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Monochromatic image reconstruction by dual energy imaging allows half iodine load computed tomography coronary angiography

Patricia Carrascosa[a,*], Jonathon A. Leipsic[c], Carlos Capunay[a], Alejandro Deviggiano[a], Javier Vallejos[a], Alejandro Goldsmit[b], Gaston A. Rodriguez-Granillo[a]

[a] *Department of Computed Tomography, Diagnostico Maipu, Buenos Aires, Argentina*
[b] *Department of Interventional Cardiology, Sanatorio Guemes, Buenos Aires, Argentina*
[c] *Medical Imaging, St. Paul's Hospital, Vancouver, BC, Canada*

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ABSTRACT

Purpose: To compare image interpretability and diagnostic performance of dual-energy CT coronary angiography (DE-CTCA) performed with 50% iodine load reduction versus single energy acquisitions (SE-CTCA) with full iodine load.

Materials and methods: The present prospective study involved patients with suspected coronary artery disease (CAD) clinically referred for CTCA. DE-CTCA with 50% iodine volume load was performed first, and after heart rate returned to baseline SE-CTCA was performed using full iodine volume load. The primary endpoint was to compare image interpretability between groups. DE-CTCA was performed by rapid switching between low and high tube potentials (80–140 kV) from a single source, allowing the generation of monochromatic image reconstructions ranging from 40 to 140 keV. Image quality assessment was performed using a 5-point Likert scale.

Results: Thirty-six patients constituted the study population. The mean heart rate before the CT scan (DE-CTCA 57.3 ± 10.7 bpm vs. SE-CTCA 58.5 ± 11.2 bpm, $p = 0.29$) and the mean effective radiation dose (3.5 ± 1.9 mSv vs. 3.8 ± 0.9 mSv, $p = 0.48$) did not differ between groups. Likert image quality scores were similar between groups (DE-CTCA 4.42 ± 0.98 vs. SE-CTCA 4.43 ± 0.84, $p = 0.67$). Signal-to-noise and contrast-to-noise ratios were significantly lower with DE-CTCA, driven by lower signal density levels at 60 keV compared to SE-CTCA. The sensitivity and specificity for the detection of stenosis >50% was indistinguishable between groups (DE-CTCA 84.4% (69.9–93.0%), 87.1% (81.6–91.2%); SE-CTCA 84.4% (69.9–93.0%), 87.1% (81.6–91.2%).

Conclusions: In this pilot, prospective study, dual energy CTCA imaging with half iodine load achieved comparable interpretability than full iodine load with single energy CTCA.

1. Introduction

Based on robust evidence collected during the past two decades, computed tomography coronary angiography (CTCA) has gained a role in the evaluation of symptomatic patients with low to intermediate likelihood of coronary artery disease (CAD) [1–3]. Since the incidence of contrast-induced acute kidney injury is closely related to iodine volume load and concentration, there is an essential need for technical developments that can achieve a significant reduction in the iodinated contrast load [4,5].

Previous investigators have achieved a 20% contrast volume reduction using a lower tube voltage, although at the expense of higher tube current thus leading to persistently elevated effective dose radiation levels [6]. Dual-energy CT (DECT) allows the reconstruction of low and high energy projections and generation of monochromatic image reconstructions [7]. Consequently, higher intravascular attenuation levels can be attained through low energy monochromatic imaging, since with the administration of iodine vessels portray higher attenuation levels at lower energies than at higher energies due to the fact that lower energies are closer to 33.2 keV, the K edge of iodine [8]. We previously demonstrated that aortic CT angiography using DECT imaging allows up to 60% iodine volume reduction with similar image quality and interpretability

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Abbreviations: DECT, dual energy computed tomography; SECT, single energy computed tomography; CTCA, computed tomography coronary angiography; CAD, coronary artery disease.

[*] Corresponding author at: Av Maipú 1668, Vicente López (B1602ABQ), Buenos Aires, Argentina. Fax: +5411 48377596.

E-mail address: investigacion@diagnosticomaipu.com.ar (P. Carrascosa).

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than full iodine load with conventional single energy CTA imaging [9]. Accordingly, we attempted to explore whether we could extrapolate those findings to the evaluation of the coronary tree using CTCA.

2. Methods

2.1. Study population

The present was a single-center, investigator driven, prospective study, that involved patients with suspected CAD clinically referred for CTCA due to chest pain, anginal equivalents, or inconclusive stress tests. All patients underwent dual energy (DE) CTCA with 50% iodine volume load and, subsequently, single energy (SE) CTCA with full iodine volume load. All patients included were more than 40 years old, in sinus rhythm, able to maintain a breath-hold for 15 s; without a history of contrast related allergy, renal failure, or hemodynamic instability. Additional exclusion criteria comprised a body mass index >32 kg/m^2, a history of previous myocardial infarction within the previous 30 days, previous percutaneous coronary revascularization or coronary bypass graft surgery, or chronic heart failure. Patients with pacemakers or implantable devices were excluded.

