MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2017; 23: 4351-4359
DOI: 10.12659/MSM.902917

Received: 2016.12.19
Accepted: 2017.02.27
Published: 2017.09.09

Low-Dose Scanning Technology Combined with Low-Concentration Contrast Material in Renal Computed Tomography Angiography (CTA): A Preliminary Study

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Source of support: This work was supported by the Science and Technology Development Plan Project of Shandong Province (No. 2014GSF118091and No. 2015ZRE27252), and the Youth Fund of the Natural Science Fund project of Shandong Province

Background: This study is to investigate the feasibility of low iodine concentration contrast material (CM) combined with low tube voltage and adaptive statistical iterative reconstruction (ASIR) in renal computed tomography angiography (CTA).

Material/Methods: A total of 136 patients were enrolled in this prospective trial, and randomly divided into two groups: group A (n=68) and group B (n=68). Group A received 120-kVp and iopromide (370 mg/mL) with filtered back projection (FBP) reconstruction, and group B received 100-kVp and iodixanol (270 mg/mL) with ASIR 40% ($ASIR_{40}$). An equal iodine dose (300 mg/kg body weight) and the same iodine delivery rate (1,500 mg I/s) were given to all patients. Density, image noise, signal-to-noise ratio (SNR), and contrast-to-noise ratio (CNR) were measured, and the image quality and visualization of renal arteries were scored. Dose-length product (DLP) and CT dose index volume (CTDIvol) were recorded, and effective doses (ED) were calculated.

Results: There was no significant difference in image noise between groups A and B (p>0.05). The vessel attenuation, SNR, and CNR were significantly higher in group B than group A (all p<0.05). The subjective image quality and visualization of renal artery branches were similar in these two groups (p>0.05). Compared with group A, the CTDIvol, DLP, and ED in group B were decreased by 38.58%, 37.24%, and 37.24%, respectively (p=0.000).

Conclusions: Compared with 120-kVp with FBP reconstruction, the protocol of 100-kVp with $ASIRP_{40}$ reconstruction provided high-quality renal CTA results, which allowed for reduced iodine concentration and decreased radiation dose.

MeSH Keywords: Angiography • Four-Dimensional Computed Tomography • Microscopy, Acoustic

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/902917

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Background

Computed tomography angiography (CTA) is a minimally invasive diagnostic procedure commonly used in the assessment of vascular lesions in clinical settings [1–5]. In CTA, the arterial enhancement partially depends on the concentration of contrast material (CM) [6,7]. Therefore, administration of high-concentration CM has become the routine clinical practice to increase the vascular attenuation of small and large vessels [2]. Along with the more popular application of CTA with high-concentration CM in clinical practice, public concerns have risen regarding the potential harms to patients that might be caused by radiation exposure and contrast-induced nephropathy (CIN) [8–11]. Therefore, reducing the CT radiation dose and CM concentration without compromising image quality is of great importance and significance.

Several approaches to achieve dose reduction have been reported for body CT, one of which is to reduce the tube voltage [1,12–16]. Low tube voltage with standard convolution filtered back projection (FBP) reconstruction algorithm can allow for reduced radiation dose and increased vessel density in patients undergoing contrast-enhanced CT, but it cannot compensate for high image noise in dose-saving strategies [1,17]. Compared with FBP reconstruction, adaptive statistical iterative reconstruction (ASIR) can reduce the quantum noise and improve the image quality [14,17–21]. The purpose of the current study was to prospectively evaluate whether low-concentration CM (270 mg/mL) with low tube voltage (100-kVp) and 40% ASIR ($ASIR_{40}$) reconstruction could reduce the radiation dose without decreasing the image quality in renal artery CTA.

