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ORIGINAL PAPER

Validation of a new contrast material protocol adapted to body surface area for optimized low-dose CT coronary angiography with prospective ECG-triggering

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Abstract In patients with large total blood volume contrast material (CM) dilution decreases coronary attenuation in CT coronary angiography (CTCA). As increased blood volume is well paralleled by body surface area (BSA) we assessed a BSA-adapted CM protocol to compensate for dilution effects. Low-dose CTCA with prospective ECG-triggering was performed in 80 patients with a BSA-adapted CM bolus ranging 40–105 ml and injection rate ranging 3.5–5.0 ml/s for a BSA of <1.70 to ≥2.5 m^2. Eighty control patients matched for BSA who had previously undergone routine CTCA with a fixed CM protocol of 80 ml at 5 ml/s served as reference group. The average vessel attenuation from the proximal right (RCA) and the left main coronary artery (LMA) was assessed. Correlation of BSA with vessel attenuation was assessed in both groups. BSA-matching of all patients was successful (BSA-adapted group 1.98 ± 0.15 m^2, range 1.66–2.39 m^2 versus reference group 1.98 ± 0.17 m^2, range 1.59–2.38 m^2; $P = 0.74$). Mean CM bolus was significantly smaller in the BSA-adapted versus the reference group (70.9 ± 14.1 vs. 80.0 ± 0 ml, $P < 0.001$). There was no correlation in the BSA-adapted group ($r = -0.07$, $P = 0.53$, SEE = 0.15), while coronary attenuation was inversely related to BSA in the reference group ($r = -0.59$, $P < 0.001$, SEE = 0.14). We have successfully validated a BSA-adapted contrast material protocol which results in a comparable coronary contrast enhancement independent of individual BSA. This was achieved despite a significant reduction in the overall contrast material amount.

Keywords Coronary vessel attenuation · BSA adaptation · Contrast material protocol · Computed tomography coronary angiography · Prospective ECG-triggering

Introduction

Coronary artery disease (CAD) is one of the major causes of morbidity and mortality in western countries. Computed tomography coronary angiography (CTCA) is a lately introduced non-invasive cardiac imaging method, which has been shown to reliably detect significant CAD (greater than 50% luminal narrowing) [1]. Prospective ECG-triggering has allowed to substantially reduce radiation dose of

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CTCA from about 15–20 mSv down to 1–3 mSv at maintained image quality [2] and accuracy [3, 4] so that the clinical acceptance of CTCA is growing. Coronary vessel attenuation may affect the accuracy of CTCA [5–7] as for an accurate detection of coronary plaque an appropriate amount of contrast material (CM) is needed. While coronary vessels can not be differentiated properly from the surrounding tissue with too little CM, coronary blooming artefacts caused by too large CM amounts may hamper the detection of coronary plaque.

The attenuation of coronary vessel is influenced by the individual patients weight, height (expressed by body mass index (BMI) and body surface area (BSA)) and cardiac output [8–13], as well as by technical factors related to the type and iodine concentration of the CM [7], the technique for bolus timing [6], the injection volume and rate [14], and tube voltage [15]. Previous CTCA protocols [2, 16–18] did not adapt to patients individual body mass or cardiac output. Consequently, vessel attenuation in CTCA has been shown to vary strongly [6–9], depending on BMI and to affect the optimal detection of coronary plaque. Recently a BMI adapted protocol was introduced in order to reduce the impact of BMI on image noise. However, coronary contrast remained subject to large variations [19], presumably due to bolus dilution depending on blood volume. As increased blood volume is well paralleled by BSA we identified BSA as the most promising parameter to be of potential value for adjusting the contrast bolus in future protocols. Therefore, we aimed at assessing a BSA-adapted CM protocol to compensate for dilution effects and the interindividual BSA-related differences in coronary attenuation.

Methods

Patients

Eighty patients underwent for clinical indication a 64-slice CTCA using prospective ECG-triggering with a contrast material protocol adapted to BSA (Table 1). For comparison, a control group of 80 patients matched for BSA were retrospectively recruited from a pool of patients ($n = 230$) who had previously undergone CTCA with prospective ECG-gating and a fixed CM protocol of 80 ml.

Table 1 Protocol for BSA-adapted contrast-material (CM) bolus and flow rate

BSA (m^2)	CM bolus (ml)	Flow rate (ml/s)
<1.70	40	3.5
1.70–1.79	45	4.0
1.80–1.94	60	4.0
1.95–2.04	80	4.5
2.05–2.14	80	5.0
2.15–2.24	85	5.0
2.25–2.49	95	5.0
≥2.5	105	5.0

CM contrast-material, *BSA* body surface area

Exclusion criteria for CTCA were: hypersensitivity to iodinated CM, renal insufficiency (creatinine levels >150 μmol/l), non-sinus rhythm, or haemodynamic instability.