The primary endpoint of the study was to evaluate image interpretability of DE-CTCA with half iodine load compared to SE-CTCA with full iodine load. The secondary endpoint was to compare the diagnostic performance between groups in a subset of patients who underwent invasive coronary angiography. The institution's Ethics Committee approved the study protocol, which complied with the Declaration of Helsinki, and written informed consent was obtained from all patients.

2.2. Image acquisition

Patients were scanned using a 64-slice high definition scanner (Discovery HD 750, GE Healthcare, Milwaukee, USA), after intravenous administration of iodinated contrast (iobitridol, Xenetix 350TM, Guerbet, France) through an antecubital vein. Patients with a heart rate of >65 beats per minute received 50 mg oral metoprolol one hour prior to the scan or 5 mg intravenous propralonol if needed in order to achieve a target heart rate of less than 60 bpm. In order to avoid any potential presence of residual intravascular contrast material, DE-CTCA with 50% iodine volume load was performed first and, 15–20 min later and after heart rate returned to baseline. SE-CTCA was performed using full iodine volume load.

All studies were acquired using prospective ECG-gating applying a 100 m sec padding centered at 75% of the cardiac cycle for patients with a heart rate lower than 60 bpm, a 200 m sec padding centered at 60% of the cardiac cycle for patients with a heart rate between 60 and 74 bpm, and a 100 m sec padding centered at 40% of the cardiac cycle for patients with a heart rate higher than 74 bpm. DE-CTCA was performed by rapid switching (0.3–0.5 milliseconds) between low and high tube potentials (80–140 kV) from a single source, thereby allowing the reconstruction of low and high energy projections and generation of monochromatic image reconstructions ranging from 40 to 140 keV. Other scanner-related parameters were a gantry rotation speed of 350 ms, collimation width of 0.625 mm, 600–640 mA, a slice interval of 0.625 mm, and a temporal resolution of 175 ms. Maximum tube voltage and current for SE-CTCA were adjusted according to the body habitus (100 kV or 120 kV for patients with body mass index <30 kg/m2 or larger, respectively). All SE-CTCA acquisitions were obtained using the high-definition mode.

For SE-CTCA with full iodine volume load acquisitions (body mass index *0.9), iodinated contrast volume was injected using a three-phase injection protocol, as follows. Phase 1:50% of the total iodinated contrast volume being injected undiluted at a rate of 4.5–5.0 ml/sec; phase 2: the other 50% of the contrast medium mixed at a 60:40 saline dilution, injected at a rate of 4.5–5.0 ml/sec; and phase 3: a 40 ml saline chasing bolus at a rate of 4.5–5.0 ml/sec. DE-CTCA angiograms with half iodine volume load were obtained using a three-phase protocol, as follows. Phase 1:50% of the total iodinated contrast volume mixed at a 50:50 saline dilution being injected at a rate of 4.0–5.0 ml/sec; phase 2: the other 50% of the contrast medium mixed at a 30:70 saline dilution, injected at a rate of 4.0–5.0 ml/sec; and phase 3: a 40 ml saline chasing bolus at a rate of 4.0 to 5.0 ml/sec. All patients received a 40 ml timing bolus to synchronize the data acquisition with the arrival of contrast material in the aorta, consisting of a combination of 20 ml contrast medium and 20 ml of saline at a rate of 5.5 ml/sec. Image acquisition was performed after sublingual administration of 2.5–5 mg of isosorbide dinitrate.

All reconstructions were performed using a standard kernel. SE-CTCA studies were reconstructed using a standard iterative reconstruction algorithm, at 40% ASIR (Adaptive Statistical Iterative Reconstruction). DE-CTCA studies were reconstructed at independent monochromatic energy levels ranging from 40 keV to 80 keV with incremental levels of 10 keV, in order to establish the lowest energy level (hence with higher signal density) with the highest contrast-to noise-ratio (CNR) and signal-to-noise ratio (SNR) and consequently use it for comparison against SE-CTCA. Based on an interim analysis (data not shown), 60 keV with iterative reconstruction algorithm (ASIR) was the lowest energy level with the highest CNR and SNR, therefore it was used for further comparisons against SE-CTCA.

2.3. Image analysis

DE-CTCA image analyses were performed off-line on a dedicated workstation, using a commercially available dedicated software tool (AW 4.6, GE Healthcare) by consensus of two experienced level 3—certified coronary CTCA observers (PC, AD), blinded to the clinical data [10]. SE-CTCA were analyzed two weeks later by the same observers blinded to the clinical data. Axial planes, curved multiplanar reconstructions, and maximum intensity projections at 1–5 mm slice thickness were used according to 18-segment Society of Cardiovascular Computed Tomography Classification [11]. Images were evaluated on a per segment basis and per territory basis. Segments with a reference diameter lower than 1.5 mm were not included in the analysis. Each segment was graded as follows: normal; non-significant stenosis (<50%); significant stenosis (≥50%); or uninterpretable. Uninterpretable segments due to motion artifacts or severe calcification were assumed as positive for the diagnostic performance analysis.