Material and Methods

Study patients

A consecutive series of 155 patients who were scheduled to undergo renal CTA were identified from October 2015 to September 2016, including 78 renal transplant donors, 31 patients with suspected primary renal artery disease, and 46 patients with suspected abdominal aorta disease. Exclusion criteria included patients with serum creatinine level >120 µmol/L or anaphylactic reaction to iodinated CM. Eight patients were excluded because of either prior anaphylactic reaction to iodinated CM (n=3) or serum creatinine level >120 µmol/L (n=5). After examination, 11 patients were excluded based on evaluation of renal arteries: aortic-iliac thrombosis (n=4), aortic-iliac dissection (n=5), nephrectomy (n=1), and breath-hold failure (n=1). Consequently, 136 eligible patients were enrolled (Figure 1) and randomly divided into two groups. Group A (n=68) received 120-kVp and iopromide 370 mg/mL with FBP reconstruction, and group B (n=68) received 100-kVp and iodixanol 270 mg/mL with $ASIR_{40}$. This study was approved by the local Ethics Committee, and prior written informed consent was obtained from all patients.

Contrast-enhanced CTA protocols

All examinations were performed on a 64-row multi-detector CT system (Discovery CT 750 HD; GE Healthcare, Milwaukee, WI, USA). All patients were scanned in supine position with their hands over their heads, and the scanning range was from the aortic hiatus to the iliac crest. The scanning parameters were described in Table 1. In group A, CT examination was performed on each patient with a routine dose protocol noise index (NI) of 8.0. In group B, $ASIR_{40}$ blend was applied according

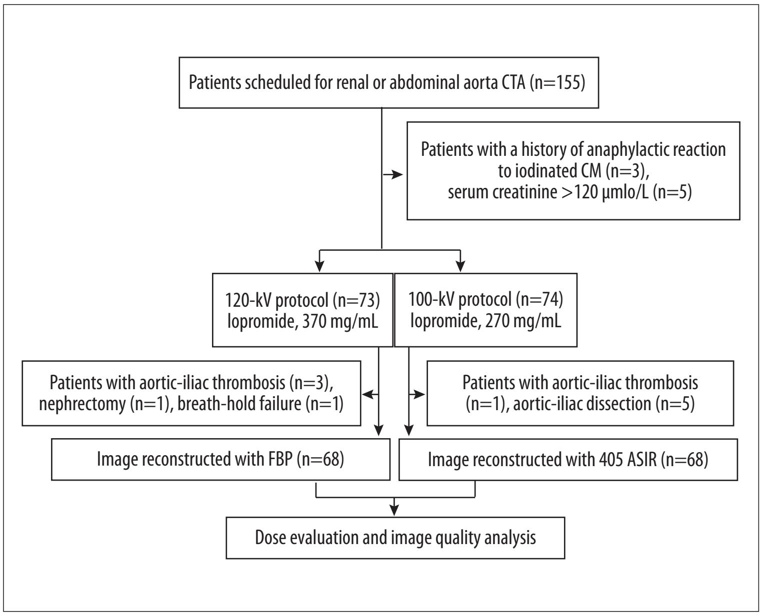

Figure 1. Study flowchart. A total of 155 consecutive patients were approached, and 136 patients were finally enrolled. Of these 136 patients, 68 were randomly selected and assigned to the 120-kVp with FBP reconstruction protocol, while the other 68 were subjected to the 100-kVp with $ASIR_{40}$ reconstruction protocol. The CM concentrations were 370 mg/mL and 270 mg/mL iodine, respectively.

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Table 1. Scanning protocol for renal CTA.

	Group A	Group B
Tube voltage (kVp)	120	100
Tube current control	ATCM	ATCM
mA min/max	100–550	100–550
Noise index	8	11
Rotation time (s)	1	1
Pitch	0.984: 1	0.984: 1
Detector collimation (mm)	5	5
Reconstruction algorithm	FBP	ASIR
Reconstruction interval (mm)	0.625	0.625
Reconstruction thickness (mm)	0.625	0.625

ATCM – automatic tube current modulation; FBP – filtered back projection.

to a previous study [14], and a NI of 11.0 was chosen based on our early clinical experience, and related publications [22,23]. The angiographic phases in groups A and B were obtained at high-concentration CM (iopromide, 370 mg/mL, Ultravist 370, Schering) and low-concentration CM (iodixanol, 270 mg/mL, Visipaque 270, Schering), respectively. An equal iodine delivery rate (1,500 mg I/s) and the same iodine dose (300 mg/kg body weight) were given to all patients, followed by a 45-mL saline flush at the same flow rate as the corresponding CM. For each patient, CM was administered with a high-pressure syringe injector through the right median cubital vein. Bolus tracking was used in both groups with a trigger level of 150 HU.