All 160 patients were referred for evaluation of known ($n = 23$) or unknown CAD ($n = 137$), based on symptoms such as dyspnoea ($n = 18$), typical angina pectoris ($n = 27$), atypical chest pain ($n = 75$), or without symptoms for pre-operative rule-out of CAD in high-risk patients ($n = 40$).

The study protocol was approved by the institutional review board (local ethics committee of the University Hospital Zurich) and written informed consent was obtained from each patient.

Body surface area (BSA)

Body surface area (BSA) is an index which is widely used in clinical practice. For many clinical purposes BSA is a better indicator of metabolic mass than body weight because it is less affected by abnormal adipose mass. To obtain the BSA (m^2) we divided the square root of (height × weight) by 60 as previously reported by Mosteller [20] as this is the most widely used method recommended by most authorities including the British Columbia Cancer Agency for calculating chemotherapy dosage [21].

Data acquisition and image analysis

To achieve a target heart rate <65 bpm, intravenous metoprolol (5–20 mg) (Beloc, AstraZeneca, London, UK) was administered prior to the CTCA examination if necessary. Furthermore, all patients received

2.5 mg isosorbiddinitrate sublingual (Isoket, Schwarz Pharma, Monheim, Germany) 2 min prior to the scan for which iodixanol (Visipaque 320, 320 mg/ml, GE Heathcare, Buckinghamshire, UK) followed by 50 ml saline solution was injected into an antecubital vein via an 18-gauge catheter. Amount and flow rate of CM were gradually increased (40–105 ml, 3.5–5.0 ml/s, corresponding to an iodine delivery rate ranging from 1.1 to 1.6 g/s) to parallel increases in BSA in the BSA-adapted scanning protocol group (Table 1), while in the non-adapted scanning protocol group the amount and flow rate of contrast material were kept constant at 80 ml and 5 ml/s (iodine delivery rate 1.6 g/s). Bolus tracking was performed and image acquisition was started as soon as the CM appeared in the ascending aorta, where the region of interest was placed.

All CTCA examinations were performed on a 64-slice LightSpeed VCT XT scanner (GE Healthcare) with prospective ECG-triggering, using the following scanning parameters: slice acquisition 64 × 0.625 mm, smallest X-ray window (only 75% of the RR-cycle), z-coverage 40 mm with an increment of 35 mm, gantry rotation time 350 ms. Tube voltage and current were adapted to BMI as previously described [2] to avoid increases in noise due to increased BMI (Table 2). The total effective radiation dose was calculated by multiplying the dose length product (provided by the scanner) times a conversion factor (0.017 mSv/cGy/cm) as previously suggested [22]. All images were analyzed on an external workstation (AW 4.4, GE Healthcare).

Vessel attenuation (in Hounsfield units, HU) were measured twice by two independent readers (A.P. and L.H., both experience level 3 [23]) in the proximal RCA and the LMA, which served as regions of interest (ROI) drawn as large as possible, carefully avoiding calcifications, plaques, and stenoses, as previously described in detail [8]. The mean of the measurements by both readers in both ROI's was defined as "coronary vessel attenuation" and used for further analysis.

Table 2 Protocol for BMI-adapted tube parameters (according to ref. 25)

BMI (kg/m^2)	Tube voltage (kV)	Tube current (mA)
<22.5	100	450
22.5–24.9	100	500
25–27.4	120	550
27.5–29.9	120	600
30–40	120	650
>40	120	700

BMI body mass index

Statistical analysis

All statistical analysis was performed using SPSS software (SPSS 15.0, Chicago, ILL, USA). Quantitative variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as frequencies and percentages. Differences between the two groups regarding coronary artery attenuation and amount of applied contrast material were tested for significance by using Mann–Whitney-*U*-tests. Linear regression analysis was performed to correlate BSA and coronary artery attenuation, and multiple regression analysis was performed to compare this relationship between both groups. Standard error of the estimate (SEE) was determined. A P value of <0.05 was considered to indicate statistical significance.

