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SYSTEMATIC REVIEW

Low tube voltage prospectively ECG-triggered coronary CT angiography: a systematic review of image quality and radiation dose

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Objective: This study aimed (1) to perform a systematic review on scanning parameters and contrast medium (CM) reduction methods used in prospectively electrocardiography (ECG)-triggered low tube voltage coronary CT angiography (CCTA), (2) to compare the achievable dose reduction and image quality and (3) to propose appropriate scanning techniques and CM administration methods.

Methods: A systematic search was performed in PubMed, the Cochrane library, CINAHL, Web of Science, ScienceDirect and Scopus, where 20 studies were selected for analysis of scanning parameters and CM reduction methods.

Results: The mean effective dose (H_E) ranged from 0.31 to 2.75 mSv at 80 kVp, 0.69 to 6.29 mSv at 100 kVp and 1.53 to 10.7 mSv at 120 kVp. Radiation dose reductions

of 38 to 83% at 80 kVp and 3 to 80% at 100 kVp could be achieved with preserved image quality. Similar vessel contrast enhancement to 120 kVp could be obtained by applying iodine delivery rate (IDR) of 1.35 to 1.45 g s⁻¹ with total iodine dose (TID) of between 10.9 and 16.2 g at 80 kVp and IDR of 1.08 to 1.70 g s⁻¹ with TID of between 18.9 and 20.9 g at 100 kVp.

Conclusion: This systematic review found that radiation doses could be reduced to a rate of 38 to 83% at 80 kVp, and 3 to 80% at 100 kVp without compromising the image quality.

Advances in knowledge: The suggested appropriate scanning parameters and CM reduction methods can be used to help users in achieving diagnostic image quality with reduced radiation dose.

INTRODUCTION

Coronary CT angiography (CCTA) has emerged as a non-invasive modality of choice for the detection of coronary artery disease, particularly for the investigation of symptomatic patients with low-to-intermediate cardiovascular risk (approximately 20 to 70%).^{1,2} However, radiation exposure and the administration of contrast medium (CM) are reasons of concern in patients undergoing CCTA. Several techniques have been developed to reduce radiation exposure. These include low tube voltage protocol,³ electrocardiography (ECG)-dependent tube current modulation,⁴ prospectively ECG-triggered protocol,^{5,6} high-pitch helical scanning with dual-source CT,⁷ application of noise reduction filters⁸ and optimisation of scan length.⁹

Prospectively ECG-triggered protocol has been recommended as the first line default technique for CCTA examination, which should be used whenever possible and practical.¹⁰ The scanning is mostly performed using

standard peak voltage of 120 kVp and iodinated CM. The iodine delivery rate (IDR) ranges from 0.99 to 2.22 g s⁻¹ and total iodine dose (TID) is between 11.1 to 56.0 g.¹¹

In the last decade, various studies have tried to reduce radiation exposure in CCTA by lowering the tube voltage to 80 and 100 kVp, together with reduced iodine doses.¹²⁻¹⁹ The low tube voltages will generate less X-ray photons in the CT tube when the same tube current is applied. This can be explained with technical reasons, such as lower tube effectiveness at low tube voltage and the heavy filtering of low-kV photons.^{20,21} At the same time, as the mean photon energy of low tube voltage approaches the iodine K-edge energy of 33 keV, it produces better image contrast, meaning an equivalent vessel contrast enhancement can be achieved at a lower amount of administered iodine.^{22,23}

Despite its advantages, increased image noise remains a drawback in the low tube voltage protocol. Since tube

output is proportional to the square of tube voltage, a reduction from 120 to 100 kVp will result in 31% less X-ray photons being produced, and this figure will increase to 56% with further reduction to 80 kVp. Image noise is proportional to the square root of X-ray photons, thus more noise will be generated when using lower tube voltage at the same tube current. One solution to improve image quality is to increase the tube current to balance image noise. However, this may end up increasing the radiation dose, especially for larger-sized patients.²⁰

To address this issue, CT scanner manufacturers have introduced different protocols based on lower tube voltage and/or tube current combined with iterative reconstruction (IR) and other radiation dose-reducing techniques, together with CM reduction method.²⁴ The scanning parameters are dependent on hardware (CT scanner) specifications. There is no consensus on the extent of radiation dose reduction and how the image quality can be preserved when different scanning techniques and CM reduction methods are applied.

Therefore, this study aims to systematically review the current prospectively ECG-triggered low tube voltage CCTA protocols to provide an overview of various scanning techniques and CM reduction methods, to assess reported achievable radiation dose reduction and image quality. We also summarise and propose appropriate scanning techniques and CM administration methods for achieving diagnostic image quality with low dose exposure.

METHODS AND MATERIALS

Data sources and study selection

This review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.²⁵ A systematic search of PubMed, the Cochrane library, CINAHL, Web of Science, ScienceDirect and Scopus was performed without publication date limitation. The following Medical Subject Heading terms and the free keywords were used to identify studies on low tube voltage CCTA protocol: (“heart” OR “cardiac” OR “coronary”) AND (“tomography, X-ray computed” OR “computed tomography angiography”) OR (“tomography” AND “X-ray” AND “computed”) OR “X-ray computed tomography” OR [(“computed” AND “tomography”) OR (“computed tomography”)] AND [(low AND voltage) OR (tube AND voltage)] (last search, 30 September, 2017). Furthermore, the reference lists of retrieved articles were manually scrutinized to identify potential relevant studies.

The inclusion criteria included: (1) study that compared radiation dose and/or image quality between 120 kVp and low tube voltage protocols; (2) scanning was performed using a multidetector CT scanner with minimum 64 detector-row; (3) prospectively ECG-triggered CCTA protocol was used; (4) quantitative measurement of vessel contrast enhancement and/or the following parameters: image noise, signal-to-noise ratio (SNR), contrast-to-noise ratio (CNR); qualitative image quality; and air-kerma length product (P_{KL}) and (5) published in peer reviewed journals written in English language.

