportions and percentages. Analysis was performed on an intent-to-diagnose basis: Segments with a non-diagnostic image quality at CTCA were rated as positive for disease. Sensitivity, specificity, positive (PPV), and negative predictive value (NPV) as well as accuracy were obtained from contingency tables; their 95% confidence intervals (CI) were calculated from binomial expression. CA served as the standard of reference.

Additionally to LGE, PERF, COMB and CTCA alone, the following combinations were tested:

1) Low-dose CTCA in combination with perfusion-CMR,
2) low-dose CTCA in combination with LGE, and
3) low-dose CTCA in combination with perfusion-CMR and LGE.

For these combinations, a patient or artery was classified as being positive for disease if any of the tests was positive.

Agreement between methods was assessed by using unweighted Cohen's kappa statistics. A *P*-value <0.05 was considered to indicate a significant difference. Statistical analyses were performed using commercially available software (SPSS, release 15.0, Inc., Chicago, IL).

Results

Conventional coronary angiography

CA revealed >50% diameter stenoses in 114/688 segments (16.6%) corresponding to 68/129 (57.7%) coronary arteries of 29/43 (70%) patients (Fig. 1). Stenoses >70% diameter were depicted in 85/688 (12.4%) segments corresponding to 57/129 (44.2%) coronary arteries in 28/43 (65%) patients.

Low-dose CTCA

During low-dose CTCA, all patients were in sinus rhythm; the average heart rate was 61 ± 7 bpm (range 43–69 bpm).

Of the 688 possible coronary artery segments, 111 (16.3%) segments were not present or were less than 1 mm in diameter at their origin and could therefore not be included into analysis. Eight (1.2%) segments were located distally to a coronary occlusion. Hence, 569/688 (82.7%) segments were included into the analysis.

Image quality of low-dose CTCA was diagnostic in 561/569 (98.6%) segments in 40/43 (93%) patients, comparable to previous reports [6, 18]. Five segments were not assessable due to motion artifacts and three segments were not assessable due to severe vessel wall calcification. No stair step artifacts, image noise, or insufficient contrast attenuation were found as cause of non-diagnostic image quality in the remaining 561 segments.

Low-dose CTCA revealed stenoses >50% in 127/561 (22.6%) segments, corresponding to 72/129 (55.8%) coronary arteries in 30/43 (70%) patients (Fig. 1). Thirty of these stenotic arteries were located in the LAD, 20 in the LCX, and 22 in the RCA. Stenoses of >70% were depicted in 86/561 (15.3%) segments, corresponding to 62/129 (48.1%) coronary arteries in 29/43 (67%) patients.

CMR

After adenosine-injection, no adverse effects leading to discontinuation of CMR were observed. Image quality of perfusion-CMR and LGE images was diagnostic in all myocardial segments of all patients. Myocardial defects were found in 140/688 (20.3%) segments corresponding to the territories of 57/129 (44.2%) coronary arteries in 26/43 (61%) patients (Fig. 1). Nineteen of the arteries positive for CAD were assigned to the LAD, 16 to the LCX, and 22 to the RCA.

Diagnostic performance

Low-dose CTCA

Sensitivity, specificity, NPV, PPV, and accuracy of low-dose CTCA for the detection of coronary stenoses in the artery-based analysis were 95.6, 88.5, 94.7, 90.3, and 92.2%, respectively, and 100, 92.9, 100, 96.7, and 97.7%, respectively, in the patient-based analysis (Table 2) when taking <50% stenosis as cutoff value. One false-positive rating occurred in a patient having a less than 50% stenosis according to CA in the proximal LAD. At low-dose CTCA, this stenosis was judged to be significant (Fig. 2). When the threshold is increased to >70% for significant stenosis, the values for diagnostic accuracy of CTCA slightly decrease as now two patients are overestimated by low-dose CTCA as shown in Table 3.

Overall agreement between low-dose CTCA and CA for the detection of coronary stenoses was 92.2% (kappa 0.8) and 97.7% (kappa 0.95), respectively, in the artery- and patient-based analysis.

CMR

The sensitivity, specificity, NPV, PPV, and accuracy of perfusion-CMR combined with LGE images in the artery-based analysis was 69.1, 83.6, 70.8, 82.5, and 76%, respectively, and 89.7, 100, 82.4, 100, and 93%, respectively, in the patient-based analysis (Table 2). Adding LGE to perfusion-CMR showed an increase in sensitivity and NPV and was based on the detection of significant CAD in two patients with no perfusion deficits but myocardial infarction (Fig. 3). When the threshold for significant stenosis is raised to <70%, the sensitivity and NPV of CMR slightly increases as the specificity and PPV slightly decrease as shown in Table 3.

