

Prognostic Performance of Prospective versus Retrospective Electrocardiographic Gating

in Coronary Computed Tomographic Angiography

Pradnya Velankar, MD
Kongkiat Chaikriangkrai,
MD
Ninad Dewal, PhD
Sayf Khaleel Bala, MD
Belqis Elferjani, MD
Sama Alchalabi, MD
Su Min Chang, MD

Key words: Cardiac-gated imaging techniques; coronary angiography/methods/standards; coronary artery disease/diagnostic imaging; coronary vessels/pathology; image processing, computer-assisted; models, cardiovascular; predictive value of tests; radiation dosage; retrospective studies; tomography, x-ray computed/methods

From: Department of Internal Medicine (Drs. Chaikriangkrai and Velankar), Houston Methodist Hospital; Human Genome Sequencing Center (Dr. Dewal), Baylor College of Medicine; and Division of Cardiovascular Imaging, Department of Cardiology (Drs. Alchalabi, Bala, Chang, and Elferjani), The Methodist DeBakey Heart and Vascular Center; Houston, Texas 77030

Address for reprints:
Su Min Chang, MD,
6550 Fannin St., Suite 1901,
Houston, TX 77030

E-mail: SMChang@
houstonmethodist.org

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Coronary computed tomographic angiography (CCTA) with prospective electrocardiographic gating reduces radiation exposure, but its prognostic power for predicting cardiovascular risk in patients with suspected CAD has not been fully validated. To determine whether prospective gating performs as well as retrospective gating in this population, we compared these scan modes in patients undergoing 64-slice CCTA.

From January 2009 through September 2011, 1,407 patients underwent CCTA; of these, 915 (mean age, 57.8 ± 13.5 yr; 54% male) had suspected coronary artery disease at the time of CCTA and were included in the study. Prospective gating was used in 195 (21%) and retrospective gating in 720 (79%). The mean follow-up duration was 2.4 ± 0.9 years.

Overall, 390 patients (42.6%) had normal results on CCTA, 382 (41.7%) had nonobstructive coronary artery disease, and 143 (15.6%) had obstructive disease. Major adverse cardiac events occurred in 32 patients (3.5%): 11 cardiac deaths, 15 late revascularizations, and 6 nonfatal myocardial infarctions. Total event occurrences were similar in both groups (retrospective, 3.8%; prospective, 2.6%; $P=0.42$), as were the occurrences of each type of event. On adjusted multivariate analysis, nonobstructive ($P=0.015$) and obstructive ($P<0.001$) coronary artery disease were independently associated with major adverse cardiac events. Scan mode was not a predictor of outcome. The mean effective radiation dose was 4 ± 2 mSv for prospective compared with 12 ± 4 mSv for retrospective gating ($P<0.01$).

The prognostic value of CCTA with prospective electrocardiographic gating compares favorably with that of retrospective gating, and it involves significantly less radiation exposure. (*Tex Heart Inst J* 2018;45(4):214-20)

Coronary angiography is the gold standard for diagnosing coronary artery disease (CAD); however, it is invasive and can cause complications. In recent years, coronary computed tomographic angiography (CCTA) with multi-detector computed tomography (MDCT) has gained acceptance as a noninvasive option for evaluating low- to intermediate-risk patients in whom CAD is suspected.

The primary computed tomographic (CT) scanning technique has been helical CT with retrospective electrocardiographic (ECG) gating (RG); it produces superb images, enabling diagnostic accuracy and prognostic power.¹⁻³ However, RG exposes patients to radiation continuously throughout the cardiac cycle, so various techniques have been used to reduce exposure.^{4,5} One of the most valuable is axial CT with prospective ECG gating (PG), which substantially reduces radiation exposure.⁶ It works on a step-and-shoot basis, meaning that image data are acquired only during the mid-to-late diastolic phase of the cardiac cycle.

Several investigators⁶⁻¹⁰ have shown that the image quality and diagnostic accuracy of low-dose CCTA with PG are comparable to those of CCTA with RG, but the prognostic value of PG has not been established. We therefore compared the 2 scan modes in patients with suspected CAD.

Patients and Methods

This retrospective, observational cohort study received institutional review board (IRB) approval. The IRB did not require informed consent, because the study posed minimal risk to patients. We used relevant data obtained during routine clinical care and from follow-up telephone calls.

We queried our database and found 1,407 patients who had presented with chest pain and undergone CCTA at our institution from January 2009 through September 2011. We then excluded 324 who had atrial fibrillation, aortic stenosis necessitating transcatheter aortic valve replacement, an established diagnosis of CAD documented by coronary angiography, or a history of percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) (Fig. 1). An additional 168 patients were excluded because of inadequate clinical follow-up; none of these patients were documented as deceased in the Social Security Death Index.