Studies that involved paediatric populations were excluded to avoid bias in radiation dose and image quality assessment due to use of different cardiac CT scanning protocols in paediatric patients when compared to adult cardiac patients. Furthermore, radiation dose measurement using *ex vivo* phantoms only were excluded. However, for studies that involved both phantoms and human participants, the data from human participants were included in this review. The methodological quality of included studies were assessed by using the QUADAS-2 checklist.²⁶ Two authors screened all articles and extracted the data independently. Disagreement on inclusion of eligible studies was resolved by consensus between the two authors.

Data extraction

Publications considered eligible were scored using a standardised extraction form, which included the first author, publication date, title, journal, participant characteristics, CM injection parameters, type of CT system, image acquisition techniques and parameters, image reconstruction techniques, reported dose and image quality measurements.

The primary outcomes were effective dose (H_E) (mSv), quantitative [vessel contrast enhancement (HU), image noise, SNR and CNR] and qualitative image quality. H_E was calculated by multiplying the P_{KL} with the conversion coefficient of 0.014 mSv·mGy⁻¹·cm⁻¹ for the chest region. For quantitative and qualitative image quality assessment, the differences were classified as “improved”, “similar” or “lower” compared with 120 kVp protocol. A statistically significant ($p < 0.05$) improvement of image quality was classified as “improved”, non-statistically significant difference ($p > 0.05$) was classified as “similar” and a statistically significant ($p < 0.05$) decrease in image quality was classified as “lower”. The scanning parameters used in the selected studies were summarised and the optimum protocols were suggested.

Statistical analysis was performed using SPSS software (v. 23.0, IBM Corporation, Armonk, NY). Correlations between H_E and publication year were tested using Spearman’s rank correlation test. 95% confidence interval was used and a p -value below 0.05 was considered as statistically significant.

RESULTS

Study selection

In the primary literature search, 1357 articles were identified, of which 789 were duplicates, leaving 568 potential articles for analysis. A total of 336 articles were excluded due to irrelevant topics. Of the remaining 232 full text articles, 188 articles were excluded during the screening process because they either (i) did not fulfil inclusion criteria ($n = 65$); (ii) did not involve human subjects ($n = 28$); (iii) focused on other goal ($n = 65$); (iv) focused on other field of interest ($n = 9$); (v) focused on paediatrics ($n = 18$); and (vi) involved non-contrast studies only ($n = 3$). Of the remaining 44 articles, 24 were excluded because the studies were addressing other technical aspects. Therefore, only 20 studies were finally selected for analysis.^{15–19,27–41} A detailed overview of the inclusion and data extraction processes is shown in Figure 1.

Figure 1. The study selection flow.

Study characteristics

The study characteristics are provided in [Tables 1 and 2](#). The studies were published in 2008 ($n = 1$), 2011 ($n = 2$), 2013 ($n = 3$), 2014 ($n = 1$), 2015 ($n = 7$) and 2016 ($n = 6$). Among all, 4 studies compared the radiation dose and image quality produced at 80 and 120 kVp, 11 studies involved the comparison between 100 and 120 kVp, while 5 studies involved the comparison between 80, 100 and 120 kVp.

In five studies, H_E was recalculated from P_{KL} because the reported H_E was calculated with a different P_{KL} -to- H_E conversion coefficient (0.017 and $0.028 \text{ mSv} \cdot \text{mGy}^{-1} \cdot \text{cm}^{-1}$, respectively).^{16,27,35,36,39} There was no correlation between publication year and H_E for 80 kVp ($p = 0.829$, $r = -0.085$), 100 kVp ($p = 0.392$, $r = 0.222$) and 120 kVp ($p = 0.447$, $r = -0.171$).

Quantitative assessment of image quality was performed in 19 studies while qualitative assessment was performed in all the studies, mostly using 2- to 5-point Likert scale (3 studies were scored by 1 observer; 16 studies were scored by 2 observers; and 1 study was scored by 3 observers).

Radiation dose and image quality

The mean H_E reported in the selected studies ranged from 0.31 to 2.75 mSv at 80 kVp, 0.69 to 6.29 mSv at 100 kVp and 1.53 to 10.7 mSv at 120 kVp. The radiation doses were reduced by 38 to 83% at 80 kVp and 3 to 80% at 100 kVp when compared with 120 kVp. The lowest doses at 80 kVp (0.31 mSv), 100 kVp (0.69 mSv) and 120 kVp (1.53 mSv) were reported by Durmus et al which combined automated tube voltage selection (ATVS) and automatic tube current modulation (ATCM) techniques.²⁸ Nine

studies reported increase in image noise at 80 kVp ($n = 4$) and 100 kVp ($n = 5$). Overall, improved or similar image quality was achieved in all the studies when using lower tube voltage, except in one study³² which reported deteriorating qualitative image quality at 100 kVp as compared to 120 kVp.

Scanning techniques used in prospectively ECG-triggered low tube voltage CCTA protocol

Different scanning techniques were used in the selected studies to achieve dose reduction and maintain image quality at low tube voltage settings ([Table 3](#)). The scanning techniques are categorized into three stages of CCTA examination: patient selection, image acquisition and image reconstruction.

Manual and automatic processes were used to select patients. Manual selection was performed based on the patients' body mass index (BMI) ($n = 5$) and chest circumference (CC) ($n = 1$). Automatic selection was used in three recent publications, involving a dedicated software (Care kV, Siemens Healthcare, Forchheim, Germany) to select the tube voltage based on the patients' size and attenuation characteristics estimated from their topograms, or scout view (CT projection radiograph) acquired from an anteroposterior scan direction.