Quantitative image quality assessment was performed using a 5-point Likert scale, as follows: (1) and (2) Non-diagnostic, impaired image quality due to motion artifacts or severe calcification that precluded appropriate assessment; (3) Suboptimal but sufficient, reduced image quality due to motion artifacts, image noise or low contrast attenuation, but sufficient to rule out obstructive disease; (4) Good, presence of mild motion artifacts, image noise, coronary calcifications or low contrast, but preserved ability to evaluate the presence of stenosis as well as to identify the presence mild atherosclerosis; and (5) Excellent, absence of motion artifacts, high intraluminal attenuation and clear delineation of vessel walls, with the ability to evaluate both the presence of obstructive disease and mild atherosclerosis.

The extent of vascular attenuation (in Hounsfield units) was measured using standardized regions of interest of 20 mm^2 at the aortic root and at the epicardial fat. Signal density (mean Hounsfield units), noise (mean standard deviation of the signal density), and signal-to-noise ratio (SNR) were further calculated. Contrast-to-noise ratio (CNR) was defined as the difference between the mean signal density at the aortic root and at the epicardial fat divided by the mean image noise.

CT effective radiation dose was derived by multiplying the dose-length product with the weighting (k) value of 0.014 mSv/mGy/cm for chest examinations, as suggested by the Society of Cardiovascular Computed Tomography [12].

2.4. Invasive angiography acquisition and analyses

All procedures were performed in accordance to standard techniques. Coronary angiograms were obtained in multiple projections after administration of intracoronary nitrates. Quantitative coronary angiography analysis was performed by an independent observer blinded to the CTCA data (AG). The catheter tip was cleared of contrast for accurate calibration. Lesion measurements were performed using the "worst" view of an end-diastolic frame.

2.5. Statistical analysis

Discrete variables are presented as counts and percentages. Continuous variables are presented as means ± SD. Comparisons among groups were performed using paired samples *t*-test, and McNemar' test, as indicated. To determine the diagnostic accuracy of DE-CTCA using half iodine load versus SE-CTCA with full iodine load for the detection of stenoses ≥50% by invasive angiography, we calculated the sensitivity, specificity, and likelihood ratios, accounting for potential non-uniform distribution (95% confidence intervals). To evaluate the interobserver agreement (Cohen's kappa) for each group, two experienced observers independently evaluated the subset of patients who underwent invasive angiography for obstructive (stenosis ≥ 50 %) and non-obstructive lesions. For this purpose, dual energy and single energy analyses were separated by a 2-week window period. Statistical analyses were performed using SPSS software, version 13.0 (Chicago, Illinois, USA). A two-sided *p* value of less than 0.05 indicated statistical significance.

Table 1
Demographical characteristics ($n = 36$).

	N(%)
Age (years ± SD)	55.8 ± 9.9
Male (%)	27 (73.0%)
Body mass index (kg/m2)	27.1 ± 3.2
Diabetes (%)	3 (8.1%)
Hypertension (%)	16 (43.2%)
Hypercholesterolemia (%)	20 (54.1%)
Current smoking (%)	6 (16.2%)
Previous smoking (%)	14 (37.8%)
Previous PCI (%)	10 (27.0%)
Serum creatinine (mg/dl)	0.97 ± 0.24
Heart rate (bpm ± SD)	57.9 ± 11.0

3. Results

Thirty-seven patients were prospectively included in the study protocol. One patient was excluded from the analysis due to a significant increment in heart rate after DE-CTCA leading to a SE-CTCA scan with severe motion artifacts and early contrast wash-out. The mean age of the 36 patients that comprised the study population was 55.8 ± 9.9 years, 27 (73%) patients were male, and 3 (8%) had diabetes (Table 1). The mean heart rate before the CT scan (DE-CTCA 57.3 ± 10.7 bpm vs. SE-CTCA 58.5 ± 11.2 bpm, $p = 0.29$) and the mean effective radiation dose (DE-CTCA 3.8 ± 0.9 mSv vs.