Image reconstruction and post-processing

Raw data from groups A and B were reconstructed with FBP and $ASIR_{40}$, respectively. The reconstruction thickness was 0.625 mm, at an interval of 0.625 mm. Then, the image datasets for each patient were post-processed with the GE Volume Share 4 AW4.4 workstation (GE Healthcare), including volume-rendering (VR), multiple-planar-reformation (MPR), and maximum-intensity-projection (MIP).

Radiation dose

To analyze the CT radiation dose, the dose-length product (DLP) and CT dose index volume (CTDIvol) of the arterial phase were recorded. The effective dose (ED) was obtained from the DLP via multiplying by a standardized abdominal conversion factor of 0.015 mSv/mGy cm.

Qualitative evaluation

Post-processed images were independently assessed with two radiologists, one with five-years of experience and the other with eight-years of experience in interpreting 3D visceral vascular images; the radiologists were unaware of the scanning protocols. Image quality and renal artery visualization were assessed with the 5-point scale system, based on the luminal border, image noise, and diagnostic acceptability [24]. The 5-point score was defined as: 1, non-diagnostic (blurring luminal border and unacceptable image noise); 2, poor but still diagnostic (notable blurring luminal border, significant image noise, and diagnostic with limitations); 3, moderate (less blurring luminal border, average image noise, and diagnostic with minor limitations); 4, good (sharp luminal border, less image noise, and diagnostic without significant limitations); and 5, excellent (sharp luminal border, no image noise, and diagnostic without limitations). The branch order of renal arteries was also visualized and assessed with a 5-point scale [25]: 1, poor (main vessels not seen); 2, suboptimal (first-order branch); 3, diagnostic (second-order branch); 4, superior (third-order branch); and 5, excellent (forth-order branch).

Quantitative evaluation

For quantitative image analysis, the attenuation values (CT value in Hounsfield units) and standard deviation (SD) of both renal arteries and abdominal aorta near the level of celiac artery were measured, respectively. The measurement was performed by manually outlining a region of interest (ROI) in the center of the vessel lumen (as large as possible, but away from the vessel wall or plaques to avoid artifacts and partial volume effects). In addition, the attenuation value of the sacrospinal muscle in the same slice of the corresponding artery was measured as the background noise. The signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of the vessels were obtained using the following formula: SNR=vessel attenuation value/SD, and CNR=(vessel attenuation value-sacrospinal muscle attenuation value)/SD.

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Table 2. Patients' profile between Group A and Group B.

	Group A (n=68)	Group B (n=68)
Male/female	36/32	35/33
Age (years)	56.77±12.51	57.93±15.39
Weight (kg)	67.77±9.99	66.84±10.08
Height (m)	1.66±0.07	1.67±0.07
BMI (kg/m^2)	24.42±5.1	23.90±4.8

BMI – body mass index.

Table 3. Radiation doses for Groups A and B.

	CTDIvol (mGy)	DLP (mGy-cm)	ED (mSv)
Group A	26.13±6.82	827.80±230.04	12.42±3.45
Group B	16.04±3.94	519.55±123.31	7.79±1.84
t Value	–8.493	–7.833	–7.833
P Value	0.000	0.000	0.000

CTDIvol – CT dose index volume; DLP – dose length products; ED – effective dose.

Table 4. Qualitative analysis of images between Group A and Group B.

Parameters	Group A	Group B	P value
Image quality score	4.53±0.42	4.69±0.56	0.502
LRA score	4.12±0.38	4.27±0.43	0.558
RRA score	4.20±0.34	4.37±0.54	0.423

CTDIvol – CT dose index volume; DLP – dose length products; ED – effective dose.