In image acquisition, manual adaptation and automatic modulation of tube current were applied. A few studies manually adapted the tube current to patients' BMI ($n = 5$) and CC ($n = 1$). Whereas for the rest of the studies ($n = 14$), ATCM software developed by four CT scanner manufacturers (Smart mA and Auto mA, GE Healthcare, Milwaukee, WI; DoseRight, Philips Healthcare, Cleveland, OH; CareDose 4D, Siemens

Table 1. Baseline characteristics of studies that compared between 80 and 120 kVp protocols

Study characteristics		80 kVp group	BMI (kg m ⁻²)	Techniques			Mean H _E (mSv)		Decrease in H _E (%)	Vessel contrast enhancement	Image quality		
Author/ year of publication	Total no. of patient			Patient selection	Image acquisition	Image reconstruction	80 kVp	120 kVp			Noise	SNR	Qualitative image quality
Nakaura et al 2013 ¹⁸	68	35	NR	NIL	ATCM (Ref. image)	iDose4 ^a	1.40	5.40	74	=	=	NR	=
Zheng et al 2014 ⁴¹	100	25	20.90	BMI < 25	ATCM (300 mAs ref.)	SAFIRE ^a	0.41	2.37	83	NR	=	NR	=
Oda et al 2015 ³³	60	30	22.20	NIL	ATCM (SD of noise)	AIDR 3D ^b	1.50	2.40	38	↑	=	NR	↑
Zhang et al 2015 ³⁸	101	31	21.89	BMI < 23	ATCM (Noise index, 100–700 mA)	ASIR ^a	1.51	4.92	69	↑	↑	=	=
Zhang et al 2015 ⁴⁰	90	30	22.10	NIL	ATCM (400 mAs ref.)	FBP ^a	2.75	9.29	70	↑	↑	=	=
Durmus et al 2016 ³⁸	302	56	22.80	ATVS	ATCM (398 mAs ref.)	FBP ^a	0.31	1.53	80	NR	↑	NR	=
Iyama et al 2016 ¹⁷	60	30	NR	NIL	ATCM (Ref. image)	IMR ^a	1.40	5.40	74	↑	=	NR	↑
Mangold et al 2016 ³¹	153	39	26.60	ATVS	ATCM (mAs ref.)	ADMIRE ^b	2.40	10.7	78	↑	↑	=	=
Wu et al 2016 ¹⁹	154	75	23.70	NIL	ATCM (285 mAs ref.)	SAFIRE ^a	0.88	2.39	63	=	=	=	=

ADMIRE, Advanced Modelled Iterative Reconstruction; AIDR 3D, Adaptive Iterative Dose Reduction 3D; ASIR, Adaptive Statistical Iterative Reconstruction; ATCM, automatic tube current modulation; ATVS, automated tube voltage selection; BMI, body mass index; CNR, contrast-to-noise ratio; H_E, effective dose; IMR, Iterative Model Reconstruction; NIL, non-existent; NR, not reported; SAFIRE, Sinogram-Affirmed Iterative Reconstruction; SNR, signal-to-noise ratio.

^a↓, lower with low tube voltage protocol; ↑, improved with low tube voltage protocol; =, similar with low tube voltage protocol.

^bfiltered back projection (FBP) reconstruction at 120 kVp.
^citerative reconstruction (IR) at 120 kVp.

Table 2. Baseline characteristics of the studies compared between 100 and 120 kVp protocols

Study characteristics			100 kVp group		Techniques			Mean H _E (mSv)				Vessel contrast enhancement	Image quality			
Author /year of publication	Total no. of patient	No. of patient	BMI (kg m ⁻²)	Patient selection	Image acquisition	Image reconstruction	100 kVp	120 kVp	Decrease in H _E (%)			Noise	SNR	CNR	Qualitative image quality	
Alkadhi et al 2008 ²⁷	68	40	22.80	BMI ≤ 25	ATCM (190 mAs ref.)	FBP ^a	1.11	2.38	53		NR	NR	NR	NR	=	
Gagarina et al 2011 ¹⁶	70	70	25.80	NIL	BMI adapted-tube current	FBP ^a	0.81	4.06	80		=	=	=	=	=	
Zhang et al 2011 ³⁹	107	40	22.26	BMI < 25	BMI adapted-tube current	FBP ^a	1.75	3.79	54		=	=	NR	=	=	
Khan et al 2013 ²⁹	78	33	23.00	BMI < 27	BMI adapted-tube current	FBP ^a	3.71	5.31	30		=	=	=	=	=	
Nakaura et al 2013 ³²	100	50	NR	NIL	ATCM (Reference image)	FBP ^a	2.80	5.20	46		↑	↑	NR	=	↓	
Zheng et al 2014 ⁴¹	100	25	25.44	NIL	ATCM (300 mAs ref.)	SAFIRE ^a	1.14	2.37	52		=	=	NR	NR	=	
Lu et al 2015 ³⁰	185	53	23.10	CC ≤ 90 cm	CC-adapted tube current	FBP ^a	2.36	3.82	38		↑	=	↑	↑	=	
Shen et al 2015 ³⁵	100	50	24.40	NIL	ATCM (350 mAs ref.)	SAFIRE ^a	3.62	5.55	35		=	=	=	=	=	
Sun et al 2015 ³⁶	179	92	28.00	NIL	BMI adapted-tube current	AIDR 3D ^a	1.59	2.90	45		↓	↑	=	=	=	
Yin et al 2015 ³⁷	231	115	24.90	NIL	ATCM (mAs ref.)	SAFIRE ^a	2.30	3.50	34		=	=	=	=	=	
Zhang et al 2015 ³⁸	101	34	25.24	23 < BMI < 28	ATCM (Noise index, 150–660 mA)	ASIR ^a	2.59	4.92	48		↑	↑	=	=	=	
Zhang et al 2015 ⁴⁰	90	30	21.10	ATVS	ATCM (400 mAs ref.)	FBP ^a	6.29	9.29	32		↑	↑	=	=	=	
Cesare et al 2016 ¹⁵	200	100	26.65	NIL	ATCM (33 HU SD of noise, 50–550 mA)	AIDR 3D ^b	2.80	2.89	3		↑	=	↑	↑	↑	
Durmus et al 2016 ²⁸	302	125	25.90	ATVS	ATCM (228 mAs ref.)	FBP ^a	0.69	1.53	55		NR	↑	NR	=	=	
Mangold et al 2016 ³¹	153	40	29.90	ATVS	ATCM (mAs ref.)	ADMIRE ^b	5.90	10.7	45		↑	=	=	=	=	

