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Diagnostic accuracy of computed tomography coronary angiography and evaluation of stress-only single-photon emission computed tomography/computed tomography hybrid imaging: comparison of prospective electrocardiogram-triggering vs. retrospective gating

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Aims To determine diagnostic accuracy, effective radiation dose, and potential value of computed tomography coronary angiography (CTCA) for hybrid imaging with single-photon emission computed tomography (SPECT) comparing prospective electrocardiogram (ECG)-triggering vs. retrospective ECG-gating.

Methods and results Two hundred patients underwent standard myocardial stress/rest- SPECT perfusion imaging, which served as standard of reference. One hundred consecutive patients underwent 64-slice CTCA using prospective ECG-gating, and were compared with 100 patients who had previously undergone CTCA using retrospective ECG-gating. For predicting ischaemia, CTCA with prospective ECG-triggering and a stenosis cut-off >50% had a per-vessel sensitivity, specificity, negative, and positive predictive value of 100, 84, 100, and 30%; respective values for CTCA with retrospective ECG-gating were similar (P = n.s.): 86, 83, 98, and 33%. Combining CTCA with stress-only SPECT revealed 100% clinical agreement with regard to perfusion defects, and provided additional information in half the patients on preclinical coronary findings. Effective radiation dose was 2.2 $\pm$ 0.7 mSv for CTCA with prospective ECG-triggering, and 19.7 $\pm$ 4.2 mSv with retrospective ECG-gating ($P < 0.001$) (5.4 $\pm$ 0.8 vs. 24.1 $\pm$ 4.3 mSv for hybrid imaging).

Conclusion Prospective ECG-triggering for CTCA reduces radiation dose by almost 90% without affecting diagnostic performance. Combined imaging with stress-only SPECT is an attractive alternative to standard stress/rest-SPECT for evaluation of coronary artery disease, offering additional information on preclinical atherosclerosis.

Keywords Low dose CT • Prospective ECG-triggering • Retrospective ECG-gating • Computed tomography coronary angiography • Diagnostic accuracy • Hybrid imaging • Stress-only SPECT

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Introduction

In the past years computed tomography coronary angiography (CTCA) had been used increasingly in the assessment of coronary artery disease (CAD), as it offers high diagnostic accuracy in stenosis detection,[1–4] short examination time, and minimal side effects apart from the potential harm of radiation-induced neoplasms, which has evoked a vivid controversy on the clinical benefit of CTCA. This has induced the search for strategies to minimize the radiation dose while maintaining image quality. Several technical advances have allowed to decrease the dose from originally 20–25[4] to 10–15 mSv by use of electrocardiogram (ECG)-gated tube modulation[5] and even below 10 mSv by further optimizing scanning parameters of CTCA with retrospective ECG-gating.[6] A recent milestone for wide clinical acceptance of CTCA was the introduction of prospective ECG-triggering, by which scanning is limited to a narrow predefined end-diastolic phase resulting in a massive reduction of radiation exposure to a range of 1–3 mSv.[7] The validity of this new low-dose protocol has been confirmed in a larger unselected patient population[8] and preliminary reports encourage the use of this protocol in latest generation CT scanners with 320 slices.[9] However, at present no data exist on the performance of CTCA with retrospective ECG-gating vs. CTCA with prospective ECG-triggering in comparison to a standard of reference for ischaemia.

As objective proof of ischaemia is the main determinant for clinical decision making in chronic stable CAD,[10–12] we have used myocardial perfusion imaging (MPI) with single-photon emission computed tomography (SPECT) as standard of reference. However, as CTCA visualizes coronary artery stenoses directly, and MPI identifies ischaemia, both methods may also provide complementary information on CAD,[13] and hybrid examinations may facilitate a comprehensive interpretation of coronary lesions and their pathophysiological relevance.[13–16] Effective radiation doses for hybrid imaging with SPECT MPI and CTCA using retrospective ECG-gating of up to 41 mSv[17] have been reported in the literature, precluding its widespread clinical use, while prospective ECG-triggering may overcome this drawback. A further decrease in radiation dose of hybrid imaging could be achieved by confining the SPECT scan to stress-only, as recently suggested for low pre-test probability populations.[18]

Therefore, the purpose of the present study was two-fold: First, to compare the diagnostic accuracy of CTCA with low-dose prospective ECG-triggering vs. standard retrospective gating for detecting haemodynamic relevant coronary lesions; and second, to validate a new algorithm for evaluation of unknown CAD by hybrid imaging combining CTCA with low-dose stress-only SPECT; standard stress/rest-SPECT served as the standard of reference for both aims.