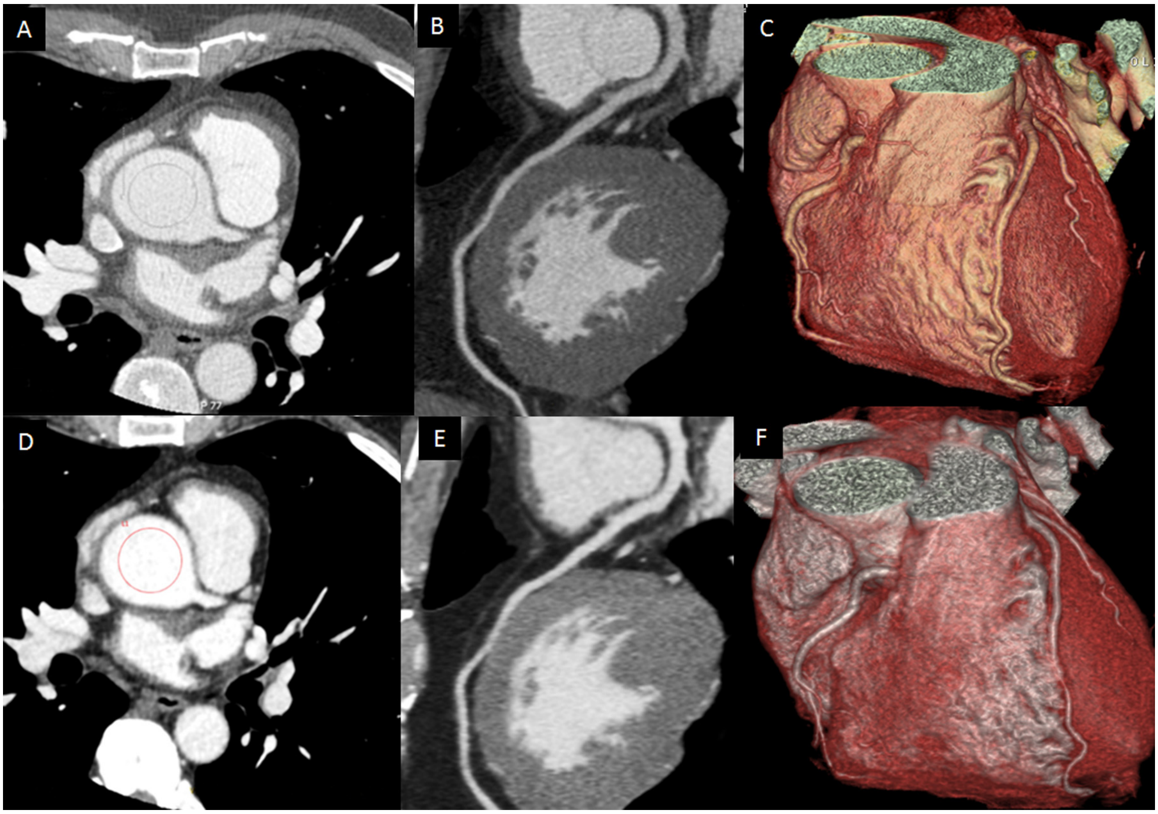

Fig. 1. Fifty-three year old male with normal coronary arteries. Single energy CT coronary angiography (above, panels A–C) performed with 70 ml of iodinated contrast and dual energy CT coronary angiography performed with 35 ml of contrast and reconstructed at 60 kev with 40% ASIR. In panels A and D, the region of interest shows a mean signal density of 328HU and 304HU, and a mean noise of 34 HU and 19 HU for SE-CTCA and DE-CTCA, respectively.

Table 2
Quantitative assessment of image quality.

Signal intensity (HU)	Dual energy (60 keV IR)	Single energy	p value vs. 60 keV IR
Heart rate	57.3 ± 10.7	58.5 ± 11.2	0.29
Aorta	321.6 ± 63.1	374.0 ± 88.1	0.001
Left ventricle	310.3 ± 106	380.0 ± 97.0	0.001
Left main	300.0 ± 50.1	363.4 ± 89.4	<0.001
Left anterior descending	288.9 ± 49.9	339.7 ± 79.0	<0.001
Left circumflex	256.9 ± 41.4	339.9 ± 76.6	<0.001
Right coronary artery	279.9 ± 47.0	368.3 ± 88.2	<0.001
Noise (HU)			
Aorta	25.2 ± 7.9	31.2 ± 8.2	<0.001
Left ventricle	25.5 ± 7.1	32.9 ± 10.1	<0.001
Left main	24.2 ± 7.5	36.3 ± 57.4	0.21
Left anterior descending	27.0 ± 14.0	28.4 ± 14.8	0.62
Left circumflex	29.4 ± 14.9	33.9 ± 19.5	0.19
Right coronary artery	27.0 ± 12.1	26.3 ± 14.4	0.82
SI and noise measurements			
Mean signal density (HU)	281.3 ± 49.3	352.8 ± 83.6	<0.001
Mean noise (HU)	26.9 ± 12.5	31.2 ± 31.9	0.11
Signal-to noise ratio	11.6 ± 7.1	14.5 ± 8.9	<0.001
Contrast-to-noise ratio	15.5 ± 9.6	18.0 ± 11.5	0.02

IR refers to iterative reconstruction.

SE-CTCA 3.5 ± 1.9 mSv, $p = 0.48$) did not differ between groups. The mean contrast volume administrated was 63.4 ± 8.3 ml for SE-CTCA acquisitions and 31.7 ± 4.1 ml for DE-CTCA acquisitions, ($p < 0.0001$). The mean iodine delivery rate was 1.63 ± 0.1 gI/s with SE-CTCA acquisitions and 1.59 ± 0.1 gI/s for DE-CTCA acquisitions, ($p = 0.002$); whereas the mean total administrated iodine was 25.0 ± 3.3 g with SE-CTCA acquisitions and 12.5 ± 1.6 g for DE-CTCA acquisitions, ($p < 0.0001$).