Results

CTCA was successfully performed in all 160 patients. Baseline characteristics of all patients included in this study are given in Table 3. BSA-matching of all patients was successful (BSA-adapted

Table 3 Patient baseline characteristics

	Non-adapted scanning protocol (n = 80)	BSA-adapted scanning protocol (n = 80)
Female/male	21/59	12/68
Age (years)	59 ± 11 (34–82)	57 ± 11 (31–85)
BSA (m^2)	1.98 ± 0.17 (1.59–2.38)	1.98 ± 0.15 (1.66–2.39)
Weight (kg)	82 ± 12 (55–115)	82 ± 12 (60–118)
Height (cm)	172 ± 8 (156–193)	174 ± 5 (149–183)
Heart rate (bpm)	56 ± 7 (36–74)	56 ± 7 (40–72)

BSA body surface area, *bpm* beats per minute

group 1.98 ± 0.15 m^2, range 1.66–2.39 m^2 vs. reference group 1.98 ± 0.17 m^2, range 1.59–2.38 m^2; P = n.s.).

As part of their baseline medication, 40 of 160 patients (25%) were on beta blocker treatment. To achieve a target heart rate <65 bpm intravenous metoprolol was given prior to CTCA in 103 patients (64%). The mean dose length product from CTCA was 139 ± 43 mGycm (range 65–318 mGycm) resulting in an estimated mean effective radiation dose of 2.4 ± 0.7 mSv (range 1.1–3.9 mSv).

Mean of the interobserver differences (between L.H. and A.P.) in coronary artery attenuation measurements was 7.0 ± 23.9 HU. In the BSA-adapted group, mean attenuation values from both readers were 378 ± 56 HU (range 262–490 HU) for LMA and 363 ± 49 HU (range 260–510 HU) for RCA, resulting in a mean coronary vessel attenuation of 370 ± 49 HU (range 268–500 HU). In the non-adapted group, mean attenuation values were 424 ± 110 HU (range 280–712 HU) for LMA and 413 ± 103 HU (range 248–688 HU) for RCA, resulting in a mean coronary vessel attenuation of 418 ± 104 HU (range 264–700 HU).

Coronary attenuation was inversely related to BSA in the reference group ($r = -0.59$, $P < 0.001$, SEE = 0.14), while there was no correlation in the BSA-adapted group ($r = -0.07$, P = n.s, SEE = 0.15) (Fig. 1).

The mean applied amount of CM was significantly lower in the BSA-adapted versus the reference group (70.9 ± 14.1 ml vs. 80.0 ± 0, $P < 0.001$).

Discussion

The findings of the present study document that the BSA-adapted CM administration protocol is feasible and successful as the inverse correlation between BSA and coronary attenuation found in our control group, and also documented in previous reports [13, 19], could be abolished. As a result, range and standard deviation of coronary attenuation were smaller in the BSA-adapted group compared to the control group indicating a well balanced consistent contrast enhancement throughout a large range of BSA (Fig. 2). Furthermore, by using the BSA-adapted protocol a significantly lower average amount of contrast medium was injected, which may help preventing contrast induced nephropathy and its sequelae [24]. Although the resulting average coronary attenuation was slightly lower than in controls, the range of coronary attenuation obtained with our protocol (300–400 HU) compares well to the values suggested by Becker et al. (250–300 HU) [5] and Cademartiri et al. (>300 HU) [7] for adequate coronary visualization and optimal stenosis detection even in relatively small coronary arteries.

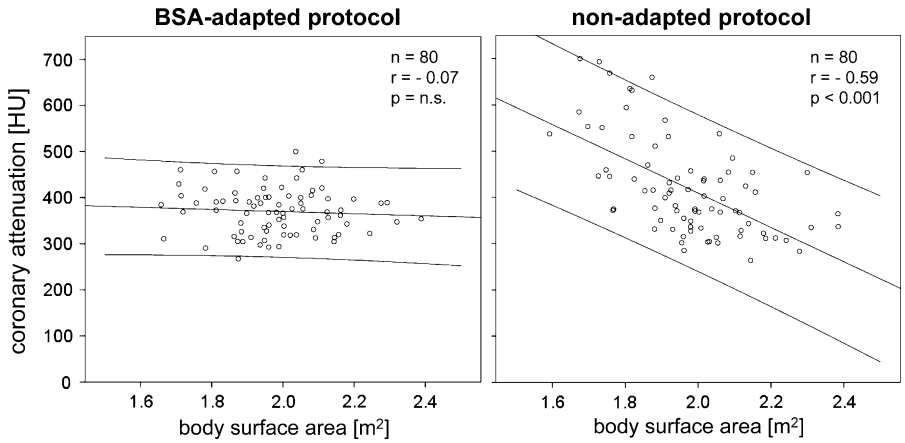

Fig. 1 Linear regression of body surface area against coronary artery attenuation. Linear regression analysis (with 95% confidence interval lines) of body surface area (BSA) against coronary artery attenuation in the groups scanned with the BSA-adapted protocol (*left panel*) and with the non-adapted contrast material protocol (*right panel*). The significant inverse correlation documented with the non-adapted protocol disappears after adapting for BSA