(Continued)

Table 2. (Continued)

Study characteristics		100 kVp group		Techniques			Mean H _E (mSv)				Image quality			
Author /year of publication	Total no. of patient	No. of patient	BMI (kg m ⁻²)	Patient selection	Image acquisition	Image reconstruction	100 kVp	120 kVp	Vessel contrast enhancement		Noise	SNR	CNR	Qualitative image quality
Pan et al 2016 ³⁴	48	24	33.80	NIL	BMI adapted-tube current	AIDR 3D ^d	1.61	3.64	=	56	=	=	=	=

ADMIRE, Advanced Modelled Iterative Reconstruction; AIDR 3D, Adaptive Iterative Dose Reduction 3D; ASIR, Adaptive Statistical Iterative Reconstruction; ATCM, automatic tube current modulation; ATVS, automated tube voltage selection; BMI, body mass index; CC, chest circumference; CNR, contrast-to-noise ratio; H_E, effective dose; HU, Hounsfield unit; NIL, non-existent; NR, not reported; SAFIRE, Sinogram-Affirmed Iterative Reconstruction; SD, standard deviation; SNR, signal-to-noise ratio.

↓, lower with low tube voltage protocol; ↑, improved with low tube voltage protocol; =, similar with low tube voltage protocol.

^afiltered back projection (FBP) reconstruction at 120 kVp.

^biterative reconstruction (IR) at 120 kVp.

Healthcare, Forchheim, Germany; SureExposure 3D, Toshiba Medical Systems Corporation, Otawara, Japan) were used. The ATCM software tools were categorised into four groups based on their operation methods: noise index based, reference image based, reference effective tube current-time product based, and standard deviation (SD) based.

In terms of image reconstruction, majority of the studies applied IR techniques (12 out of 19 studies). Two types of IR algorithms were used; the statistical or hybrid IR and the knowledge-based iterative model IR. In general, statistical or hybrid IR involves a combination of filtered back projection (FBP) (analytical method) and IR algorithms (statistical method) in the image reconstruction process. Knowledge-based model IR is the latest technology using a full IR algorithm in the image reconstruction process.

Different statistical or hybrid IR algorithms were used namely the Advanced Modelled Iterative Reconstruction (ADMIRE, Siemens Healthcare, $n = 1$), Adaptive Iterative Dose Reduction (AIDR 3D, Toshiba Medical Systems Corporation, $n = 4$), Adaptive Statistical Iterative Reconstruction (ASIR, GE Healthcare, $n = 1$), iDose4 (iDose4, Philips Healthcare, $n = 1$) and Sinogram-Affirmed Iterative Reconstruction (SAFIRE, Siemens Healthcare, $n = 4$). Only one study applied knowledge-based model IR [Iterative Model Reconstruction (IMR), Philips Healthcare] at 80 kVp.

The H_E values from IR were compared to FBP at 80, 100 and 120 kVp. At 80 kVp, the median H_E was 1.40 mSv (0.41 to 2.40 mSv) for IR and 1.53 mSv (0.31 to 2.75 mSv) for FBP. At 100 kVp, the median H_E was 2.45 mSv (1.14 to 5.90 mSv) for IR and 2.06 mSv (0.69 to 6.29 mSv) for FBP. At 120 kVp, the median H_E was 2.89 mSv (2.40 to 10.7 mSv) for IR and 3.82 mSv (1.53 to 9.29 mSv) for FBP.

CM reduction and vessel contrast enhancement

Improved or similar vessel contrast enhancement was observed in all studies when low tube voltage was used, except in one study that reported lower vessel contrast enhancement at 100 kVp compared to 120 kVp (Tables 1 and 2). Table 4 shows the CM injection parameters used in the studies.

Three injection patterns were applied: uniphasic ($n = 3$), biphasic ($n = 16$) and triphasic ($n = 1$). Uniphasic injection involved the administration of a single bolus of undiluted CM. Biphasic injection utilises two boluses; an initial undiluted contrast bolus followed by a diluted contrast bolus or a saline flush. Whereas for triphasic injection, three distinct boluses were used; an initial undiluted contrast bolus followed by a CM and saline mixture, and then completed by a saline flush. Compared to 120 kVp, CM reduction was applied in seven studies at 80 kVp^{17–19,31,33,38,41} and eight studies at 100 kVp.^{27,34–39,41} However, only two studies at 80 kVp,^{18,19} and five studies at 100 kVp^{34,35,37,39,41} reported similar vessel contrast enhancement compared to those at 120 kVp.

