Multimodality Imaging of Anatomy and Function in Coronary Artery Disease

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Chapter 22

Comprehensive Cardiac Assessment with MSCT: Evaluation of Left Ventricular Function and Perfusion in addition to Coronary Anatomy in Patients with Previous Myocardial Infarction

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Abstract

Background

In patients with previous infarction comprehensive assessment is needed for optimal risk stratification, including assessment of coronary artery stenoses, left ventricular (LV) function and perfusion. Currently, different imaging modalities are needed to provide the information, but multi-slice computed tomography (MSCT) may be able to provide all information from a single data set. The purpose of the study was to evaluate a comprehensive MSCT protocol in patients with previous infarction, including assessment of coronary artery stenoses, LV function and perfusion.

Methods

16-slice MSCT was performed in 21 patients with previous infarction; from the MSCT data, coronary artery stenoses, (regional and global) LV function and perfusion were assessed. Invasive coronary angiography and gated single photon emission computed tomography (SPECT) served as the gold standard for coronary artery stenoses and LV function/perfusion respectively.

Results

In total, 236 of 241 (98%) coronary artery segments were interpretable on MSCT. The sensitivity and specificity for detection of stenoses were 91% and 97%. Pearson's correlation showed excellent agreement for assessment of LV ejection fraction between MSCT and SPECT, respectively 49±13% vs 53±12%, r=0.85. Agreement for assessment of regional wall motion was excellent (92%, κ statistic 0.77). Finally, in 68 of 73 (93%) segments, MSCT correctly identified a perfusion defect as compared to SPECT, whereas the absence of perfusion defects was correctly detected in 277 of 284 (98%) segments.

Conclusions

MSCT permits accurate, non-invasive assessment of coronary artery stenoses, LV function and perfusion in patients with previous infarction. All parameters can be assessed from a single data set.

Introduction

The evaluation of patients with previous myocardial infarction is extensive but mandatory to allow optimal risk stratification. Coronary angiography is needed for precise assessment of the location and severity of obstructive coronary artery lesions. Information on systolic function (left ventricular ejection fraction, LVEF) needs to be evaluated, since this is an important prognostic factor. LVEF can be assessed by 2D echocardiography, nuclear imaging with gated SPECT, or invasively by left ventricular (LV) angiography. Finally, assessment of perfusion in the infarct region is of importance; this can be performed by gated single photon emission computed tomography (SPECT). An imaging modality that could provide all this information during one acquisition would be preferred. Over the past few years, multi-slice computed tomography (MSCT) has emerged as a non-invasive imaging modality that allows the acquisition of high resolution 3D images of the entire heart within 25 seconds. The technique allows non-invasive coronary angiography, with sensitivities and specificities for the detection of significant stenoses ranging from 70% to 98%[1-5]. Since MSCT data acquisition is gated to the electrocardiogram (ECG), LV function can be derived from the same dataset[1,6]. In particular, both global LV function (LVEF) and regional LV function (wall motion) can be assessed. Moreover, due to the acquisition of images during the first pass of a contrast agent, hypoenhanced areas can be identified, indicating reduced perfusion. Accordingly, a single MSCT examination could potentially provide all this information, but currently no data are available on the value of MSCT on this topic. The purpose of the present study was to evaluate the feasibility of MSCT to assess all these parameters during a single acquisition. Conventional modalities were used as gold standard to compare these different parameters, including invasive coronary angiography to assess coronary stenoses and nuclear perfusion imaging with SPECT to assess resting perfusion. Moreover, since the SPECT studies were assessed in gated mode, global (LVEF) and regional LV function (wall motion) could also be derived from SPECT.

Methods

Patients and study protocol

Twenty-one patients with a history of myocardial infarction (>3 months before the study) underwent MSCT and resting gated SPECT using technetium-99m. In 20 patients also invasive coronary angiography was performed. Patients with atrial fibrillation were excluded, as well as patients with renal insufficiency (serum creatinine >120 mmol/L), known allergy to iodine contrast media, severe claustrophobia, and pregnant patients. All patients provided informed consent to the study protocol, which was approved by the local ethics committee.