3.1. Image interpretability and diagnostic performance

All assessable segments at full iodine load with SE-CTCA imaging were also assessable with half iodine load using DE-CTCA imaging. Image quality was similar between groups (mean Likert score DE-CTCA = 4.43 ± 0.84 vs. SE-CTCA 4.42 ± 0.98, $p = 0.67$). Eleven (2.1%) segments were deemed non-assessable within DE-CTCA, compared to 26 (5.0%) segments within SE-CTCA ($p = 0.003$ by McNemar's test). Within DE-CTCA, the best energy level was 60 keV in all cases, with the best subjective balance between increased signal density and decreased image noise. A good agreement between observers was found for the identification of obstructive lesions among both groups (DE-CTCA = k 0.85, $p < 0.0001$; SE-CTCA = k 0.83, $p < 0.0001$).

Seventeen patients underwent invasive coronary angiography, and diagnostic performance was assessed within these patients on a per segment basis (224 AHA segments). The sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio for the detection of stenosis > 50% was indistinguishable between groups [DE-CTCA84.4% (69.9–93.0%), 87.1% (81.6–91.2%), 6.5 (4.5–9.5), 0.18 (0.09–0.35), respectively; and SE-CTCA 84.4% (69.9–93.0%), 87.1% (81.6–91.2%), 6.5 (4.5–9.5), 0.18 (0.09–0.35), respectively].

3.2. Signal density and signal to noise ratio

At the aortic root, SE-CTCA acquisitions with full iodine load achieved mean signal density levels of 374.0 ± 88.1 HU and mean noise levels of 31.2 ± 8.2 HU; whereas mean signal density and noise levels of DE-CTCA acquisitions with half iodine load at 60 keV reconstructions with iterative reconstruction were 321.6 ± 63.1 HU and 25.2 ± 7.9 HU ($p < 0.0001$ for both comparisons), respectively.

The average signal density of the four coronary arteries (left main, left anterior descending, left circumflex, and right coronary artery) was 352.8 ± 83.6 HU for SE-CTCA acquisitions and 281.3 ± 49.3 for DE-CTCA acquisitions at 60 keV with iterative reconstruction ($p < 0.0001$), whereas image noise was higher (SE-CTCA 31.2 ± 31.9HU vs. DE-CTCA 26.9 ± 12.5HU, $p = 0.11$). Overall, signal-to-noise ratio (SE-CTCA 14.5 ± 8.9 vs. DE-CTCA 11.6 ± 7.1, $p < 0.001$) and contrast-to-noise ratio (SE-CTCA 18.0 ± 11.5 vs. DE-CTCA 15.5 ± 9.6, $p = 0.02$) were higher among SE-CTCA acquisitions. Table 2 and Figs. 1 and 2 depict signal density and noise levels, signal-to-noise ratio and contrast-to-noise ratio at different regions of interest of SE-CTCA and DE-CTCA acquisitions.

4. Discussion

Our main findings can be summarized as follows: (1) DE-CTCA allowed 50% iodine load reduction, with comparable image interpretability than full iodine load with conventional SE-CTCA imaging; (2) In the subset of patients who underwent invasive coronary angiography, iodine load reduction did not have an impact on the diagnostic performance.

The incidence of contrast-induced acute kidney injury is highly associated with traditional cardiovascular risk factors [13]. Indeed, a recent study established that diabetic patients with preserved renal function are at higher risk of renal function deterioration after CTCA [14]. An incidence of contrast-induced acute kidney injury contrast-induced acute kidney injury of up to 11% has been reported in the outpatient setting of contrast-enhanced CT angiograms [15]. Several prophylactic strategies have been attempted, although none has conclusively achieved overall satisfactory results. In this respect, the lack of adequate oral hydration has been identified as an independent predictor of worsening renal function after CTCA, and therefore sufficient oral fluid intake appears so far as the most cost-effective prevention strategy [16,17]. Contrast volume reduction has emerged as an important modifiable risk factor, and several technical and procedural developments have been implemented in the last decade aimed at reducing iodine volume load, even by means of central superior vena cava contrast injection [4,18].

In the present study, we reduced the iodine volume load required in CTCA by 50% by using low energy monochromatic imaging which is related to higher intravascular attenuation levels [8].

Fig. 2. Seventy-three year old female with effort dyspnea. Curved multiplanar reconstructions portray a ≥99% lesion (arrows) at the proximal left circumflex using single energy CT (panel A) performed with 64 ml of iodinated contrast, and dual energy CT (panel B) performed with 32 ml of contrast and reconstructed at 60 kev with 40% ASIR. The invasive coronary angiography (panel C) confirms the findings. The mean signal density at the aortic root was 361 HU for single energy CT and 357 HU for dual energy CT, whereas the mean noise was 33 HU for single energy CT and 20 HU for dual energy CT.