Overall agreement between perfusion-CMR combined with LGE images and CA was 76% (kappa 0.52) and 93% (kappa 0.85), respectively, in the artery- and patient-based analysis.

Combination of low-dose CTCA and CMR

Combinations of low-dose CTCA and perfusion-CMR and/or LGE revealed minor increases in sensitivity and NPV as compared to low-dose CTCA alone. Values for specificity, PPV and accuracy decreased at the same time. None of the changes in diagnostic performance as compared to that of low-dose CTCA alone was significant (see Tables 2, 3).

Discussion

This study is the first to directly compare the diagnostic performance of low-dose CTCA and CMR for the detection of significant CAD in one patient population. Taking CA as the standard of reference, low-dose CTCA outperformed CMR with regard to sensitivity and NPV. On the other hand, CMR was more specific and had a higher PPV than did low-dose CTCA in a patient-based analysis. Any combination of the two non-invasive imaging tests did not improve the diagnostic performance as compared to that of low-dose CTCA alone.

Table 2 Diagnostic performance of low-dose CTCA, CMR, and combinations thereof in comparison with catheter coronary angiography. (Cut-off value for CA: > 50%)

	Sensitivity (CI;n)	Specificity (CI;n)	NPV (CI;n)	PPV (CI;n)	Accuracy (CI;n)
Per-artery analysis					
CT					
Low-dose CTCA	95.6%* (90–100; 65/68)	88.5% (80–97; 54/61)	94.7%* (88–100; 54/57)	90.3% (83–98; 65/72)	92.2% (87–97; 119/129)
CMR					
PERF	60.3% (48–73; 41/68)	86.9% (78–96; 53/61)	66.3% (55–77; 53/80)	83.7% (72–95; 41/49)	72.9% (65–81; 94/129)
LGE	26.5% (15–38; 18/68)	93.4% (86–100; 57/61)	53.3% (43–63; 57/107)	81.8% (63–100; 18/22)	58.1% (49–67; 75/129)
COMB	69.1%* (68–81; 47/68)	83.6% (74–94; 51/61)	70.8%* (60–82; 51/72)	82.5% (72–93; ; 47/57)	76% (68–84; 98/129)
CT and CMR					
CTCA/LGE	95.6% (90–100; 65/68)	86.9% (78–96; 53/61)	94.6% (88–100; 53/56)	89% (81–97; 65/73)	91.5% (86–97; 118/129)
CTCA/PERF	97.6% (92–100; 66/68)	78.7% (68–90; ; 48/61)	96% (90–100; 48/50)	83.5% (75–92; 66/79)	88.4% (83–94; 114/129)
CTCA/COMB	97.6% (92–100; 66/68)	78.7% (68–90; 48/61)	96% (90–100; 48/50)	83.5% (75–92; 66/79)	88.4% (83–94; 114/129)
Per-patient analysis					
CT					
Low-dose CTCA	100% (98–100; 29/29)	92.9% (76–100; 13/14)	100% (96–100; 13/13)	96.7% (89–100; 29/30)	97.7% (92–100; 42/43)
CMR					
PERF	82.8% (67–98; 24/29)	100% (96–100; 14/14)	73.7% (51–96; 14/19)	100% (98–100; 24/24)	88.4% (78–99; 38/43)
LGE	51.7% (32–72; 15/29)	100% (96–100; 14/14)	50% (30–70; 14/28)	100% (97–100; 15/15)	67.4% (52–83; 29/43)
COMB	89.7% (77–100; 26/29)	100% (96–100; 14/14)	82.4% (61–100; 14/17)	100% (98–100; 26/26)	93% (84–100; 40/43)
CT and CMR					
CTCA/LGE	100% (98–100; 29/29)	92.9% (76–100; 13/14)	100% (96–100; 13/13)	96.7% (89–100; 29/30)	97.7% (92–100; 42/43)
CTCA/PERF	100% (98–100; 29/29)	92.9% (76–100; 13/14)	100% (96–100; 13/13)	96.7% (89–100; 29/30)	97.7% (92–100; 42/43)
CTCA/COMB	100% (98–100; 29/29)	92.9% (76–100; 13/14)	100% (96–100; 13/13)	96.7% (89–100; 29/30)	97.7% (92–100; 42/43)