MSCT, data acquisition

MSCT examinations were performed with a 16-slice Toshiba Multi-slice Aquilion 16 system (Toshiba Medical Systems, Otawara, Japan). Collimation was 16 x 0.5 mm (if arterial grafts were present, a collimation was 16 x 1.0 mm was used to decrease scan time), and rotation time was 400, 500 or 600 ms, depending on heart rate. Tube current and tube voltage were 250 mA and 120 kV, respectively. Total contrast dose for the scan varied from 120 to 150 ml, depending on total scan time, with an injection rate of 4 ml/s through the antecubital vein (Xenetix 300, Guerbet, Aulnay S. Bois, France), followed by a saline flush of 40 ml. To time the scan, automated detection of peak enhancement in the aortic root was used. All images were acquired during an inspiratory breath hold, while the ECG was registrated simultaneously for retrospective gating of the data. With the aid of a segmental reconstruction algorithm, data of 2 or 3 consecutive heartbeats were used to generate a single image. Estimated radiation dose was 8 mSv for men and 10 mSv for women.

Evaluation of coronary artery stenoses

For evaluation of coronary artery stenoses, images with a slice thickness of 0.5 mm were reconstructed at typically 75% of the cardiac cycle. In case of motion artifacts, reconstructions at 40% to 50% were explored. Subsequently, images were transferred to a remote workstation (Vitrea2, Vital Images, Plymouth, Mn, USA) for post- processing.

Evaluation of LV function and resting perfusion

For evaluation of LV function and resting perfusion, 2.0-mm slices were reconstructed in the short-axis orientation at 20 time points, starting at early systole (0% of cardiac cycle) to end-diastole (95% of cardiac cycle) in steps of 5%. Images were transferred to a remote workstation with dedicated cardiac function analysis software (MR Analytical Software System, Medis, Leiden, The Netherlands).

MSCT, data analysis

Assessment of significant coronary artery stenoses

For the assessment of significant coronary artery stenoses, the MSCT angiograms were evaluated by 2 experienced observers, blinded to the results of conventional coronary angiography**.** Coronary arteries were divided in 17 segments according to the guidelines of the American Heart Association/ American College of Cardiology [7]. Only segments with a diameter ≥2.0 mm were included. First, segments were classified as evaluable or not. Thereafter, the interpretable segments were evaluated for the presence of significant narrowing (≥50% decrease in luminal diameter). In case of previous bypass surgery and patent bypass grafts, only segments distal to the anastomosis were evaluated.

LV function

To determine LV function, an independent observer outlined endocardial borders manually on the short-axis cine images. The papillary muscles were regarded as being part of the LV cavity. The LV