Previous studies have shown the feasibility of reducing contrast volume by means of low voltage and/or DE-CTCA at different vascular territories, including pulmonary CTA, aortic CTA, and CTCA [8,9,19,20]. Recently, Liu et al. reported a significant reduction in contrast volume administration using high-pitch mode CTCA. Nevertheless, the lack of sizeable differences in signal density values might have been influenced by the fact that the reference standard already had a significant reduction in iodine volume injection (0.7 ml/kg), possibly attributed to the fact that Asian patients have in general a low body mass index [21]. In another study, third-generation high-pitch CTCA at lower tube voltage (70 kV) resulted in comparable image quality, at significantly reduced radiation dose and contrast medium volume [22]. Nonetheless, dual source scanners are not widely available and high-pitch acquisitions are eligible only for non-obese patients with stable low heart rate, preferably ≤60 bpm [23]. In parallel, it has been very recently reported that 320-row CT scanners might generate strong contrast enhancement due to decreased photon energy, thus enabling a significant reduction in contrast volume and radiation dose [24].

Our study demonstrated the feasibility of performing CTCA with half iodine load using DE-CTCA imaging, with similar interpretability than conventional SE-CTCA acquisitions. In turn, signal-to-noise and contrast-to-noise ratios were significantly lower with DE-CTCA, mainly driven by the fact that signal density levels at 60 keV were lower than those with SE-CTCA. It should be noted though, that DE-CTCA at lower energy levels (40/50 keV) achieved greatly higher CT values, although at detriment of increased image noise. To date, iterative reconstruction algorithms are available only from 60 keV, whereas current work-in-progress aimed at developing algorithms for the lowest energy levels are expected to attain a significant reduction in noise levels. This might improve signal-to-noise ratio at 40/50 keV, potentially leading to further contrast volume reductions without compromise of image quality. In parallel, the ability of DE-CTCA to reconstruct images at a wide energy spectrum might potentially enhance the evaluation of coronary atherosclerosis at different stages, being lower monochromatic energy levels more appropriate to evaluate soft tissues and higher energy levels more suitable for hard tissues such as calcium and stents [25]. Moreover, in a subset of patients who underwent invasive coronary angiography, diagnostic performance was similar between groups. Finally, it is worth mentioning that one of the main strengths of our study was the fact that patients underwent both protocols thus avoiding selection bias in this regard.

In a contemporaneous study to the present investigation in which we were also involved, DE-CTCA allowed a 50% reduction in iodine administration while maintaining diagnostic interpretability, signal-to-noise ratio, and contrast-to-noise ratio; with slight compromise in subjective image quality scores [26]. Two main differences can be recognized between these studies. Firstly, Raju et al. randomly assigned patients to SE-CTCA or DE-CTCA, whereas in our study all patients underwent DE-CTCA and SE-CTCA. And secondly, our study included a subset of patients who underwent invasive coronary angiography, providing exploratory findings regarding the potential impact of iodine volume load reduction on the diagnostic performance.

Our findings add to the increasing evidence supporting the reduction of contrast material administration during CTCA studies without significant compromise in image quality. A substantial reduction in iodine load might have major clinical implications in selected populations such as diabetics, patients with impaired renal function, and in the elderly. As a matter of fact, in patients with chronic kidney disease undergoing invasive angiography the use of ultra low (<50 ml) contrast volume was associated with a reduction in contrast-induced acute kidney injury, with each additional 20 ml leading to a twofold increase in risk [27]. In our study, a similar image interpretability and diagnostic performance was achieved with a mean contrast volume within the DE-CTCA group of 32 ml. Accordingly, though preliminary and hypothesis generating since we neither tested at risk patients, nor we screened serum creatinine levels before and after the scans, our findings might potentially have relevant clinical implications for patients at risk for contrast-induced acute kidney injury.

A number of limitations should be acknowledged. The relatively small sample size might lead to selection bias. Given the fact that all patients underwent both DE-CTCA and SE-CTCA on a per-protocol basis, including a larger population was discouraged by the Ethics committee due to obvious ethical reasons. Since we excluded patients with a history of previous coronary revascularization and those with a body mass index > 32 k/m^2, our results cannot be extrapolated to all patients referred to CTCA. Moreover, it should be recognized that the primary outcome was the evaluation of image quality and interpretability therefore diagnostic performance analysis, based on a subset of 17 patients who underwent invasive angiography, should be considered as exploratory. Likewise and for the same reason, analyses on a per patient basis were not performed. In addition, low energy DE-CTCA imaging is contraindicated in obese patients since it is associated to increased image noise. Finally, the test bolus consisting in 20 ml of further contrast material might be avoided shortly with the advent of a bolus tracking technique that will enable a synchronized scan with respect to the arrival of contrast at the level of the coronary arteries .

5. Conclusions

In this pilot, prospective study, dual energy CTCA imaging with half iodine load achieved comparable interpretability than full iodine load with single energy CTCA.

Conflict of interest

We declare that Dr. Patricia Carrascosa and Jonathon Leipsic are Consultants of GE. There are no competing interests related to the manuscript for any of the other authors.