NPV negative predictive value, *PPV* positive predictive value, *CI* 95%-confidence interval; *PERF* adenosine stress-/rest-perfusion; *LGE* late gadolinium-enhancement; *COMB* adenosine stress-/rest-perfusion and late gadolinium-enhancement; *CTCA* computed tomography coronary angiography

* Differences are significant ($P < 0.05$)

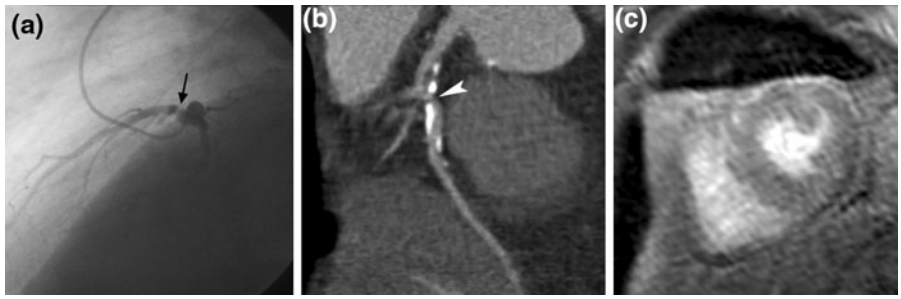

Fig. 2 76-year-old male with clinical suspicion of CAD. CA revealed a non-significant stenosis at the origin of the LAD (**a**, *arrow*). At low-dose CTCA, this stenosis was judged as being significant (**b**, *arrowhead*). Perfusion-CMR showed no perfusion deficit (**c**, *adenosine stress*). No late gadolinium enhancement was found (not shown)

Low-dose CTCA

CTCA using prospective ECG-gating was recently shown to be feasible in selected patients having a regular heart rate yielding radiation dose values as low as 1–4 mSv [6]. The diagnostic performance of CTCA known from previous single-source and dual-source 64-slice CT studies conducted in the retrospective ECG-gating mode [3, 4] could be maintained using the low-dose technique. The comparable diagnostic accuracy of CTCA as compared to CA has been shown in previous studies and could again be confirmed by our results [3, 6, 19, 20]. The most important clinical value of CTCA derives from its high sensitivity and NPV, allowing to reliably ruling-out CAD with the non-invasive test. On the other hand, specificity and PPV of CTCA are known to be lower, usually because of false-positive ratings occurring in the presence of severe vessel wall calcifications. These performance characteristics of CTCA could be confirmed in this study. In one patient, a heavily calcified stenosis at the origin of the LAD was overestimated with low-dose CTCA as being significant, whereas CA only showed a stenosis less than 50%. A total of two patients were overestimated with low-dose CTCA when taking >70% as the cutoff value for significant stenosis. Overestimation of stenosis grading must not be considered a specific drawback of prospective ECG-gating itself [21], but similarly occurs with retrospective ECG-gating in the helical mode [3, 4].

CMR

First pass perfusion under rest and adenosine-induced stress is a widely accepted CMR-technique for the detection of reduced myocardial blood flow. In addition to perfusion-CMR, LGE images are also acquired and help in the detection and quantification of infarcted myocardium. Thus, it is the rule to combine these two CMR-techniques for improving the non-invasive detection of CAD [17]. It is important, however, to recognize that LGE can be caused by other diseases apart from CAD, such as hypertrophic or dilated cardiomyopathy [22, 23]. Also, unrecognized myocardial infarction as depicted by LGE can occur as the result of a spontaneous thrombolysis and recannulation of an acute coronary lesion [24]. On the other hand, coronary stenosis in patients with CAD not necessarily leads to scarification of the myocardium, which is underlined by the low sensitivity of LGE imaging in our patient cohort.

Our study results regarding perfusion-CMR with LGE are in line with the data reported in the literature [25]. Most importantly, CMR showed an excellent specificity and PPV for the diagnosis of hemodynamically relevant CAD. On the other hand, a relatively low sensitivity and NPV was found, indicating the above stated fact that not every "morphologic" stenosis >50% irrevocably leads to a perfusion defect in the corresponding myocardial segment. When raising the threshold for significant stenosis to >70%, patients with coronary artery stenosis between 51 and 70% with ischemia as depicted on CMR are now rated to be false-positive. Therefore, the slight increase in sensitivity and NPV of CMR is accompanied by a slight decrease in specificity and PPV.