Statistical analysis

Data were expressed as mean ± SD. SPSS 19.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The age, height, weight, body mass index (BMI), and radiation dose were compared using the Student *t*-test for unpaired samples, and the Fisher exact test was used for gender composition analysis. Image quality scores were compared using the Mann-Whitney *U* test, and the inter-observer variability was estimated by the Cohen's kappa test. The *k* values indicated poor (<0.40), moderate (0.41–0.60), good (0.61–0.80), and excellent (0.81–1.00) agreements, respectively.

Results

Patient demographics and radiation doses

Patient demographics were shown in Table 2. Our results showed that there were no significant differences in the patients' gender, age, height, weight, and BMI between groups A and B. For the CT radiation doses, as shown in Table 3, the CTDIvol, DLP, and ED in group B were all significantly less than those in group A (p=0.000). Compared with group A, CTDIvol, DLP, and ED in group B decreased by 38.58%, 37.24%, and 37.24%, respectively. These results suggest that the protocol in group B was a pragmatic approach significantly reducing radiation dose.

Qualitative analysis

Qualitative analysis indicated the subjective image quality score showed no significant difference between groups A and B (p>0.05) (Table 4, Figure 2). Compared with group A, the image quality in group B was not decreased. Moreover, the *k* value of inter-observer agreement for the subjective image quality was 0.73, indicating good inter-observer agreement between the two observers. Assessment of the renal artery branch orders indicated that there was no difference between these two groups (p>0.05) (Table 4, Figure 3). Again, the inter-observer

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Figure 2. Volume-rendering (VR) images of renal artery and abdominal aorta. (**A**) Image of a 43-year-old woman obtained with the protocol of 120-kVp, iopromide 370 mg/mL and FBP reconstruction (the subjective score of 5). (**B**) Image of a 59-year-old man obtained with 100-kVp, iodixanol 270 mg/mL and $ASIR_{40}$ reconstruction (the subjective score of 5).