References

[1] Taylor AJ, Cerqueira M, Hodgson JM, Mark D, Min J, O'Gara P, Rubin GD, American College of Cardiology Foundation Appropriate Use Criteria Task Force, Society of Cardiovascular Computed Tomography, American College of Radiology, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, North American Society for Cardiovascular Imaging, Society for Cardiovascular Angiography, Interventions, Society for Cardiovascular Magnetic Resonance, Kramer CM, Berman D, Brown A, Chaudhry FA, Cury RC, Desai MY, Einstein AJ, Gomes AS, Harrington R, Hoffmann U, Khare R, Lesser J, McGann C, Rosenberg A, Schwartz R, Shelton M, Smetana GW, Smith Jr SC. Accf/scct/acr/aha/ase/asnc/nasci/scai/scmr 2010 appropriate use criteria for cardiac computed tomography. A report of the american college of cardiology foundation appropriate use criteria task force, the society of cardiovascular computed tomography, the american college of radiology, the american heart association, the american society of echocardiography, the american society of nuclear cardiology, the north american society for cardiovascular imaging, the society for cardiovascular angiography and interventions, and the society for cardiovascular magnetic resonance. J Am Coll Cardiol 2010;56:1864–94.

[2] Wright RS, Anderson JL, Adams CD, Bridges CR, Casey Jr DE, Ettinger SM, Fesmire FM, Ganiats TG, Jneid H, Lincoff AM, Peterson ED, Philippides GJ, Theroux P, Wenger NK, Zidar JP, Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey Jr DE, Chavey WE, 2nd Fesmire FM, Hochman JS, Levin TN, Lincoff AM, Peterson ED, Theroux P, Wenger NK, Zidar JP, American College of Cardiology Foundation/American Heart Association Task Force on Practice G. 2011 accf/aha focused update incorporated into the acc/aha 2007 guidelines for the management of patients with unstable angina/non-st-elevation myocardial infarction: A report of the american college of cardiology foundation/american heart association task force on practice guidelines developed in collaboration with the american academy of family physicians, society for cardiovascular angiography and interventions, and the society of thoracic surgeons. J Am Coll Cardiol 2011;57:e215–367.

[3] Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, Caso P, Dudek D, Gielen S, Huber K, Ohman M, Petrie MC, Sonntag F, Uva MS, Storey RF, Wijns W, Zahger D. Guidelines ESCCfP. Esc guidelines for the management of acute coronary syndromes in patients presenting without persistent st-segment elevation: The task force for the management of acute coronary syndromes (acs) in patients presenting without persistent st-segment elevation of the european society of cardiology (esc). Eur Heart J 2011;32:2999–3054.

[4] Nyman U, Bjork J, Aspelin P, Marenzi G. Contrast medium dose-to-gfr ratio: a measure of systemic exposure to predict contrast-induced nephropathy after percutaneous coronary intervention. Acta Radiol 2008;49:658–67.

[5] Laville M, Juillard L. Contrast-induced acute kidney injury: how should at-risk patients be identified and managed? J Nephrol 2010;23:387–98.

[6] Kidoh M, Nakaura T, Nakamura S, Nakamura S, Sakaino N, Harada K, Uemura S, Yamashita Y. Low-contrast-dose protocol in cardiac ct: 20% contrast dose reduction using 100 kvp and high-tube-current-time setting in 256-slice ct. Acta Radiol 2013;55:545–53.

[7] So A, Lee TY, Imai Y, Narayanan S, Hsieh J, Kramer J, Procknow K, Leipsic J, Labounty T, Min J. Quantitative myocardial perfusion imaging using rapid kvp switch dual-energy ct: preliminary experience. J Cardiovasc Comput Tomogr 2011;5:430–42.

[8] Yuan R, Shuman WP, Earls JP, Hague CJ, Mumtaz HA, Scott-Moncrieff A, Ellis JD, Mayo JR, Leipsic JA. Reduced iodine load at ct pulmonary angiography with dual-energy monochromatic imaging: comparison with standard ct pulmonary angiography–a prospective randomized trial. Radiology 2012;262:290–7.

[9] Carrascosa P, Capunay C, Rodriguez-Granillo GA, Deviggiano A, Vallejos J, Leipsic JA. Substantial iodine volume load reduction in ct angiography with dual-energy imaging: insights from a pilot randomized study. Int J Cardiovas Imaging 2014;30:1613–20.

[10] Pelberg R, Budoff M, Goraya T, Keevil J, Lesser J, Litwin S, Newton C, Ridner M, Rumberger J, Teague S, Winkler M. Society of cardiovascular computed T. training competency, and certification in cardiac ct: a summary statement from the society of cardiovascular computed tomography. J Cardiovasc Comput Tomogr 2011;5:279–85.

[11] Leipsic J, Abbara S, Achenbach S, Cury R, Earls JP, Mancini GJ, Nieman K, Pontone G, Raff GL. Scct guidelines for the interpretation and reporting of coronary ct angiography: a report of the society of cardiovascular computed tomography guidelines committee. J Cardiovasc Comput Tomogr 2014;8:342–58.