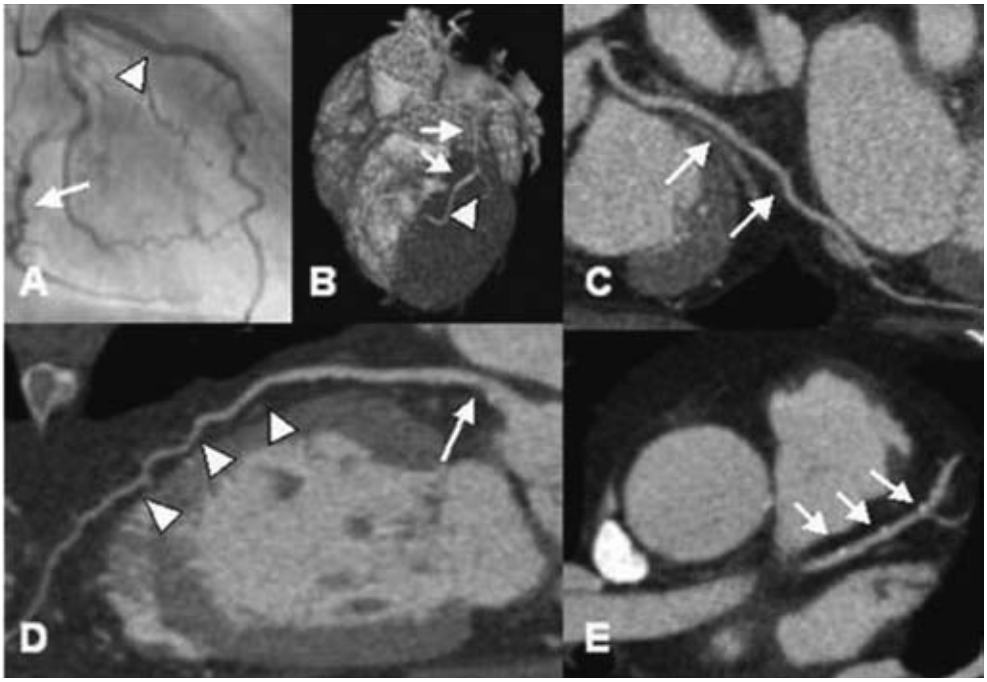

Figure 1. Example of MSCT coronary angiography.
Panel (A) Conventional angiography showing the LCX (white arrow) and the LAD (white arrow head).
Panel B-E: Corresponding MSCT images. (B) MSCT 3D volume-rendered reconstruction depicting the LAD (white arrows) and the D1 (white arrowhead). (C) MPR of the LCX (white arrows). (D) MPR of the LAD (white arrow heads) with soft plaque (white arrow). (E) Transaxial image of the LAD (white arrows) demonstrating small calcifications.

end-systolic and end-diastolic volumes were calculated and the LVEF was derived. Regional wall motion was assessed visually using the short-axis slices in cine-loop mode, by one observer blinded to all other data using a 17- segment model [8]. A three-point scale was used to assign to each segment a wall motion score (1 = normokinesia, 2 = hypokinesia, 3 = a- or dyskinesia) [9].

Myocardial perfusion

To assess myocardial perfusion, the transmural extent of the LV wall showing reduced perfusion was evaluated in terms of transmurality of decreased signal intensity. A five-point scoring system was used with 0 = no perfusion defect, 1 = a perfusion defect involving 1% - 25% of the LV wall, 2 = a defect involving 26% - 50% of the LV wall, 3 = a defect involving 51% - 75% of the LV wall, and 4 = a defect involving >75% of the LV wall, using the same 17-segment model as described for the assessment of regional wall motion [10].

Resting gated SPECT

Myocardial perfusion SPECT imaging with technetium-99m tetrofosmin (500 MBq, injected at rest) was performed using a triple head SPECT camera system (GCA 9300/HG, Toshiba Corp.) equipped with low

energy high-resolution collimators. Around the 140-KeV energy peak of technetium-99m tetrofosmin, a 20% window was used. A total of 90 projections (step and shoot mode, 35 seconds per projection, imaging time 23 minutes) were obtained over a 360-degree circular orbit. Data were stored in a 64 x 64, 16-bit matrix. Resting perfusion was assessed using segmental tracer activity (0 = ≥75% of maximum tracer activity, 1 = 50% - 75% of maximum tracer activity, 2 = 25% - 50% of maximum tracer activity, 3 = ≤25% of maximum tracer activity), using a similar 17-segment model as described above[11].
LV volumes were calculated from the gated short-axis images using previously validated and commercially available automated software (quantitative gated SPECT, QGS, Cedars-Sinai Medical Center, Los Angeles, California)[12]. After segmentation of the LV, endo- and epicardial surfaces are estimated and displayed, the LV end-systolic and end-diastolic volumes are calculated and the LVEF can be derived. Regional wall motion was evaluated using the same 17-segment model and three-point scale as described for MSCT.

Invasive coronary angiography

Conventional coronary angiography was performed according to the standard techniques. To obtain vascular access the femoral approach with the Seldinger technique was used. An experienced observer blinded to the MSCT data performed visual evaluation of the coronary angiograms. Coronary arteries were divided in 17 segments according to the guidelines of the American Heart Association/American College of Cardiology [7]. Consequently, the segments with a diameter ≥2.0 mm were evaluated for the presence of significant narrowing (defined as ≥50% decrease in luminal diameter). In case of previous bypass surgery and patent bypass grafts, only segments distal to the anastomosis were evaluated.