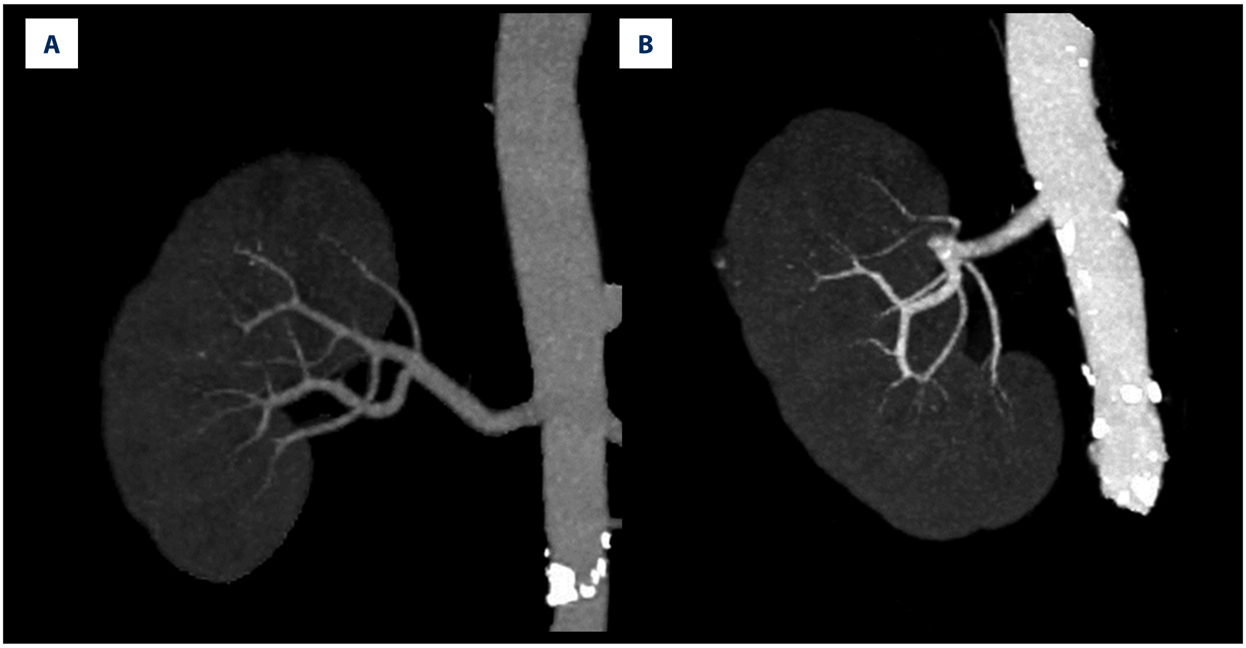

Figure 3. Renal artery branch characterization in MIP images. MIP images were obtained from a 62-year-old man and a 53-year-old woman subjected to the protocols (**A**): 120-kVp, iopromide 370 mg/mL and FBP reconstruction and (**B**): 100-kVp, iodixanol 270 mg/mL and $ASIR_{40}$ reconstruction, respectively. The two images show the same characterization of the renal artery branches.

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Table 5. Quantitative analysis of images between Groups A and B.

Vessel	Parameters	Group A	Group B	t value	P value
AA	CT value	396.55±55.13	452.07±37.88	5.504	0.000
	Noise	19.55±2.63	20.31±2.79	1.311	0.193
	SNR	17.42±2.44	19.67±4.00	3.172	0.002
	CNR	20.41±2.54	22.73±4.14	3.172	0.002
LRA	CT value	376.39±53.72	432.55±34.61	5.828	0.000
	Noise	19.73±2.44	20.53±2.14	1.623	0.108
	SNR	16.40±2.69	18.16±2.83	2.990	0.004
	CNR	19.23±2.84	21.32±3.01	3.343	0.001
RRA	CT value	384.11±51.41	427.77±43.83	4.285	0.000
	Noise	20.22±3.27	20.72±2.35	0.833	0.408
	SNR	16.44±2.59	17.81±3.26	2.192	0.031
	CNR	19.26±2.84	20.94±3.43	2.482	0.015

AA – abdominal aorta; LRA – left renal artery; RRA – right renal artery.