Combining low-dose CTCA and CMR

It is known that the morphological assessment of a coronary lesion with CA or CTCA does not necessarily correlate with the impairment in myocardial

Table 3 Diagnostic performance of low-dose CTCA, CMR, and combinations thereof in comparison with catheter coronary angiography. (Cut-off value for CA: > 70%)

	Sensitivity (CI;n)	Specificity (CI;n)	NPV (CI;n)	PPV (CI;n)	Accuracy (CI;n)
Per-artery analysis					
CT					
Low-dose CTCA	89.4% (80–98; 51/57)	84.7% (75–93; 61/72)	91% (83–98; 61/67)	82.2% (71–92; 51/62)	86.8% (80–93; 112/129)
CMR					
PERF	61.4% (47–74; 35/57)	80.5% (70–90; 58/72)	72.5% (62–82; 58/80)	71.4% (57–85; 35/49)	72% (63–80; 93/129)
LGE	31.5% (18–44; 18/57)	94.4% (88–100; 68/72)	63.5% (53–73; 68/107)	81.8% (63–100; 18/22)	66.6% (58–75; 86/129)
COMB	71.9% (59–84; 41/57)	77.7% (67–88; 56/72)	77.7% (67–88; 56/72)	71.9% (59–84; 41/57)	75.1% (67–83; 97/129)
CT and CMR					
CTCA/LGE	91.2% (83–99; 52/57)	81.9% (72–91; 59/72)	92.1% (84–99; 59/64)	80% (69–90; 52/65)	86% (79–92; 111/129)
CTCA/PERF	94.7% (88–101; 54/57)	73.6% (62–84; 53/72)	94.6% (87–101; 53/56)	73.9% (63–84; 54/73)	82.9% (76–89; ; 107/129)
CTCA/COMB	94.7% (88–101; 54/57)	72.2% (61–83; 52/72)	94.5% (87–101; 52/55)	72.9% (62–83; 54/74)	82.1% (75–89; 106/129)
Per-patient analysis					
CT					
Low-dose CTCA	96.4% (87–105; 27/28)	86.6% (66–107; 13/15)	92.8% (75–109; 13/14)	93.1% (82–104; 27/29)	93% (84–101; 40/43)
CMR					
PERF	82.1% (66–98; 23/28)	93.3% (77–109; 14/15)	73.6% (51–96; 14/19)	95.8% (85–105; 23/24)	86% (74–97; 37/43)
LGE	50% (29–70; 14/28)	93.3% (77–109; 14/15)	50% (29–70; 14/28)	93.3% (77–109; 14/15)	65.1% (49–80; 28/43)
COMB	89.2% (76–102; 25/28)	93.3% (77–109; 14/15)	82.3% (61–103; 14/17)	96.1% (86–105; 25/26)	90.6% (80–100; 39/43)
CT and CMR					
CTCA/LGE	96.4% (87–105; 27/28)	86.6% (66–107; 13/15)	92.8% (75–109; 13/14)	93.1% (82–104; 27/29)	93% (84–101; 40/43)
CTCA/PERF	96.4% (87–105; 27/28)	86.6% (66–107; 13/15)	92.8% (75–109; 13/14)	93.1% (82–104; 27/29)	93% (84–101; 40/43)
CTCA/COMB	96.4% (87–105; 27/28)	86.6% (66–107; 13/15)	92.8% (75–109; 13/14)	93.1% (82–104; 27/29)	93% (84–101; 40/43)

NPV negative predictive value, *PPV* positive predictive value, *CI* 95%-confidence interval; *PERF* adenosine stress-/rest-perfusion; *LGE* late gadolinium-enhancement; *COMB* adenosine stress-/rest-perfusion and late gadolinium-enhancement; *CTCA* computed tomography coronary angiography