The final cohort comprised 915 patients with complete clinical follow-up as of 31 March 2013. They were divided into 2 groups based on scanning method: 720 patients (79%) had undergone CCTA with RG, and 195 (21%) with PG (Table I).

The indications for CCTA were chest pain suspicious for CAD, an abnormal or equivocal stress test, or both. No predefined guidelines or criteria had been used to select patients for PG. Board-certified readers with level III training determined the scan mode. In general, patients were considered for PG only if their heart rates were steady and slower than 65 beats/min. No investigator in this study was involved in the clinical management of enrolled patients beyond interpreting their images and making follow-up telephone inquiries.

Patients' baseline characteristics, cardiac symptoms, and medications were retrieved during chart review. Follow-up information was obtained through chart

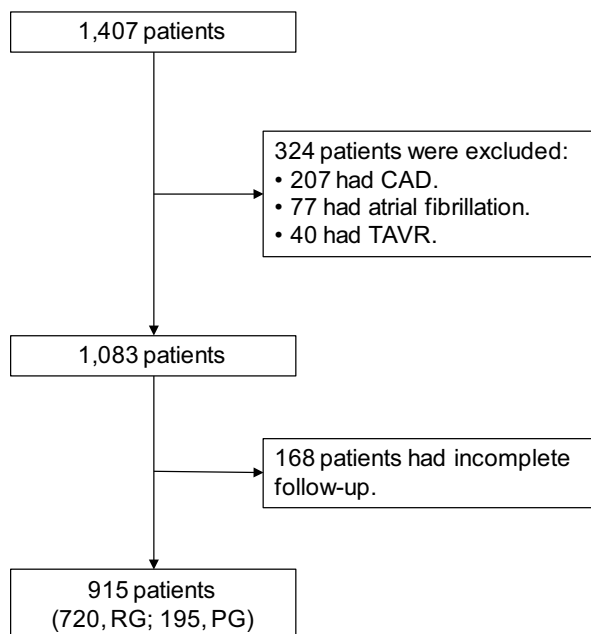


Fig. 1 Flow chart shows patient selection.

CAD = coronary artery disease; PG = prospective electrocardiographic gating; RG = retrospective electrocardiographic gating; TAVR = transcatheter aortic valve replacement

review, telephone interviews with use of a structured questionnaire approved by the IRB, and Social Security Death Index verification.

The primary endpoints of the study were major adverse cardiac events (MACE), defined as cardiac death, nonfatal myocardial infarction (MI), or late (>30 d) revascularization (PCI or CABG). Cardiac death was defined as death caused by acute MI, ventricular arrhythmias, or refractory heart failure. Nonfatal MI was defined by the presence of positive biomarkers (troponin I) in addition to ECG abnormalities, physical symptoms suggesting myocardial ischemia, or both.

Image Acquisition and Analysis

Patients were prepared and images were gathered in accordance with Society of Cardiovascular Computed Tomography guidelines.¹¹ Patients were given 50 mg of metoprolol tartrate orally and 5 mg intravenously as needed to achieve a heart rate <65 beats/min. Patients were also given 0.4 mg of nitroglycerin sublingually unless their systolic blood pressure was <100 mmHg.

A Brilliance 64 CT Scanner (Philips Healthcare) was used to acquire the images (collimation width, 64 × 0.625 mm). The x-ray tube voltage was set at 120 kV, and the current was 500 to 900 mA. Retrospective ECG gating was performed with dose modulation (maximal tube output in mid-diastole or 75% phase of R-R interval), and images were reconstructed for every 10% of the R-R interval. For PG, the x-ray window was set at mid-diastole (75% phase of R-R interval), and no padding was applied. The z-axis was from just above the carina to below the caudal border of the left ventricle. Images were reconstructed and analyzed with use of a Brilliance workstation (Philips). The CT images were read by a board-certified cardiac imager.

A 17-segment model of the coronary arteries was used to evaluate the extent of disease. The left anterior descending, left circumflex, and right coronary arteries, and the diagonal, ramus intermedius, and obtuse marginal branches were all divided into 3 segments: proximal, mid, and distal. The left main, posterolateral, and posterior descending coronary arteries were not divided into segments. Each segment was graded according to the presence of plaque and the severity of stenosis within the coronary artery: 0 = no plaque, 1 = nonobstructive CAD (<50% stenosis), and 2 = obstructive CAD (≥50% stenosis).^{2,3,12} Arteries <1.5 mm in diameter were considered to be uninterpretable.