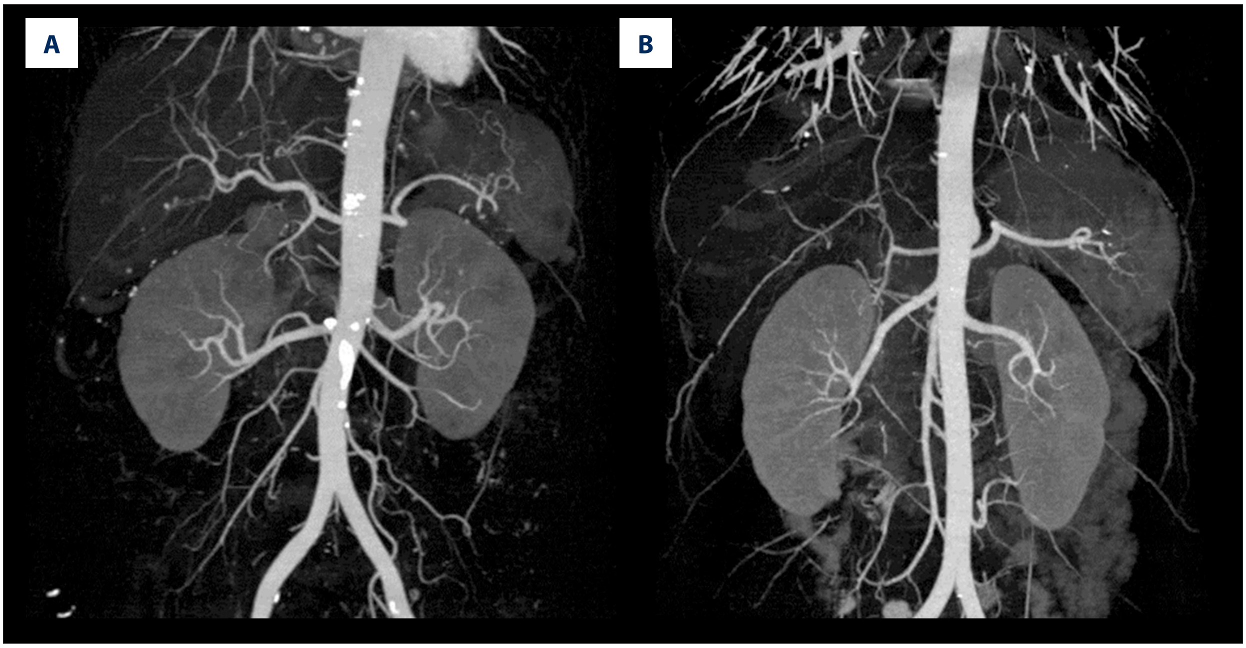

Figure 4. Analysis of MIP images. MIP images were obtained from a 68-year-old man and a 64-year-old woman subjected to the protocols of (**A**) 120-kVp, iopromide 370 mg/mL and FBP reconstruction and (**B**) 100-kVp, iodixanol 270 mg/mL and $ASIR_{40}$ reconstruction, respectively. The CT attenuation values, SNRs, and CNRs at the left renal arteries were 381.53 HU, 17.3, 18.9, and 437.08 HU, 19.2, 21.1, respectively.

agreement in the values of left and right renal arteries between the two observers was good (*k*=0.66 and 0.72, respectively).

Quantitative analysis

The CT values, image noise, SNR, and CNR were analyzed and compared between groups A and B. As shown in Table 5, group B showed significantly higher CT value than group A, in the renal arteries and abdominal aorta (all *p*=0.000) (Figure 4). For the image noise, there was no significant difference between groups A and B (*p*>0.05). The evaluation showed higher SNR and CNR in group B than in group A (*p*<0.05) (Figure 4). Taken together, these results suggest that, our protocol can provide superior diagnostic quality images.

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Discussion

In this study, the effects of CM with low iodine concentration administered in an intra-individual setting and low tube voltage with $ASIR_{40}$ on the image quality and radiation dose were investigated. Our results showed that, compared with the conventional protocol (using high iodine concentration CM iopromide 370 mg/mL and 120-kVp with FBP reconstruction), the application of iodixanol 270 mg/mL combined with 100-kVp and $ASIR_{40}$ lead to significant vascular attenuation, higher SNR and CNR, and comparable image quality (with reductions of 38.58% in CTDIvol, 37.24% in DLP, and 37.24% in ED). These findings indicated that our "double-low" protocol was a promising approach significantly reducing the radiation dose while providing superior diagnostic quality images, and as such should be recommended for use in renal CTA examinations.

CTA plays a very important role in the assessment of vascular diseases. However, the administration of high iodine concentration CM always yields high vascular attenuation in the large and tiny vessels [7]. Particularly in clinical practice, application of high iodine concentration CM might increase the risk of CIN, not only because of the high concentration but also the high viscosity and osmolality. The chemical properties (especially the viscosity) are important factors involved in toxic side effects [9,10]. Application of low iodine concentration CM with moderate viscosity and osmolality is essential to reduce the iodine burden in the kidneys. In this study, the iso-osmolar CM iodixanol 270 mg/mL with viscosity of 5.80 mPa·s at 37°C was used to increase the vascular attenuation in CTA, which may be crucial to patients who have CTA examination without recognizing the risk of poor renal function.