Methods

Study design

Each patient underwent low-dose stress/high-dose rest-SPECT, and CTCA for clinical indication.

First step: Findings from both CTCA acquisition protocols were separately analysed and compared with SPECT results.

Second step: Two independent blinded readers analysed either the paired stress-SPECT plus CTCA (CTCA/stress-SPECT) or the stress-SPECT plus the rest-SPECT scan (stress/rest-SPECT).

Clinical study endpoints were, first, the direct comparison of total effective radiation dose and diagnostic accuracy of both CTCA protocols, and, second the comparison of hybrid CTCA/stress-SPECT vs. standard stress/rest-SPECT with regard to: agreement on presence or absence of ischaemic coronary heart disease, information on preclinical CAD, total effective radiation dose, and total examination duration.

Patient groups

One hundred consecutive patients with suspected ($n = 85$) or known ($n = 15$) CAD referred for MPI with SPECT and CTCA using prospective ECG-triggering were prospectively enrolled in the present study, if none of the following exclusion criteria were present: hypersensitivity to iodinated contrast agent, renal insufficiency (creatinine levels >150 μmol/L, or >1.7 mg/dL), non-sinus rhythm, or previous coronary bypass surgery. These patients were compared with 100 retrospectively enrolled patients, who had previously undergone MPI and CTCA using retrospective ECG-gating; groups were matched for the presence of known CAD, heart rate, and body mass index (BMI). We decided to include 100 patients into the final analysis of this preliminary report, although no formal sample size calculation was performed due to the pilot nature of this study.

The study protocol was approved by the institutional review board and written informed consent was obtained.

Computed tomography coronary angiography data acquisition and post-processing

All 200 patients received a single dose of 2.5 mg isosorbiddinitrate sublingual (Isoket, Schwarz Pharma, Monheim, Germany) 2 min prior to the scan. In addition, intravenous metoprolol (5–20 mg) (Beloc, AstraZeneca, London, UK) was administered prior to the CTCA examination if necessary to achieve a target heart rate <65 b.p.m. For CTCA, 80 mL of iodixanol (Visipaque 320, 320 mg/mL, GE Healthcare, Buckinghamshire, UK) at a flow rate of 5 mL/s followed by 50 mL saline solution was injected into an antecubital vein via an 18-gauge catheter. Bolus tracking was performed with a region of interest placed into the ascending aorta.

All CTCA examinations were performed on a LightSpeed VCT XT scanner (GE Healthcare) using two different scanning protocols.

Prospective ECG-triggering: slice acquisition 64 × 0.625 mm, smallest X-ray window (only 75% of the R–R interval; padding set to 0 ms), z-coverage 40 mm with an increment of 35 mm, gantry rotation time 350 ms, BMI-adapted tube voltage (100–120 kV), and effective tube-current (450–700 mA).

Retrospective ECG-gating: slice acquisition 64 × 0.625 mm, z-coverage 40 mm, heart rate adapted pitch ranging between 0.18 and 0.26, gantry rotation time 350 ms, tube voltage 120 kV, BMI-adapted effective tube-current (280–750 mA), and ECG-adapted tube modulation (i.e. reduction to about 40% of nominal tube current during systole to mid-diastole). Computed tomography data sets were retrospectively reconstructed in mid- to end-diastolic phases and additional phases if needed for optimal coronary artery visualization.

Computed tomography coronary angiography image quality was assessed in all coronary segments[19] of all patients using a previously reported scoring system.[20] If one or more segments in a patient were rated 'non-diagnostic', then the examination was excluded from further analysis (for retrospective ECG-gating an examination

was excluded from further analysis, if at least one coronary segment was considered 'non-diagnostic' in all reconstructed phases of the R–R interval).