In the two studies at 80 kVp, two different methods were used to determine the CM volume for the first bolus; (i) a calculation

Table 3. Techniques used to achieve dose reduction and maintain image quality

Stages of CCTA examination	Techniques	Definition	Application examples	
Patient selection	(1) BMI = weight (kg) / height ² (m ²)	Selection of patient for low tube voltage protocol based on their BMI.	BMI ≤ 25 for 100 kVp.	Alkadhhi et al 2008 ²⁷
			30 ≥ BMI > 25 for 120 kVp.	
			BMI < 25 for 100 kVp.	
			BMI ≥ 25 for 120 kVp	Zhang et al 2011 ³⁹
			BMI < 27 for 120 kVp.	
			BMI ≥ 27 for 100 and 120 kVp.	
			BMI < 25 for 80 kVp.	Khan et al 2013 ²⁹
			BMI ≥ 25 for 100 and 120 kVp.	
			BMI < 23 for 80 kVp.	
			23 < BMI < 28 for 100 kVp.	Zheng et al 2014 ⁴¹
Image acquisition	(2) Measurement of nipple-level CC using a measuring tape. (3) ATVS algorithm	Selection of patient for low tube voltage protocol based on their CC. Automatically select tube voltage based on patients' size and attenuation characteristics estimated from topogram.	BMI ≥ 28 for 120 kVp.	Zhang et al 2015 ³⁸
			CC < 90 cm for 100 kVp.	Lu et al 2015 ³⁰
			CC ≥ 90 cm for 120 kVp.	
			Care kV (Siemens Healthcare)	Zhang et al 2015 ⁴⁰
				Durmus et al 2016 ²⁸
				Mangold et al 2016 ³¹
Image acquisition	(1) Manual tube current adaptation to: (a) BMI (b) CC	Manually set the tube current based on patients' BMI. Manually set the tube current based on patients' CC.	At 100 kVp, 200 mA for BMI = 21; 570 mA for BMI = 30.	Gagarina et al 2011 ¹⁶
			At 120 kVp, 400 mA for BMI = 21; 500 mA for BMI = 30.	
			At 100 kVp, 400–450 mA for BMI < 21; 450–500 mA for 22 ≤ BMI < 25.	Zhang et al 2011 ³⁹
			NR	Khan et al 2013 ²⁹
			Tube current was adjusted with a range of 330–480 mA	Sun et al 2015 ³⁶
			Tube current was adjusted with a range of 330–400 mA	Pan et al 2016 ³⁴
			At 100 kVp, 200 mAs for CC ≤ 85 cm; 250 mAs for 85 cm < CC < 90 cm.	Lu et al 2015 ³⁰
			At 120 kVp, 200 mAs for 90 cm ≤ CC ≤ 95 cm; 250 mAs for CC > 95 cm.	

(Continued)

Table 3. (Continued)

Stages of CCTA examination	Techniques	Definition	Application examples
Image acquisition	(2) ATCM based on:		
	(a) Noise index	Automatically modulate the tube current to a target noise index to achieve constant image noise regardless of attenuation level.	Smart mA and Auto mA (GE Healthcare). Zhang et al 2015 ³⁸
	(b) Reference image	Automatically modulate the tube current based on reference image, regardless of attenuation level. It aims to keep the same image quality as in the reference image.	DoseRight (Philips Healthcare, Cleveland). Nakaura et al 2013 ¹⁸ Nakaura et al 2013 ³² Iyama et al 2016 ¹⁷
	(c) Reference effective tube current-time product	Automatically modulate the tube current with reference to a target tube current level for a standard-sized patient to achieve constant image quality.	CareDose4D (Siemens Healthcare). Alkadhi et al 2008 ²⁷ Zhang et al 2014 ⁴¹ Shen et al 2015 ³⁵ Yin et al 2015 ³⁷
			Zhang et al 2015 ⁴⁰
			Durmus et al 2016 ²⁸
			Mangold et al 2016 ³¹
			Wu et al 2016 ¹⁹
	(d) SD (noise)	Automatically modulate the tube current to a target SD of noise to achieve constant image noise regardless of attenuation level.	Oda et al 2015 ³³ Cesare et al 2016 ¹⁵

(Continued)

Table 3. (Continued)

Stages of CCTA examination	Techniques	Definition	Application examples	
Image reconstruction	(1) Statistical/Hybrid IR	A combination of FBP and IR, not fully iterative.	ADMIRE (Siemens Healthcare)	Mangold et al 2016 ³¹
			AIDR 3D (Toshiba Medical Systems Corporation)	Oda et al 2015 ³³
				Sun et al 2015 ³⁶
				Cesare et al 2016 ¹⁵
				Pan et al 2016 ³⁴
	(2) Knowledge-based model IR	Involving full IR algorithms with both forward and backward projection steps.	ASIR (GE Healthcare)	Zhang et al 2015 ³⁸
			iDose4 (Philips Healthcare)	Nakaura et al 2013 ¹⁸
			SAFIRE (Siemens Healthcare)	Zheng et al 2014 ⁴¹
				Shan et al 2015 ³⁵
				Yin et al 2015 ³⁷
				Wu et al 2016 ¹⁹
			IMR (Philips Healthcare)	Iyama et al 2016 ¹⁷

ADMIRE, Advanced Modelled Iterative Reconstruction; AIDR 3D, Adaptive Iterative Dose Reduction 3D; ASIR, Adaptive Statistical Iterative Reconstruction; ATCM, automatic tube current modulation; ATVS, automated tube voltage selection; BMI, body mass index; CC, chest circumference; CCTA, coronary CT angiography; FBP, filtered back projection; IMR, Iterative Model Reconstruction; IR, iterative reconstruction; NR, not reported; SAFIRE, Sinogram-Affirmed Iterative Reconstruction; SD, standard deviation.