In our study, the administration protocol was different from pervious publications [1,7,9,25]. In those studies, the same injection flow rate and volume were used for different CMs. Therefore, it was not surprising that higher iodine concentration CM was found to produce higher contrast enhancement, compared with lower iodine concentration CM. In our administration protocol, an equal iodine delivery rate (1,500 mg I/s) and the same iodine dose (300 mg/kg body weight) were given to all patients. Our protocol was based on the common clinical practice that CM with moderate iodine concentration (300 mg/mL) was always administered with the empirical delivery rate of 5 mL/s. This meant that the low iodine concentration CM must be administered with a higher flow rate (in mL/s), compared with high iodine concentration CM. However, the increased injection rate would require larger needles and might result in extravasation. Actually, previous studies have reported that, when the injection rate was under 6 mL/s, there was no correlation between injection rate and extravasation incidence [26,27]. Consistent with this finding, in our study, the flow rates of 4.05 and 5.56 mL/s were applied for iopromide 370 mg/mL and iodixanol 270 mg/mL, respectively, and no extravasation occurred. Increased vascular attenuation may be achieved by using low-concentration CM in addition to low tube voltage, due to the closer proximity to the *k*-edge of iodine and the subsequently increased beam attenuation [28]. Therefore, our administration protocol was considered highly feasible.

In this study, there was a significant difference in the renal vascular contrast between the 120-kVp with iopromide 370 mg/mL and 100-kVp with iodixanol 270 mg/mL. In line with this, a previous study demonstrated that the contrast conspicuity in renal CTA could be compensated at reduced tube voltage with low iodine concentration CM, which was recommended for clinical practice [1]. However, another study showed that reduced tube voltage may result in increased image noise and background noise due to low photon flux, and might adversely affect the diagnostic accuracy of the images [29]. So image quality impairment associated with low tube voltage may present a big challenge. Fortunately, ASIR has been shown to decrease image noise and effectively increase SNR and CNR compared to FBP reconstruction [14,17,18]. ASIR depends on the mathematic model and statistical iteration of raw CT data, which selectively identifies and reduces the image noise [23]. It has the potential to maintain and improve the diagnostic ability of CT examination performed at reduced doses [30]. Our findings confirmed that 100-kVp with $ASIR_{40}$ reconstruction could significantly reduce the radiation dose in renal CTA, without compromising the image quality, compared with 120-kVp with FBP reconstruction.

In this study, the automatic tube current modulation (ATCM) technique was used, which has been reported to reduce the overall radiation dose by rapidly altering the mA as the gantry rotates around the patient, and at the same time maintain acceptable image quality. For the ATCM, an appropriate NI becomes really important to reach as low as reasonably achievable dose. The NI could alter the mA range, over which the tube current varies during the gantry rotation, producing the image noise [22,31]. In this study, our results showed that $ASIR_{40}$ technique with 100-kVp allowed 38.58% decrease in CTDIvol and 37.24% reduction in DLP, without compromising the image quality, compared with the FBP technique with 120-kVp for the renal CTA examination using the ATCM technique. Consistent with this finding, a previous study found that the ASIR technique resulted in a reduction of 24.5% to 26.5% in radiation dose compared with the FBP technique for abdominal CT examination performed with ATCM [32]. Our study observations contribute to existing data regarding the combination of low-concentration CM, low tuber voltage, and ASIR in renal CTA. Furthermore, we found no significant differences in gender distribution, mean age, and height and weight of patients between the two groups.

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There were some limitations to our study. First, the data were tested in a relatively small prospective trial, and further large multi-center prospective trials might be needed. Second, only the image quality of the renal artery was assessed, while other branches of the abdominal aorta and parenchymal organ were not involved. Third, this study only focused on the dose reduction in the abdomen, while the doses in other body parts and organs were not investigated. Fourth, only the image quality and radiation dose for the 100-kVp and $ASIR_{40}$ were estimated, and not for 100-kVp and FBP. Finally, only the image quality and radiation dose with ATCM were evaluated, not the effects of fixed current.

Conclusions

Our study demonstrated that, compared with iopromide 370 mg/mL with 120-kVp and FBP reconstruction, the combination of iodixanol 270 mg/mL with 100-kVp and $ASIR_{40}$ in renal CTA allowed effective radiation dose reduction, without compromising image quality. These findings provide evidence for the clinical application of the combination of low-concentration CM with low tube voltage and ASIR reconstruction algorithm in renal CTA.

Conflict of interests

None.

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