Single-photon emission computed tomography data acquisition and post-processing

Single-photon emission computed tomography data acquisition was performed on a dual-head detector camera (Ventri, GE Healthcare, Milwaukee, WI, USA), and all patients underwent a 1-day stress (0.14 mg/kg/min adenosine i.v.)/rest MPI protocol using a dose of ~300 and 900 MBq of ^{99m}Tc-tetrofosmin, respectively. Emission data were acquired with a parallel-hole, low-energy, high-resolution collimator with a 20% symmetric window centred at 140 keV. Further acquisition parameters were 3° rotation per stop, 180° each head, and 25 s per projection. Acquisitions were gated for 16 frames per R–R cycle with an acceptance window of 50%. All patients underwent low-dose, unenhanced CT for attenuation correction on a LightSpeed VCT XT scanner (GE Healthcare), as previously reported in detail.[21]

Diagnostic accuracy

Computed tomography coronary angiography images were evaluated and classified by two independent readers, blinded to the results of SPECT, using axial source images, multi-planar reformations, and thin-slab maximum intensity projections. Coronary arteries were visually assessed for the presence of narrowing of the coronary luminal diameter >50 and >75%.

Single-photon emission computed tomography data were analysed, blinded to the results of CTCA, with regard to the presence of reversible and/or fixed perfusion defects on short-axis, horizontal and vertical long-axes slices as well as on the polar maps. Left ventricular perfusion defects were attributed to three vascular territories: left anterior descending artery (LAD) included the apical, anterior, septal wall; circumflex artery (CX) included the lateral wall; right coronary artery (RCA) included the inferior wall.

Effective radiation dose

The total effective dose of CTCA was calculated as the product of the dose–length product (DLP) times a conversion coefficient for the chest ($k = 0.017$ mSv/mGy × cm).[5] For SPECT, the effective radiation dose was estimated as previously suggested (6.7mSv/GBq)[5] plus the dose for CT attenuation correction (DLP × conversion coefficient for the chest).

Duration of examination protocols

The routine time schedule for the standard stress/rest-SPECT protocol[22] used at our institute requires a period of 90 min between each injection of ^{99m}Tc-tetrofosmin and the following data acquisition. Computed tomography coronary angiography is routinely performed between the application of the tracer at stress and the first SPECT data acquisition. For all patients the total time for both protocols was assessed.

Statistical analysis

Quantitative variables were expressed as mean ± standard deviation and categorical variables as frequencies and percentages. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated, stress/rest MPI with SPECT was considered the standard of reference. Because of the interdependencies between different vessels, the statistics were also calculated on a per-patient basis (presence of at least one significant coronary artery stenosis or absence of any significant stenosis in each patient). We took into account the clustered nature of the data (i.e. the fact that there were not 600 independent vessels but instead clusters of vessels in 200 patients). For these analyses, a proportion-procedure for survey data of the Stata software (Stata 10.0, StataCorp, College Station, TX) with the patient as primary sample unit was performed to address dependencies between the vessels.[23] Differences between the two matched patient populations regarding diagnostic performance were tested for significance by using χ^2-tests for comparison of cross tables. For further comparison, Mann–Whitney *U*-tests were performed for: total effective radiation dose, heart rate, BMI, and age. χ^2-tests were used to determine differences in gender, coronary risk factors, clinical symptoms, and prevalence of known CAD. Differences between CTCA/stress-SPECT and standard stress/rest-SPECT in total radiation dose and total time between both protocols were determined using a paired Student's *t*-test. A *P*-value of <0.05 was considered to indicate statistical significance, all reported *P*-values were two-sided and were not adjusted for multiple testing. SPSS software (SPSS 15.0, Chicago, IL, USA) was used for statistical testing.

Results

The present study aimed at including 100 consecutive patients scanned with prospective ECG-triggering (CAD) and a matched control group scanned with retrospective ECG-gating. After initial assessment, seven additional patients did not meet the inclusion criteria because CTCA was not feasible due to non-sinus rhythm ($n = 5$), high heart rate despite beta-blocker administration ($n = 1$), and elevated creatinine levels ($n = 1$). Of these resulting 100 initially included patients, 15 patients had to be excluded because of non-diagnostic CTCA image quality in at least one coronary segment, due to breathing ($n = 5$) or motion artefacts ($n = 10$). The control group was retrospectively recruited from a large pool of patients who had undergone CTCA with retrospective ECG-gating. We identified 193 patients who had undergone SPECT in addition to CTCA, of these, 100 patients were selected who showed the best match with regard to presence of known CAD, BMI, and heart rate. Of these resulting 100 initially included patients, 13 patients were excluded because of breathing artefacts ($n = 6$), occurrence of a premature ventricular beat during scanning ($n = 1$), or coronary motion artefacts ($n = 6$). Demographics of the final two patient populations are given in *Table 1*.