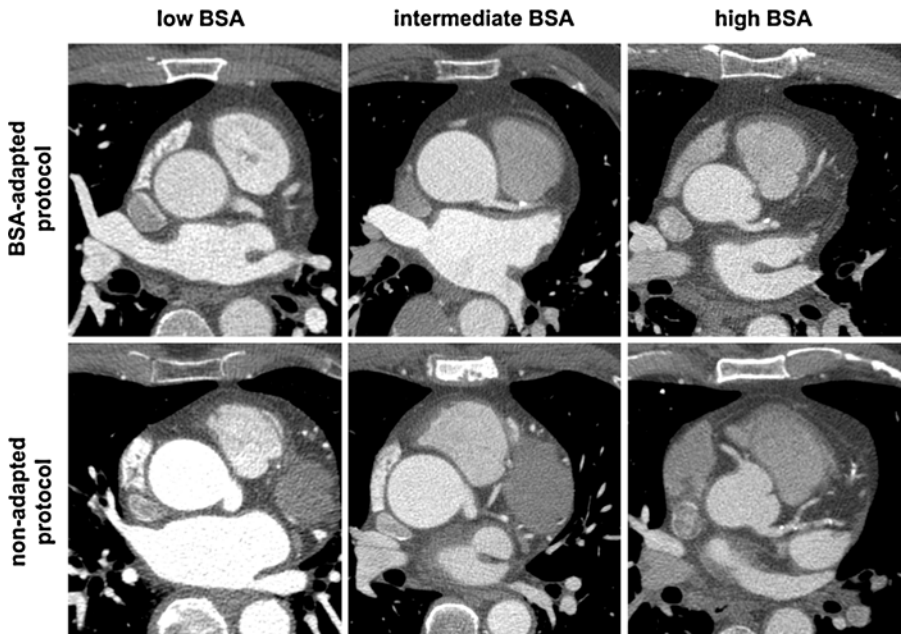

Fig. 2 CTCA images in patients with different body surface area. CTCA images of patients with low (<1.8 m^2), intermediate (1.8–2.2 m^2) and high (>2.2 m^2) body surface area (BSA). Images of the BSA-adapted protocol show an equivalent coronary attenuation independent of individual BSA (top row), while differences in attenuation can be seen in the control group depending on individual BSA (bottom row)

Attenuation of coronary vessel in CTCA is closely related to several factors including patient specific characteristics on one side such as body mass, blood volume and cardiac output [8, 9, 11, 13] as well as protocol related parameters on the other side such as concentration and injection rate of the administered CM [7, 19, 25]. In patients with increased body mass CTCA image quality is degraded by an unfavorable shift in the signal-to-noise ratio due to increase in noise and loss of attenuation. Introduction of scan protocols with body mass index-adapted tube current and voltage have allowed to overcome the adverse effects of body mass on image noise [25]. By contrast, the adverse effect of body mass on coronary attenuation is less well understood but recent reports have suggested increased CM dilution due to higher blood volume as explanation. Consequently, the hypothesis has been generated that BSA would be the most promising parameter to be used for CM protocol adjustment [13, 19]. Our study provides the evidence to approve this hypothesis. As our protocol has included BMI adaptation of tube current and voltage, our results suggest that an ideal protocol should integrate both BMI adaptation of tube parameters (noise minimization) and CM adjustment according to BSA (signal optimization). This may help differentiating coronary plaque from surrounding tissue and avoid blooming artefacts caused by excursive intracoronary CM concentration.

We acknowledge the following limitations to the present study: First, the case matching of the control group was retrospective, which may have introduced bias. Second, the determination of the BSA-adapted contrast material protocol was arbitrary. However, the protocol was designed based on the upslope of the coronary attenuation—BSA curve previously reported [19]. Third, coronary attenuation was measured only in two proximal vessels (RCA and LMA). However, smaller vessel diameters of distal segments do not allow appropriate placing of a ROI. Further studies in larger populations are needed to confirm the added value of greater consistency in coronary artery attenuation regarding the accuracy of CTCA.

The proposed BSA-adapted contrast material protocol results in an adequate coronary vessel attenuation independent of individual BSA.

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