Statistical analysis

Sensitivity, specificity, positive and negative predictive values were calculated to detect significant coronary artery stenoses (≥50% decrease in luminal diameter) on MSCT using invasive angiography as the gold standard. Pearson's correlation coefficient r was calculated for the linear regression analysis of the LVEFs (MSCT versus gated SPECT). Bland-Altman analysis was performed for each pair of values of LVEF to calculate the limits of agreement and systematic error between the 2 modalities (MSCT versus gated SPECT) [13]. A P value <0.05 was considered statistically significant.
A 3 x 3 table using weighted κ statistics was applied to express the agreement for regional wall motion between MSCT and gated SPECT. A κ value of < 0.4 represents poor agreement, a κ value between 0.4 and 0.75 fair to good agreement and a κ >0.75 states excellent agreement [14].

Results

MSCT was performed successfully in all 21 patients. The study population consisted of 20 men and 1 woman, with a mean age of 61 ± 13 years. A total of 17 (81%) patients used beta-blocking agents, no additional beta-blockade was administered prior to MSCT imaging. The mean heart rate was 64 ± 9 bpm, range 51 to

Table 1. Clinical characteristics of the study population (n=21).

	n (%)
Age (yrs)	61 ± 13
Men	20 (95%)
Previous infarction	21 (100%)
Location	
Anterior	10 (48%)
Inferior	10 (48%)
Both	1 (4%)
Q wave on electrocardiogram	13 (62%)
Previous CABG	8 (38%)
Multi-vessel CAD	13 (62%)
Angina pectoris	
CCS class I/II	10 (48%)
CCS class III/IV	11 (52%)
Heart failure	
NYHA class I/II	17 (81%)
NYHA class III/IV	4 (19%)

CAD: coronary artery disease; CCS: Canadian Cardiovascular Society; NYHA: New York Heart Association.

78 bpm, duration of breath hold was approximately 20 seconds, and success rate of obtaining adequate breath hold was 100%. Clinical characteristics of the study population are summarized in Table 1.

Non-invasive coronary angiography by MSCT

Conventional, invasive coronary angiography was performed in 20 patients. In these patients, a total of 241 segments were available for evaluation. Of these segments, 236 (98%) were of sufficient image quality on MSCT to assess the presence/absence of significant stenoses. During conventional coronary angiography, significant stenoses were observed in 46 segments, with 42 (91%) correctly identified on MSCT. In 185 of 190 (97%) segments, MSCT correctly ruled out the presence of significant stenoses. Accordingly, the sensitivity and specificity were 91% and 97% respectively. In Table 2, the diagnostic accuracy of MSCT is summarized (for segments, vessels and patients). An example of MSCT coronary angiography and the corresponding conventional angiography is provided in Figure 1.

Table 2. Diagnostic accuracy of MSCT for the detection of significant (≥50% luminal narrowing) stenoses.

	Segment-based	Vessel-based	Patient-based
Evaluable (%)	98 (236/241)	99 (76/77)*	100 (20/20)
Sensitivity (%)	91 (42/46)	92 (23/25)	92 (12/13)
Specificity (%)	97 (185/190)	96 (49/51)	86 (6/7)
PPV (%)	89 (42/47)	92 (23/25)	92 (12/13)
NPV (%)	98 (185/189)	96 (49/51)	86 (6/7)

Data are percentages (segments).
* in 1 patient the LCx was uninterpretable due to its small size, whereas in 3 patients both the LAD and LCx were supplied by patent grafts. In these patients, the LM was not evaluated.
NPV: negative predictive value; PPV: positive predictive value.