Diagnostic accuracy

Prospective ECG-triggering: CTCA revealed 58 coronary vessels (23%) with stenoses >50% in 29 of 85 patients (34%), and 18 vessels (7%) with stenoses >75% in 12 patients (14%). In this group, MPI with SPECT detected perfusion defects in 20 vascular territories (8%) of 18 patients (21%); while 5 of the defects were fixed (scar) 11 were reversible (ischaemia), and 2 were partly fixed and partly reversible (mixed defects).

Retrospective ECG-gating: Sixty-two coronary vessels (24%) with stenoses >50% in 38 of 87 patients (44%), and 24 vessels (9%) with stenoses >75% in 17 patients (20%) were observed on CTCA scans. Perfusion defects in 27 (10%) vascular territories of 23 patients (26%) were detected by MPI with SPECT, i.e. 8 fixed, 15 reversible, and 4 mixed defects.

Table 1 Patient demographics

	Retrospective electrocardiogram-gating	Prospective electrocardiogram-triggering	*P*-value
Enrolled patients	100	100	
Inadequate computed tomography coronary angiography quality	13	15	0.68
Final study population	87	85	
Female/male	30/57	30/55	0.91
Age (years)	63 ± 11 (33–89)	59 ± 11 (27–85)	0.04[a]
BMI (kg/m^2)	27 ± 4 (19–50)	27 ± 4 (18–39)	0.43
Heart rate (b.p.m.)	58 ± 6 (45–73)	57 ± 6 (40–70)	0.12
Known coronary artery disease, (%)	11 (13)	12 (14)	0.78
Previous infarction, (%)	5 (6)	3 (4)	0.49
Previous stent placement, (%)	7 (8)	6 (7)	0.32
Coronary risk factors, (%)			
Smokers	24 (28)	35 (41)	0.06
Hypertension	56 (64)	50 (59)	0.46
Diabetes	11 (13)	11 (13)	0.95
Positive family history	22 (25)	29 (34)	0.21
Dyslipidaemia	41 (47)	43 (51)	0.65
Clinical symptoms, (%)			
None	35 (40)	21 (25)	0.03[a]
Typical angina	23 (26)	16 (19)	0.23
Atypical chest pain	22 (25)	38 (45)	0.003[a]
Dyspnoea	11 (13)	10 (12)	0.86

[a]Indicates statistical significance.

The diagnostic performance of CTCA by prospective ECG-triggering was comparable with retrospective ECG-gating (*Table 2*); no statistically significant differences were detected. Regardless of the scanning technique, CTCA is more sensitive and offers a higher NPV for a stenosis cut-off >50% compared with >75%. Conversely, sensitivity and NPV decrease, while specificity and the PPV increase when a cut-off >75% is chosen.

Hybrid imaging

Computed tomography coronary angiography/stress-SPECT with prospective ECG-triggering identified the same 18 patients to have abnormal perfusion, as the standard stress/rest-SPECT protocol, resulting in a clinical agreement of 100% (*Figure 1*). Computed tomography coronary angiography provided additional information in 38/85 patients (45%), i.e. intermediate coronary lesions ($n = 22$), non-stenosing coronary plaque ($n = 15$), and coronary anomaly ($n = 1$) (*Figure 2*).

Computed tomography coronary angiography/stress-SPECT with retrospective ECG-gating identified the same 23 patients to have abnormal perfusion, as the standard stress/rest-SPECT protocol, also resulting in a clinical agreement of 100%. Computed tomography coronary angiography provided additional information in 43/87 patients (49%), i.e. intermediate coronary lesions ($n = 20$), non-stenosing coronary plaque ($n = 22$), and coronary anomaly ($n = 1$).

The time schedule of the CTCA/stress-SPECT examination protocol was shorter as compared with standard stress/rest SPECT (130 vs. 245 min, $P < 0.001$), as all CTCA examinations (either with prospective ECG-triggering or with retrospective ECG-gating) were performed in the 90 min between the first injection of ^{99m}Tc-tetrofosmin and stress data acquisition.

Total effective radiation dose

The mean total effective radiation dose of CTCA with prospective ECG-triggering was 2.2 ± 0.7 mSv (range: 1.0–3.3 mSv), representing a reduction of about 90% when compared with the 19.7 ± 4.2 mSv (range: 11.5–33.0 mSv) obtained with retrospective ECG-gating ($P < 0.001$).