Table 4. CM injection parameters

Author/ year of publication	Tube voltage (kVp)	Injection pattern	Method for CM volume calculation		CM concentration (mg ml ⁻¹)	FR (mls ⁻¹)	ID (s)	IDR (gs ⁻¹)	TID (g)	CM reduction compared to 120 kVp	Saline flush (ml)	Vessel contrast enhancement
			First bolus	Second bolus								
Alkadhi et al 2008 ²⁷	100	Biphasic	0.8 ml kg ⁻¹	CM volume same as first bolus; CM : saline = 1 : 5	320	4.4	CM volume/ FR	NR	NR	Yes	NIL	NR
Gagarina et al 2011 ¹⁶	100	Biphasic	50 ml or 60 ml for body weight > 90 kg	NIL	320 or 350	5.0	10.0–12.0	1.60–1.75	16.0–21.0	No	20	=
Zhang et al 2011 ³⁹	100	Triphasic	BMI < 22, 45 ml; 22 ≤ BMI < 25, 50 ml	20 ml; CM : saline = 3 : 7	370	4.0–4.5	14.0	1.48–1.66 → 0.44– 0.50	18.9–20.7	Yes	30	=
Khan et al 2013 ²⁹	100	Biphasic	70 ml	NIL	350	5.0	14.0	1.75	24.5	No	40	=
Nakaura et al 2013 ¹⁸	80	Uniphasic	0.5 ml kg ⁻¹	NIL	370	CM volume/ ID	7.5	1.45	10.9	Yes	NIL	=
Nakaura et al 2013 ³²	100	Uniphasic	1.0 ml kg ⁻¹	NIL	370	CM volume/ ID	15.0	1.51	22.6	No	NIL	↑
Zheng et al 2014 ⁴¹	80	Biphasic	1.0 ml kg ⁻¹	NIL	270	5.0	CM volume/ FR	1.35	15.5	Yes	40	NR
	100	Biphasic	1.0 ml kg ⁻¹	NIL	270	5.0	CM volume/ FR	1.35	19.6	Yes	40	=
Lu et al 2015 ³⁰	100	Biphasic	80 ml	NIL	370	5.0	16.0	1.85	29.6	No	30	↑
Oda et al 2015 ³³	80	Biphasic	0.6 ml kg ⁻¹	NIL	370	CM volume/ ID	10.0	1.12	11.2	Yes	40 ml, 4 ml s ⁻¹	↑
Shen et al 2015 ³⁵	100	Biphasic	1.0 ml kg ⁻¹	NIL	270	5.0	CM volume/ FR	1.08	20.4	Yes	40	=
Sun et al 2015 ³⁶	100	Biphasic	0.9 ml kg ⁻¹	NIL	270	5.0	CM volume/ FR	1.35	17.4	Yes	40	↓
Yin et al 2015 ³⁷	100	Biphasic	ST × FR	30 ml; CM : saline = 3 : 7	270	5.0	CM volume/ FR	1.35 → 0.41	20.7	Yes	NIL	=
Zhang et al 2015 ³⁸	80	Biphasic	1.0 ml kg ⁻¹	NIL	300	4.0	CM volume/ FR	1.20	18.6	Yes	NIL	↑
	100	Biphasic	1.0 ml kg ⁻¹	NIL	300	4.0	CM volume/ FR	1.20	21.0	Yes	46–55	↑
Zhang et al 2015 ⁴⁰	80	Biphasic	50–70 ml	NIL	370	5.0	10.0–14.0	1.85	18.5–25.9	No	30–40	↑

(Continued)

Table 4. (Continued)

Author/ year of publication	Tube voltage (kVp)	Injection pattern	Method for CM volume calculation		CM concentration (mg ml ⁻¹)	FR (mls ⁻¹)	ID (s)	IDR (gs ⁻¹)	TID (g)	CM reduction compared to 120 kVp	Saline flush (ml)	Vessel contrast enhancement
			First bolus	Second bolus								
	100	Biphasic	50–70 ml	NIL	370	5.0	10.0–14.0	1.85	18.5–25.9	No	30–40	↑
Cesare et al 2016 ¹⁵	100	Biphasic	60 ml	NIL	320	6.0	10.0	1.92	19.2	No	40	↑
Durmus et al 2016 ²⁸	80	Biphasic	0.6 ml kg ⁻¹	NIL	370	CM volume/ ID	10.0	1.73	17.3	No	Same as first bolus	NR
	100	Biphasic	0.6 ml kg ⁻¹	NIL	370	CM volume/ ID	10.0	1.73	17.3	No	Same as first bolus	NR
Iyama et al 2016 ¹⁷	80	Uniphasic	0.6 ml kg ⁻¹	NIL	370	CM volume/ ID	12.0	1.07	12.0	Yes	NIL	↑
Mangold et al 2016 ³¹	80	Biphasic	60 ml	NIL	350	4.5	13.3	1.58	21.0	Yes	50 ml	↑
	100	Biphasic	80 ml	NIL	350	4.5	17.8	1.58	28.0	No	50 ml	↑
Pan et al 2016 ³⁴	100	Biphasic	0.8 ml kg ⁻¹	NIL	270	CM volume/ ID	12.0	1.70	20.9	Yes	30 ml	=
Wu et al 2016 ¹⁹	80	Biphasic	60 ml	NIL	270	5.0	12.0	1.35	16.2	Yes	40 ml	=

BMI, body mass index; CM, contrast medium; FR, flow rate; ID, injection duration; IDR, iodine delivery rate; NIL, non-existent; NR, not reported; ST, scanning time; TID, total iodine dose.
 ↓, lower with low tube voltage tube voltage protocol; ↑, improved with low tube voltage protocol; =, similar with low tube voltage protocol.

Figure 2. Suggested appropriate scanning techniques.