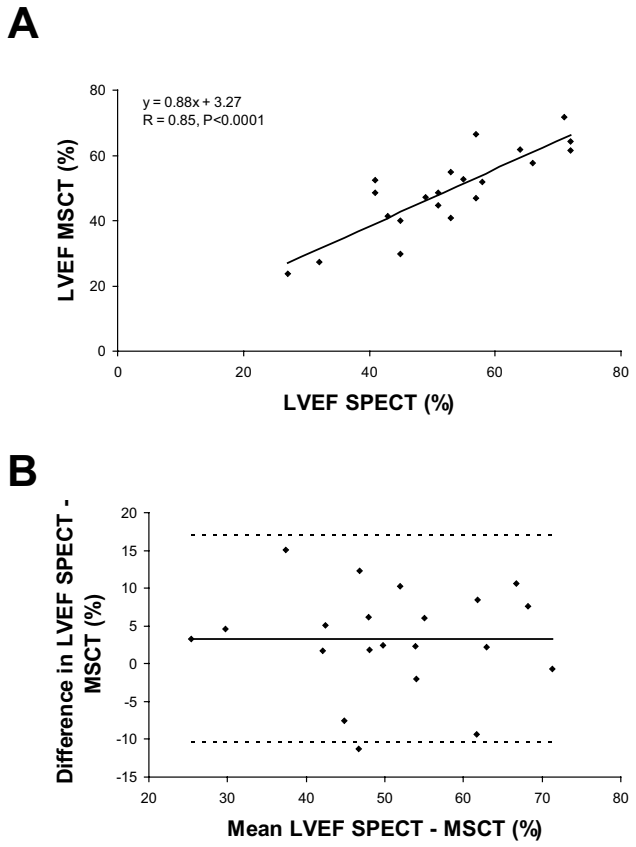

Figure 2. (A) Linear regression plot shows correlation between left ventricular ejection fraction (LVEF) as measured by SPECT and MSCT (CT). (B) Bland-Altman plot of LVEF shows the difference between each pair plotted against the average value of the same pair, i.e. mean value of differences (solid line) and mean value of differences ± 2 SDs (dotted lines).

LV function: MSCT versus gated SPECT

The average LVEF was 53 ± 12% (range 27% to 72%) on gated SPECT, as compared to 49 ± 13% (range 24% to 72%) on MSCT. An excellent correlation was demonstrated using linear regression analysis ($r = 0.85$, $P<0.0001$) (Figure 2A). Bland-Altman analysis (Figure 2B) showed a mean difference of 3.3 ± 13.6%, which was not statistically different from zero.

On resting gated SPECT, regional wall motion abnormalities were detected in 75 (21%) of 357 segments, with 40 (53%) showing hypokinesia and 35 (47%) a- or dyskinesia. In 69 (92%) of the dysfunctional segments, decreased systolic wall motion was also observed on the MSCT images (Table 3). An excellent agreement was shown between the 2 techniques, with 92% of segments scored identically on both modalities (κ statistics 0.77). Agreements for the individual gradings (1 to 3) were 96%, 75%, and 74%, respectively. An example of decreased wall motion on MSCT is provided in Figure 3.

Table 3. Agreement between assessment of regional wall motion on MSCT as compared to resting gated SPECT (agreement 92%, kappa 0.77).

	MSCT			
SPECT	**1**	**2**	**3**	**Total**
1	271	10	1	282
2	6	30	4	40
3	0	9	26	35
Total	277	49	31	357

1= normokinesia, 2=hypokinesia, 3= akinesia or dyskinesia.

Resting perfusion: MSCT versus SPECT

On the resting SPECT images, reduced tracer uptake was observed in 73 (20%) of 357 segments. Of these 73 segments, perfusion defects were detected on MSCT in 68 (93%) segments. In 277 of 284 (98%) segments with normal perfusion on SPECT, no perfusion defects were observed on MSCT as well. The degree of transmurality of the perfusion defects on MSCT paralleled the relative reduction in tracer activity on SPECT. An example of a large perfusion defect on MSCT is provided in Figure 4.