Radiation exposure from SPECT was—by definition of the study design—comparable in both groups: i.e. 9.6 ± 0.7 mSv (range: 8.2–12.5 mSv) in the prospectively triggered group, and 10.7 ± 1.1 mSv (range: 8.5–14.4 mSv) in the group with retrospective ECG-gating.

Combining stress-only SPECT with prospective ECG-triggering allows a significant reduction of total effective radiation dose, when compared with hybrid imaging with retrospective ECG-gating (5.4 ± 0.8 vs. 24.1 ± 4.3 mSv, $P < 0.001$).

Table 2 Diagnostic accuracy of computed tomography coronary angiography

All patients	Retrospective electrocardiogram-gating				Prospective electrocardiogram-triggering			
	Any perfusion defect		Reversible defects only		Any perfusion defect		Reversible defects only	
	>50%	>75%	>50%	>75%	>50%	>75%	>50%	>75%
Patient-based								
Sens. % (CI;*n*)	91 (79–100;21/23)	57 (36–77;13/23)	89 (75–100;17/19)	53 (29–76;10/19)	94 (83–100;17/18)	61 (38–84;11/18)	100 (NA;13/13)	71 (47–96;10/14)
Spec. % (CI;*n*)	73 (62–84;47/64)	94 (88–100;60/64)	73 (62–84;47/64)	94 (88–100;60/64)	76 (66–86;51/67)	97 (93–100;65/67)	76 (66–86;51/66)	97 (93–100;65/67)
NPV % (CI;*n*)	96 (90–100;47/49)	86 (77–94;60/70)	96 (90–100;47/49)	87 (79–95;60/69)	98 (94–100;51/52)	90 (83–97;65/72)	100 (NA;51/51)	94 (88–100;65/69)
PPV % (CI;*n*)	55 (39–71;21/38)	77 (56–97;13/17)	50 (33–67;17/34)	71 (47–96;10/14)	52 (34–69;17/33)	85 (64–100;11/13)	47 (28–65;13/28)	83 (61–100;10/12)
Vessel-based								
Sens. % (CI;*n*)	85 (72–99;23/27)	59 (41–77;16/27)	86 (71–100;19/22)	59 (39–79;13/22)	85 (69–100;17/20)	65 (42–‘88;13/20)	100 (NA;16/16)	75 (52–98;12/16)
Spec. % (CI;*n*)	83 (77–90;195/234)	97 (93–100;226/234)	83 (77–90;189/227)	96 (93–100;219/227)	83 (76–89;194/235)	98 (95–100;230/235)	84 (77–90;190/227)	98 (95–100;223/227)
NPV % (CI;*n*)	98 (96–100;195/199)	95 (93–98;226/237)	98 (97–100;189/192)	96 (94–99;219/228)	98 (97–100;194/197)	97 (95–99;230/237)	100 (NA;190/190)	98 (97–100;223/227)
PPV % (CI;*n*)	37 (23–51;23/62)	67 (43–90;16/24)	33 (19–48;19/57)	62 (36–88;13/21)	29 (17–42;17/58)	72 (43–100;13/18)	30 (16–44;16/53)	75 (43–100;12/16)
Unknown coronary artery disease only								
Patient-based								
Sens. % (CI;*n*)	87 (69–100;13/15)	53 (27–80;8/15)	83 (61–100;10/12)	50 (20–80;6/12)	92 (75–100;11/12)	75 (49–100;9/12)	100 (NA;9/9)	80 (54–100;8/10)
Spec. % (CI;*n*)	74 (63–85;45/61)	95 (90–100;58/61)	74 (63–85;45/61)	95 (90–100;58/61)	79 (68–89;48/61)	97 (92–100;59/61)	79 (68–89;48/60)	97 (92–100;59/61)
NPV % (CI;*n*)	96 (90–100;45/47)	89 (82–97;58/65)	96 (90–100;45/47)	91 (83–98;58/64)	98 (94–100;48/49)	95 (90–100;59/62)	100 (NA;48/48)	97 (92–100; 59/61)
PPV % (CI;*n*)	45 (26–63;13/29)	73 (45–100;8/11)	39 (19–58;10/26)	67 (38–100;6/9)	46 (25–66;11/24)	82 (58–100;9/11)	43 (23–64;9/21)	80 (54–100;8/10)
Vessel-based								
Sens. % (CI;*n*)	88 (70–100;14/16)	63 (37–88;10/16)	85 (64–100;11/13)	62 (33–90;8/13)	93 (79–100;13/14)	79 (55–100;11/14)	100 (NA;12/12)	83 (61–100;10/12)
Spec. % (CI;*n*)	84 (78–91;179/212)	97 (94–100;206/212)	84 (78–91;174/206)	97 (94–100;200/206)	85 (78–92;174/205)	98 (94–100;200/205)	86 (79–93;172/201)	98 (95–100;197/201)
NPV % (CI;*n*)	99 (97–100;179/181)	97 (95–99;206/212)	99 (97–100;174/176)	98 (95–100;200/205)	99 (98–99;174/175)	99 (97–100;200/203)	100 (NA;172/172)	99 (98–100;197/199)
PPV % (CI;*n*)	30 (15–40;14/47)	63 (34–91;10/16)	26 (11–40;11/43)	57 (26–88;8/14)	30 (14–45;31/44)	69 (37–100;11/16)	29 (13–46;12/41)	71 (35–100;10/14)