	Patient selection	Image acquisition	Image reconstruction
80 kVp	- BMI < 25 kgm⁻² - ATVS	ATCM based on default reference or targeted value for 80 kVp	- FBP - Hybrid IR - Knowledge-based model IR
100 kVp	- BMI < 30 kgm⁻² - CC < 90 cm - ATVS	25 kgm⁻² ≤ BMI < 30 kgm⁻², 500 - 570 mA - CC ≤ 85 cm, 200 mAs; 85 cm < CC < 90cm, 250 mAs - ATCM based on default reference or targeted value for 100 kVp	- FBP - Hybrid IR

ATCM, automatic tube current modulation; ATVS, automated tube voltage selection; BMI, body mass index; CC, chest circumference; FBP, filtered back projection; IR, iterative reconstruction.

based on body weight at 0.5 ml kg⁻¹ [CM concentration 370 mg ml⁻¹ and fixed injection duration (ID) 7.5 s] and (ii) a fixed volume of 60 ml [CM concentration 270 mg ml⁻¹, flow rate (FR) 5.0 mls⁻¹ and ID 12.0 s]. In the five studies at 100 kVp, three different methods were used to determine the CM volume for first bolus; a calculation based on (i) body weight of 0.8 ml kg⁻¹ ($n = 1$) and 1.0 ml kg⁻¹ ($n = 2$), (ii) BMI (BMI < 22 kg m⁻², 45 ml; 22 kg m⁻² ≤ BMI < 25 kgm⁻², 50 ml) ($n = 1$) and (iii) the product of scanning time and FR ($n = 1$). CM concentrations of 270 and 370 mg ml⁻¹ were used in these studies with the FR ranging from 4.0 to 5.0 ml s⁻¹ and ID ranging from 12.0 to 14.0 s. These resulted in IDR of 1.35 to 1.45 g s⁻¹ with TID of 10.9 to 16.2 g at 80 kVp and IDR of 1.08 to 1.70 g s⁻¹ with TID of 18.9 to 20.9 g at 100 kVp.

Suggestions of appropriate scanning techniques and CM administration methods

To propose appropriate scanning techniques in prospectively ECG-triggered low tube voltage CCTA protocol, data from all selected studies were integrated, together with consideration of guidelines set by the Society of Cardiovascular Computed Tomography (SCCT)⁴² (Figure 2).

For patient with BMI < 25 kg m⁻², the suggested tube voltage is 80 kVp. This was determined based on the highest BMI cut-off point used in the selected studies. The application of ATVS was another method for selecting patients. ATCM software based on default reference or targeted value for CCTA protocol at 80 kVp is suggested for image acquisition.

On the other hand, 100 kVp is suggested for patients with BMI < 30 kg m⁻². It was determined by comparing the highest BMI

cut-off point used in the selected studies and the SCCT guideline. Besides, CC cut-off point of less than 90 cm is an alternative reference for manual patient selection. ATVS can also be used for automatic selection of patient for 100 kVp. During image acquisition, ATCM based on default reference or targeted value for CCTA protocol at 100 kVp is suggested. Alternatively, tube current can be adapted to BMI or CC measurements.

For image reconstruction, currently available FBP and statistical or hybrid IR can be used in both 80 and 100 kVp. In addition, knowledge-based model IR is suggested to be used at 80 kVp to improve the image quality.

Suggested methods of CM administration for prospectively ECG-triggered low tube voltage CCTA protocol are shown in Figure 3. To achieve a similar vessel contrast enhancement as in 120 kVp, reference IDR of 1.35 to 1.45 g s⁻¹ and TID of 10.9 to 16.2 g are recommended for 80 kVp, whereas the reference IDR of 1.08 to 1.70 g s⁻¹ and TID of 18.9 to 20.9 g are recommended for 100kVp.

DISCUSSION

To our knowledge, this is the first systematic review of prospectively ECG-triggered low tube voltage CCTA protocol to evaluate the reported dose reductions and preservation of image quality. This systematic review found that low tube voltage protocol could substantially reduce radiation dose and produce good imaging in prospectively ECG-triggered CCTA.

Increased image noise at low tube voltage settings was observed in several studies selected in this survey. Nevertheless, the increase of vessel contrast enhancement at low tube voltage due

Figure 3. Suggested contrast medium (CM) reduction methods.

BMI, body mass index; FR, flow rate; ID, injection duration; IDR, iodine delivery rate; ST, scanning time; TID, total iodine dose.

to an increase of photoelectric effect compensated the SNR and CNR.³² Therefore, in almost all the selected studies, dose reduction was possible without the loss of quantitative and qualitative image quality.

Different quantities for radiation dose, including volume CT dose index ($CTDI_{vol}$), size-specific dose estimates, P_{KL} and H_E , were reported in the selected studies. In this review, the H_E was used as the comparative benchmark since most of the studies reported it, together with or without P_{KL} .

Different P_{KL} -to- H_E conversion coefficients (0.014, 0.017 and 0.028 $mSv.mGy^{-1}.cm^{-1}$) for chest region were used in the selected studies. The conversion coefficient of 0.017 $mSv.mGy^{-1}.cm^{-1}$ was recommended by the European Commission in 2000, which was later replaced by 0.014 $mSv.mGy^{-1}.cm^{-1}$, as recommended by the European Commission in 2004 and Public Health England (formerly National Radiological Protection Board) in 2005.⁴³⁻⁴⁵ It had been reported that these conversion coefficients might underestimate the overall radiation exposure from CCTA imaging.⁴⁶⁻⁴⁸ Subsequently, Gosling et al and Sabarudin et al had suggested that a conversion coefficient of 0.028 $mSv.mGy^{-1}.cm^{-1}$ would give a better estimation of the H_E in cardiac-specific imaging.^{46,47} However, there were no guidelines on the appropriate P_{KL} -to- H_E conversion coefficient for CCTA to date. Therefore, the most commonly used conversion coefficient of 0.014 $mSv.mGy^{-1}.cm^{-1}$ was used in this review.