Discussion

The evaluation of patients with previous infarction is extensive and different imaging modalities are needed to provide the necessary information. For efficient patient management, a comprehensive non-invasive cardiac examination would be ideal. The current study was designed to evaluate the possibility to derive additional information on LV function and perfusion from cardiac MSCT, apart from the information on coronary arteries.

Conventional coronary angiography is considered the diagnostic standard for determining the presence of coronary artery stenoses and MSCT has recently been demonstrated to assess coronary artery stenoses with high accuracy [1-5]. The current findings demonstrate that non-invasive coronary angiography with MSCT also in patients with previous myocardial infarction has a high sensitivity and specificity (91% and 97% respectively) for the detection of coronary artery stenoses, in line with previous observations in patients with known or suspected coronary artery disease [1-5]. Other parameters can also be obtained using the same data set as used for evaluation of the coronary arteries, including LV function and perfusion. In particular LVEF is an important prognostic parameter after myocardial infarction [15]. The current results demonstrated an excellent agreement between MSCT and gated SPECT for the assessment of LVEF. Previous studies have shown similar results with other imaging modalities, including magnetic resonance imaging (MRI) and 2D echo, although these studies were not specifically evaluating a selected study population after myocardial infarction, and mainly focusing on patients with relatively preserved LVEF [1;16-18].

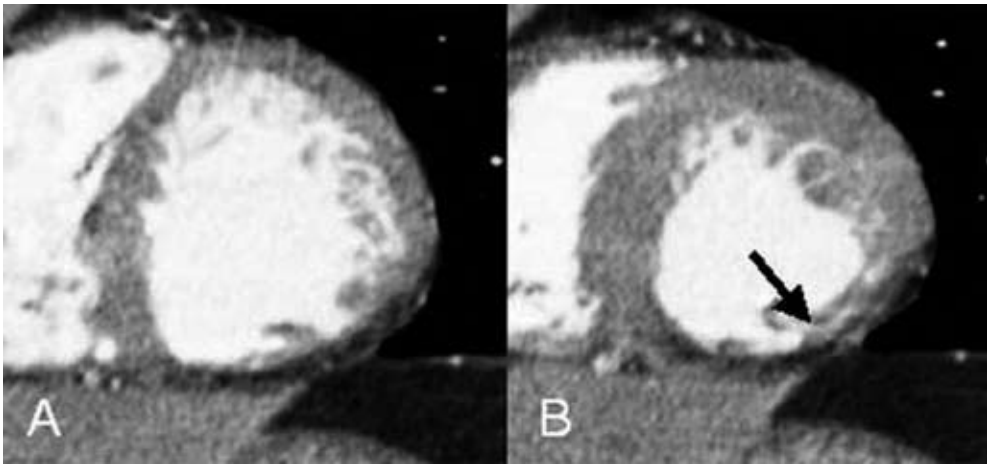

Figure 3. Example of wall motion analysis with MSCT of a patient with an inferior myocardial infarction. Short-axis images in end-diastole (A) and end-systole (B) show reduced wall thickening (black arrow) in the inferior wall.

Besides assessment of global LV function, MSCT can also be used to evaluate regional wall motion. A good agreement between MSCT and gated SPECT (κ statistics 0.77) was observed in the present study. No direct comparisons between gated SPECT and MSCT for assessment of regional wall motion have been reported, but Mahnken et al. reported a good agreement for assessment of regional wall motion between 16-slice MSCT and MRI (κ statistics 0.79) [16].