CI, 95% confidence interval; *n*, absolute numbers; Sens., sensitivity; Spec., specificity; NA, not available; NPV, negative predictive value; PPV, positive predictive value.

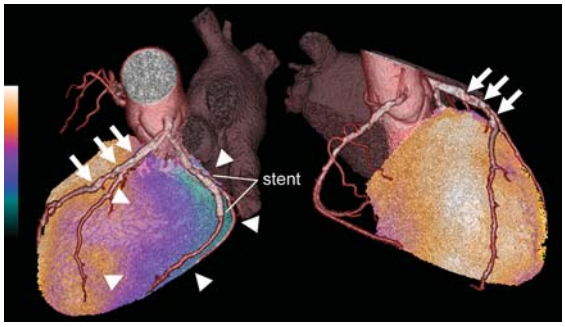

Figure 1 Fused stress ^{99m}Tc-tetrofosmin perfusion single-photon emission computed tomography/computed tomography coronary angiography image (radiation dose from computed tomography coronary angiography 2.2 mSv, from stress-single-photon emission computed tomography 2.5 mSv), showing a lateral perfusion defect (arrows heads), served by the stented circumflex artery. Sequential intermediate lesions in the left anterior descending artery (arrows) are not haemodynamically relevant (no perfusion defect).

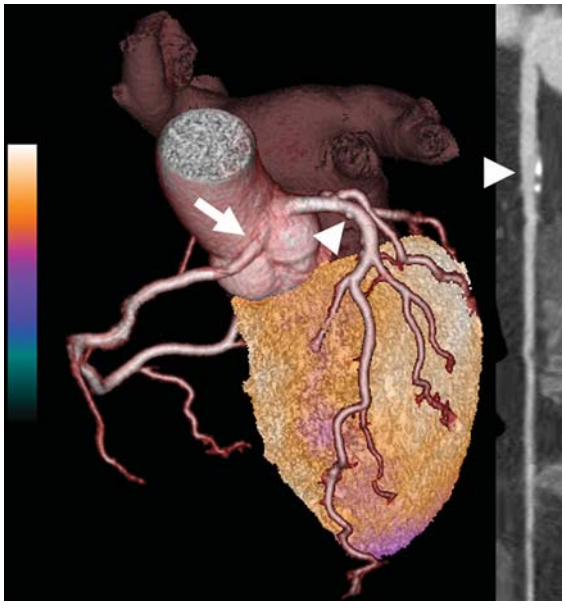

Figure 2 Fused stress ^{99m}Tc-tetrofosmin perfusion single-photon emission computed tomography/computed tomography coronary angiography image (radiation dose from computed tomography coronary angiography 1.3 mSv, from stress-single-photon emission computed tomography 2.2 mSv) reveals normal myocardial perfusion, but non-significant vessel wall irregularities in the proximal left anterior descending artery (arrows heads), as well as a coronary anomaly (arrow; origin of the right coronary artery from the left coronary sinus).

Discussion

The main findings of the present study are two-fold: first, it documents that prospective ECG-triggering provides an excellent diagnostic accuracy, comparable with retrospective ECG-gating, despite a decrease in radiation dose by about 90%. Second, we have validated a new low-dose hybrid SPECT/CTCA algorithm for assessment of CAD allowing reduction in protocol time as well as in radiation dose at maintained accuracy compared with stress/rest SPECT offering additional clinical information.