The scanning techniques in the studies were presented in three stages to provide a clear picture of performing a low-dose CCTA examination; from patient selection to image acquisition and image reconstruction. For manual patient selection based on BMI measurement, inconsistency was observed with regard to the BMI cut-off points of 80, 100 and 120 kVp, although a guideline was established by SCCT in 2014. According to the guideline, 80 kVp was recommended for performing CCTA in patients with BMI < 18 $kg.m^{-2}$; 100 kVp for patients with BMI < 30 $kg.m^{-2}$; and between 120 and 140 kVp for those classified as obese.⁴² However, rapid development and emerging capabilities of CT scan technology might cause inconsistencies in the voltage parameters. The newer machines used in recent studies

would allow for scanning of higher BMI patients at lower CT tube voltage. For instance, Pan et al reported a similar quantitative and qualitative image quality in obese patients with BMI > 30 $kg.m^{-2}$ at 100 kVp.³⁴ Hence, the guideline might need to be reviewed to eliminate inconsistencies among studies which made it difficult to draw conclusions in most of the cases.

Ghoshhajra et al reported a significant correlation between BMI and CC. The author suggested CC as a better parameter because BMI might not provide an exact estimation of body mass at heart level.⁴⁹ Although only one selected study applied CC as the reference parameter for manual patient selection and tube current adaptation, the reported result was promising at 100 kVp with 38% reduction in H_E , improvement in quantitative image quality and similar qualitative image quality.³⁰ Other parameters which were not included in this review, including the measurement of chest dimensions,⁵⁰ chest tissue composition,⁵¹ scout image attenuation⁵² and unenhanced attenuation⁵³ have also been proposed for manual tube voltage selection. However, those measurements were more complex and prone to errors.²⁸

Compared with manual selection techniques, ATVS is a fully-automated algorithm that utilises CNR as the image quality index to adjust the CT tube voltage based on patients' size and attenuation characteristics estimated from topograms.⁵⁴ Patient-specific tube current curves are generated for all tube voltage levels to achieve the desired CNR with the selected scan range on the patients' topogram. These patient-specific tube current curves are then used to calculate the estimated radiation dose for all tube voltage levels to determine the optimal dose efficiency. Subsequently, the software suggests the best tube voltage setting by taking into account the optimal dose efficiency and limitation of the scanner, such as the maximum tube current and heat capacity.⁵⁴ This systematic review found that a similar image quality at reduced radiation dose level could be achieved in prospectively ECG-triggered low tube voltage CCTA protocol by combining the application of ATVS (Care kV, Siemens Healthcare) and ATCM (CareDose 4D, Siemens Healthcare). In addition, these algorithms had provided a fast and easy way for selecting appropriate scanning parameters in CCTA examination.

ATCM software packages were installed in all CT scanners by manufacturers to reduce the radiation exposure to patients. However, with no set standards, each manufacturer had created their own ways of tube current modulation based on different image quality references. Additionally, as reported in this systematic review, even for the same ATCM software, different references, or targeted values were used in the CCTA protocol. For example, in studies using the CareDose 4D system (Siemens Healthcare), the reference effective tube current-time product of 285, 398 and 400 mAs were used at 80 kVp, whereas 190, 228, 300, 350 and 400 mAs were used at 100 kVp. The reference or targeted values could directly affect the image quality and radiation dose on patients. Therefore, a consensus regarding the default reference or targeted value for CCTA protocol at different tube voltage would be required to reduce the variation in scanning techniques.

In term of image reconstruction, most of the selected studies had investigated the performance of statistical or hybrid IR, while only one study investigated knowledge-based model IR at 80 kVp. IR techniques were used in early CT machines in the 1970s. However, due to its high computational demand and long reconstruction time, the faster and robust FBP method had been widely used in CT scans. Despite its acceptable performance, CT studies using FBP were heavily affected by image noise, especially when radiation dose was reduced.⁵⁴ With recent improvements in computer processing, using IR as a noise-suppressing technique had become more feasible in clinical setting. For the past 10 years, IR technologies had evolved from image-based denoising procedures to statistical or hybrid IR, before becoming model based IR and to the latest knowledge-based model IR.^{55–58} Knowledge-based model IR was expected to decrease the radiation dose even further. A selected study had observed improvement in quantitative image quality at 80 kVp, where there was a 78% dose reduction compared to 120 kVp. Future research should be conducted to investigate the potential of knowledge-based model IR algorithm.

Several prior systematic reviews had been conducted to assess the reduction of H_E with IR in CCTA.^{55–58} These previous reviews mainly focused on the comparison of H_E between IR and FBP in CCTA. In this present review, we have further reported the median H_E for IR and FBP at different tube voltages. The median H_E was found to be lower in studies which applied IR at 80 and 120 kVp. However, a conflicting result

was observed at 100 kVp, possibly due to the small number of studies.

Nevertheless, it is always feasible to reduce the radiation dose at the expenses of image quality. The effects on SNR can be masked by the use of IR techniques. There is a great heterogeneity in image reconstruction algorithms used in the included studies. Besides, the focus of these studies is on image quality, rather than diagnostic accuracy. Therefore, findings in this reported review need to be interpreted with caution.

Limitations

This review has several limitations. First, we excluded many articles due to strict selection criteria. By only including studies comparing prospectively ECG-triggered CCTA protocol at low tube voltages to 120 kVp, it was possible to assess the achievable dose reduction and image quality. Second, although this review suggested appropriate scanning techniques and CM administration methods, nonetheless, these are based on previous findings. Hence, a continuous effort in updating these suggestions is needed to keep pace with the development of CT technology and clinical research findings.

CONCLUSION

This systematic review provides an overview of currently available scanning techniques used in prospectively ECG-triggered low tube voltage CCTA protocol. This review found that radiation doses could be reduced between 38 to 83% at 80 kVp, and 3 to 80% at 100 kVp without compromising the image quality.

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