Finally, MSCT was used in the present study to assess resting perfusion. The results demonstrated that MSCT detected perfusion defects correctly in 93% of the segments with a perfusion defect on SPECT imaging. On the other hand, MSCT did not detect any perfusion abnormalities in 98% of the segments with normal perfusion on SPECT. In addition, the extent of transmurality of the perfusion defects on MSCT corresponded to the relative reduction in tracer activity as assessed on SPECT. Most segments with ≥75% tracer activity had no or minimal perfusion abnormalities on MSCT, whereas segments with ≤25% tracer activity had predominantly extensive, transmural perfusion defects on MSCT. Minimal information on assessment of perfusion with MSCT is currently available. Two recent studies have focused on assessment of perfusion defects (indicating scar tissue) with MSCT in comparison to MRI. Nikolaou et al. compared 16-slice MSCT with MRI for assessment of myocardial infarction, and reported a sensitivity and specificity of 91% and 79% respectively [19]. In the second study, both early-phase MSCT as well as late-enhancement MSCT were performed and compared to MRI for the evaluation of perfusion defects and infarct size in 28 patients with reperfused myocardial infarction [20]. A good agreement between MRI and MSCT for the detection of scar tissue was demonstrated. MRI is currently regarded as gold standard for the assessment of LV function, while scar tissue due to myocardial infarction can be evaluated by delayed enhancement on MRI as well. A major advantage of this technique is the lack of radiation exposure.

Several limitations of the present study need attention. The study population was relatively small, and larger studies are needed to confirm the current observations. A drawback of MSCT remains the

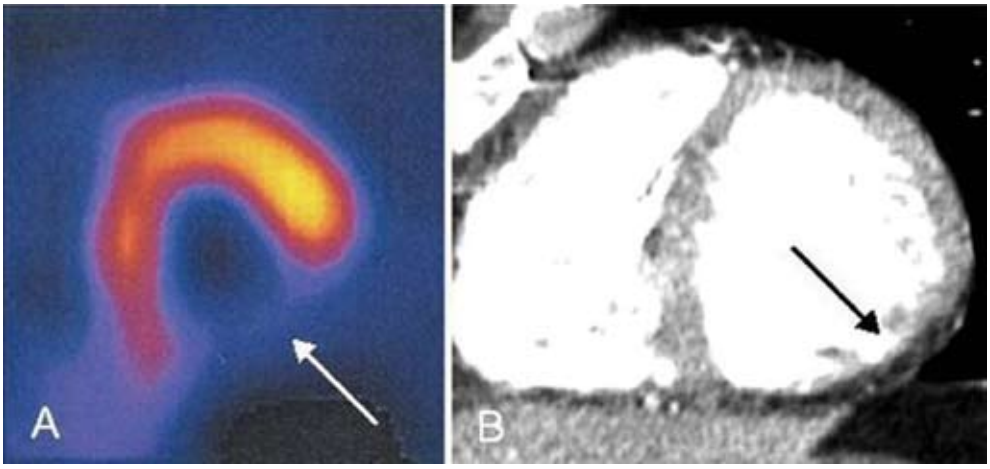

Figure 4. Example of a large perfusion defect on SPECT and MSCT of the patient depicted in Figure 3.
(A) SPECT short-axis image showing a perfusion defect in the inferior wall (white arrow) at rest, (B) corresponding MSCT short-axis image in end-diastole, revealing a hypoenhanced area (black arrow) in the inferior wall, indicating a perfusion defect.

radiation dose (8 to 10 mSv in this study, which is higher as compared to a conventional diagnostic angiography) and future developments are needed to reduce radiation. Furthermore, most MSCT parameters were evaluated qualitatively, and software allowing quantitative analysis needs to be developed. In addition, MSCT at present only provides information on resting perfusion. Additional imaging during stress conditions would allow assessment of stress perfusion and the combination of the stress and rest images would potentially allow detection of ischemia and scar tissue. However, in view of the radiation burden, such a protocol may currently not be feasible for routine clinical practice.

In conclusion, the findings in the present study demonstrate the feasibility of integrated assessment of coronary anatomy, regional and global LV function and perfusion with MSCT in patients with previous infarction. Agreement with invasive coronary angiography and gated SPECT (for assessment of function and perfusion) was excellent. In patients with previous infarction, non-invasive evaluation of the coronary arteries can be performed for the detection or exclusion of possible new significant stenoses. In patients with previous bypass surgery, non-invasive evaluation with MSCT can provide information of the patency of the grafts. The additional data on LV function as well as extent of (possibly) infarcted myocardium can be taken into account in the risk stratification in these patients; this concept needs further testing in future studies.

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