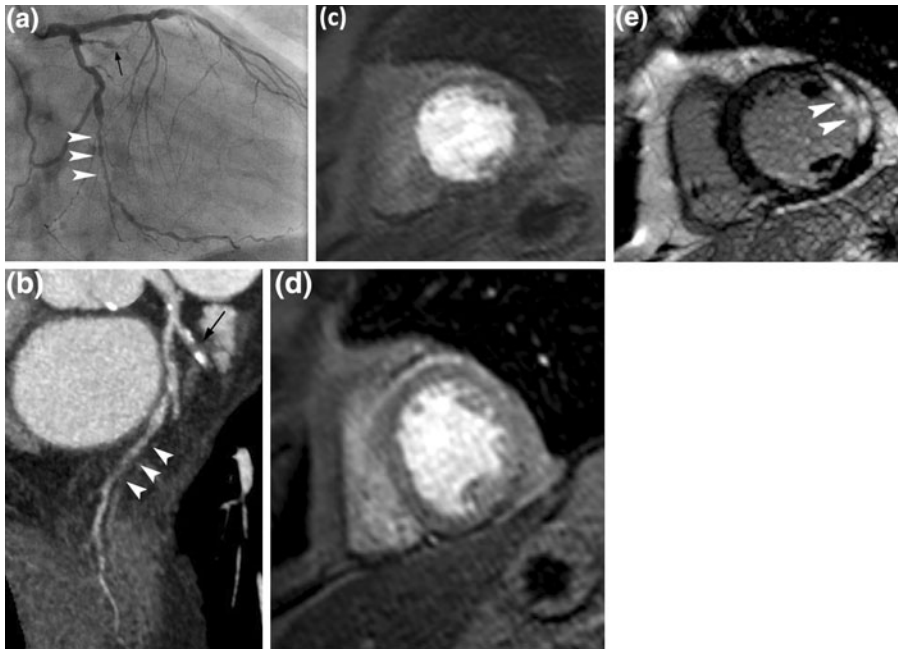

Fig. 3 60-year-old male with clinical suspicion of CAD. CA showed a significant stenosis of the distal LCX (**a**, *arrowheads*) and occlusion of the first posterolateral branch (**a**, *arrow*). Low-dose CTCA confirmed the significant stenosis (**b**, *arrowheads*) and occlusion (**b**, *arrow*). Stress-(**c**) and rest-perfusion-CMR (**d**) revealed no perfusion deficit. Late gadolinium enhancement was found in anterolateral and partially in inferolateral myocardial segments, corresponding to the LCX territory (*arrowheads*, **e**)

blood flow caused by the stenosis. Owing to the performance characteristics of low-dose CTCA, patients with no coronary stenoses can be safely discharged without further testing. On the other hand, patients with obstructive lesions at CTCA should undergo a functional test such as CMR for evaluating the hemodynamic relevance of the stenosis. CMR might qualify as a second line imaging technique in patients with non diagnostic coronary artery segments on low-dose CTCA. The three patients in our study which had one or more non-diagnostic segments all had other significant stenoses in different segments of the same vessel, therefore not influencing the results of diagnostic accuracy. In certain cases, where low-dose CTCA is not diagnostic, however, CMR can help to confirm or exclude CAD.

Thus, we did expect that the strengths and weaknesses of the two imaging tests would counterbalance each other. However, no combination between low-dose CTCA and perfusion-CMR and/or LGE did lead to a relevant increase in the diagnostic performance when compared to CTCA alone. This study result could be caused by the known variability in the coronary artery blood supply to myocardial segments [26]. Another, more probable explanation is the purely morphoanatomic nature of our reference standard.

Limitations

The number of included patients was relatively low. Our patients were referred for CA and as such represent a selected patient population. The cohort was characterised by a relatively high prevalence of CAD that may have resulted in an overestimation of the ability of DSCT to detect and to rule out stenoses [27]. Thus, our study results may not be transferred to a more unselected group of patients. Further studies are needed to confirm our results in a larger and more homogeneous patient cohort. Secondly, as mentioned above, we compared a functional imaging test taking a morphological test as the reference standard without additional functional assessment such as fractional flow reserve. This may underestimate the true diagnostic performance of CMR for the diagnosis of hemodynamically relevant CAD. On the other

hand, a comparison with CA is the standard in the majority of studies assessing the value of non-invasive cardiac testing.

Finally, CMR images were analyzed purely visually using a previously described algorithm [2, 15–17]. No semi-quantitative analysis of perfusion-CMR was performed. However, most studies investigating the diagnostic accuracy of CMR for the detection of CAD utilize purely visual evaluation [2, 15–17, 28] and the majority of centers continue to use visual analysis for the assessment of clinical myocardial perfusion scans [29]. Comparing the rest and stress scans together on a viewing platform allows the recognition of perfusion defects and discrimination from artifacts, as previously shown [30]. Recognition of artifacts is critical for accurate analysis of scans because artifacts with rapid image acquisition usually manifest themselves as dark subendocardial rims and may mimic perfusion defects.

Conclusion

Compared to CA, low-dose CTCA outperforms CMR with regard to sensitivity and NPV, whereas CMR is more specific and has a higher PPV than low-dose CTCA. Combined approaches of low-dose CTCA and CMR did not improve the performance of CTCA alone, most probably because of the use of a purely morphological imaging test as the standard of reference.

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