[12] Halliburton SS, Abbara S, Chen MY, Gentry R, Mahesh M, Raff GL, Shaw LJ, Hausleiter J. Society of Cardiovascular Computed T. Scct guidelines on radiation dose and dose-optimization strategies in cardiovascular ct. J Cardiovasc Comput Tomogr 2011;5:198–224.

[13] Boxt LM. Coronary computed tomography angiography: a practical guide to performance and interpretation. Semin Roentgenol 2012;47:204–19.

[14] Isobe S, Yamada T, Sato K, Katagiri T, Ohyama H, Hayashi M, Yoshikawa D, Ishii H, Murohara T. Diabetes with preserved renal function is an independent risk factor for renal function deterioration after coronary computed tomography angiography. J Comput Assist Tomogr 2013;37:750–4.

[15] Mitchell AM, Jones AE, Tumlin JA, Kline JA. Incidence of contrast-induced nephropathy after contrast-enhanced computed tomography in the outpatient setting. Clin J Am Soc Nephrol: CJASN 2010;5:4–9.

[16] Yoshikawa D, Isobe S, Sato K, Ohashi T, Fujiwara Y, Ohyama H, Ishii H, Murohara T. Importance of oral fluid intake after coronary computed tomography angiography: an observational study. Eur J Radiol 2011;77:118–22.

[17] Ando H, Isobe S, Amano T, Yamada T, Ohtsubo H, Yuba M, Ishii H, Murohara T. Predictors of worsening renal function after computed tomography coronary angiography: assessed by cystatin c. J Cardiovasc Comput Tomogr 2012;6:31–6.

[18] Shetty AN, Bis KG, Vyas AR, Kumar A, Anderson A, Balasubramaniam M. Contrast volume reduction with superior vena cava catheter-directed coronary ct angiography: comparison with peripheral i. V. Contrast enhancement in a swine model. AJR Am J Roentgenol 2008;190:W247–54.

[19] Faggioni L, Neri E, Sbragia P, Pascale R, D'Errico L, Caramella D, Bartolozzi C. 80-kv pulmonary ct angiography with 40 ml of iodinated contrast material in lean patients: comparison of vascular enhancement with iodixanol (320 mg i/ml) and iomeprol (400 mg i/ml). AJR Am J Roentgenol 2012;199:1220–5.

[20] Delesalle MA, Pontana F, Duhamel A, Faivre JB, Flohr T, Tacelli N, Remy J, Remy-Jardin M. Spectral optimization of chest ct angiography with reduced iodine load: experience in 80 patients evaluated with dual-source, dual-energy ct. Radiology 2013;267:256–66.

[21] Liu J, Gao J, Wu R, Zhang Y, Hu L, Hou P. Optimizing contrast medium injection protocol individually with body weight for high-pitch prospective ecg-triggering coronary ct angiography. Int J Cardiovasc Imaging 2013;29:1115–20.

[22] Meyer M, Haubenreisser H, Schoepf UJ, Vliegenthart R, Leidecker C, Allmendinger T, Lehmann R, Sudarski S, Borggrefe M, Schoenberg SO, Henzler T. Closing in on the k edge: coronary ct angiography at 100, 80, and 70 kv-initial comparison of a second-versus a third-generation dual-source ct system. Radiology 2014;273:373–82.

[23] St Noble V, Douraghi-Zadeh D, Padley SP, Rubens MB, Nicol ED. Maximizing the clinical benefit of high-pitch, single-heartbeat ct coronary angiography in clinical practice. Clin Radiol 2014;69:674–7.

[24] Oda S, Utsunomiya D, Yuki H, Kai N, Hatemura M, Funama Y, Kidoh M, Yoshida M, Namimoto T, Yamashita Y. Low contrast and radiation dose coronary ct angiography using a 320-row system and a refined contrast injection and timing method. J Cardiovasc Comput Tomogr 2015;9:19–27.

[25] Secchi F, De Cecco CN, Spearman JV, Silverman JR, Ebersberger U, Sardanelli F, Schoepf UJ. Monoenergetic extrapolation of cardiac dual energy ct for artifact reduction. Acta Radiol 2014.

[26] Raju R, Thompson AG, Lee K, Precious B, Yang TH, Berger A, Taylor C, Heilbron B, Nguyen G, Earls J, Min J, Carrascosa P, Murphy D, Hague C, Leipsic JA. Reduced iodine load with ct coronary angiography using dual-energy imaging: a prospective randomized trial compared with standard coronary ct angiography. J Cardiovasc Comput Tomogr 2014;8:282–8.

[27] Kane GC, Doyle BJ, Lerman A, Barsness GW, Best PJ, Rihal CS. Ultra-low contrast volumes reduce rates of contrast-induced nephropathy in patients with chronic kidney disease undergoing coronary angiography. J Am Coll Cardiol 2008;51:89–90.