Conventional spiral CTCA protocols using retrospective ECG-gating have been shown to be associated with high total radiation doses between 9.4 and 21.4 mSv.[4,24] With the introduction of prospective ECG-gating, however, the total radiation dose of CTCA could be reduced down to 2.1 mSv.[7] Only one study[25] has directly compared total effective radiation doses of the two protocols in a head-to-head comparison, describing a 79% decrease from CTCA with retrospective ECG-gating (20.0 mSv) to CTCA with prospective ECG-triggering (4.1 mSv), which is very similar to the results in the two matched patient populations of the present study (i.e. 2.2 and 19.7 mSv).

Our study provides evidence that accuracy of CTCA is preserved even after introducing the prospective ECG-triggering protocol. No data exists on direct comparison between the two protocols with regard to diagnostic performance, although preliminary data have proved the feasibility and documented preserved image quality with the new dose saving protocol.[7,8,25,26] The present data not only confirm the substantial reduction in effective radiation dose, but also document that the accuracy of CTCA with prospective ECG-triggering equals the accuracy of retrospectively gated CTCA. As the reduction in radiation dose is striking, the widespread use of prospective ECG-gating may now be envisaged. Our results display an excellent NPV but a modest PPV in the detection of ischaemic heart disease, especially when a cut-off for luminal narrowing is chosen at 50%. This is in line with previous results,[27–29] and concurs with the generally accepted fact that the strengths of CTCA lies in its excellent ability to rule out CAD. As a consequence most recommendations consider the use of CTCA mainly in low-to-intermediate risk populations,[30] in which event rate and mortality are low and unlikely to be further lowered by any diagnostic or therapeutic procedure. Therefore the bars are very high for any diagnostic tool to keep a positive balance between harms and benefits. This is reflected by the ongoing controversy on the potential carcinogenic risk of the effective radiation dose and its justification for a purely diagnostic application. In this context, prospective ECG-triggering represents a milestone as it allows accurate CAD assessment with low-dose CTCA, which appears to be an ideal 'gate-keeper' for the assessment of unknown CAD in selected patient populations (i.e. low-to-intermediate pre-test probability) due to its high NPV, and may offer an alternative to SPECT. Computed tomography coronary angiography is less expensive and the examination time is shorter when compared with MPI with SPECT, although new multi-headed SPECT systems may allow considerable shortening of scan duration.

In clinical routine, standard stress/rest SPECT MPI scans are important to determine the reversibility of perfusion defects in patients with a history of myocardial infarction.[22] In contrast, in a patient population with low-to-intermediate pre-test probability and unknown CAD, the aim of any test is to reveal the presence of CAD, while potential discrimination of scar from ischaemia

remains beyond the primary focus of the examination. In patients with normal myocardial perfusion at stress, however, subclinical, yet prognostically relevant[31] CAD may be present and patients may benefit from risk factor modification or even specific treatment for CAD.[32] The present study demonstrates that low dose CTCA/stress-SPECT offers such additional information on pre-clinical CAD in a large proportion of patients at no cost of additional radiation exposure. Furthermore, hybrid cardiac imaging offers a high confidence in image interpretation as the occurrence of equivocal findings in one modality may be supplemented by the other.[33] This seems to be particularly important when CTCA is acquired with the prospective ECG-gating, as the performance of this new technique may be prone to artefacts, especially at higher heart rates.[7]

We acknowledge the following limitations to our study. After the matching of two patient cohorts, several patients had to be excluded from further analysis because of non-diagnostic image quality in CTCA. This however, applies to both study groups, which therefore remained well matched with regard to heart rate and BMI or presence of known CAD. Furthermore, we have included patients with known CAD, although our CTCA/stress-SPECT algorithm appears most suitable for the assessment of patients with unknown CAD, and does not allow distinguishing reversible (ischaemia) from fixed defects (scar). Nevertheless, these patients were included for validation purposes to ascertain true positive findings and allow meaningful analysis. We did not determine whether a pathological CTCA/stress-SPECT finding should be completed by a rest-scan or directly by invasive coronary angiography, as this decision would probably be best driven by clinical context.

The use of prospective ECG-triggering for CTCA allows reduction of radiation dose by almost 90% without affecting diagnostic performance. Hybrid imaging combining CTCA with stress-only SPECT is an attractive alternative to standard stress/rest SPECT for the detection of CAD, offering additional information on pre-clinical atherosclerosis.

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