The effective radiation dose was calculated by multiplying the dose-length product by a conversion coefficient of 0.014 mSv/(mGy•cm).¹³

Statistical Analysis

Descriptive statistics are presented as mean ± SD for normally distributed variables, which include age, body mass index (BMI), systolic and diastolic blood pressures,

heart rate, and radiation dose. Non-nominally distributed variables are presented as median and range, and categorical variables, as frequency and percentage. Student *t* tests were used to identify differences in means between the 2 groups; Mann-Whitney U tests, to examine differences in medians; and χ^2 analysis, to identify significant heterogeneity in the frequencies. For survival analyses, statistical tests were performed separately for each ECG gating technique to compare prognostic performance between the two. Kaplan-Meier estimates of MACE rates and overall survival were calculated in strata defined by the scan mode and extent of disease. Two-sided log-rank tests were used to determine significance. A Cox proportional hazards model was used to calculate unadjusted and adjusted hazard ratios and corresponding 95% CIs.

The rate of MACE as a function of time was also evaluated, with use of univariate and multivariate Cox regression analysis. In multivariate analysis, baseline characteristics with *P* values <0.1 were adjusted for each CCTA parameter. Cox regression analysis results are presented as hazard ratios with 95% CI.

Statistical tests were performed with IBM SPSS 20 and PASW Statistics 18 (SPSS Inc., an IBM company). A *P* value <0.05 was considered statistically significant.

Results

The final cohort comprised 915 patients (mean age, 57.8 ± 13.5 yr). The majority were white (n=580, 63.4%),

male (n=497, 54.3%), and nonsmokers (n=669, 73.1%). Other baseline characteristics included hypertension in 427 patients (46.7%), diabetes mellitus in 125 (13.7%), and hyperlipidemia in 296 (32.3%).

Coronary computed tomography angiography with RG was performed in 720 patients (78.7%) and with PG in 195 patients (21%). The PG patients were younger (53.8 ± 13.9 vs 58.9 ± 13.5 yr; *P* <0.001) and had a lower BMI (28 ± 4.9 vs 30.3 ± 7.4 kg/m²; *P* <0.001). The frequency of a family history of CAD was higher in the PG patients (28.7% vs 11.8%; *P* <0.001), as was the use of aspirin before CCTA (29.2% vs 21.8%; *P*=0.04). The other baseline characteristics were not significantly different between the 2 groups (Table I).

Coronary Computed Tomography Angiography Findings

On CCTA, 390 patients (42.6%) had normal coronary arteries, and 525 (57.4%) had evidence of CAD. Of the 525 patients with CAD, a single coronary artery was involved in 222 (42.3%); 2 coronary arteries, in 103 (19.6%); 3 coronary arteries, in 101 (19.2%); and the left main coronary artery, in 99 (18.9%). Obstructive CAD was documented in 143 patients (27.2%). The patients who underwent PG had a lower rate of obstructive CAD than those who had RG (8% vs 18%; *P* <0.001), and they had a higher rate of normal coronary arteries (55% vs 39%; *P* <0.001). No other CCTA findings were significantly different. Table II details the extent of CAD in each group.

TABLE I. Baseline Characteristics of the 915 Patients

Variable	Value	Gating		P Value
		Retrospective (n=720)	Prospective (n=195)	
Age (yr)	57.8 ± 13.5	58.9 ± 13.2	53.8 ± 13.9	<0.001
Male	497 (54.3)	393 (54.6)	104 (53.3)	0.81
White	580 (63.4)	446 (61.9)	134 (68.7)	0.09
Body mass index (kg/m ²)	29.8 ± 7	30.3 ± 7.4	28 ± 4.9	<0.001
Diabetes mellitus	125 (13.7)	104 (14.4)	21 (10.8)	0.2
Hypertension	427 (46.7)	341 (47.4)	86 (44.1)	0.47
Hyperlipidemia	296 (32.3)	229 (31.8)	67 (34.4)	0.49
Smoking	246 (26.9)	194 (26.9)	52 (26.7)	0.33
Family history of CAD	141 (15.4)	85 (11.8)	56 (28.7)	<0.001
Aspirin use	214 (23.4)	157 (21.8)	57 (29.2)	0.04
Statin use	212 (23.2)	159 (22.1)	53 (27.2)	0.15
Heart rate before CCTA (beats/min)	60.3 ± 11.5	60.7 ± 11.5	59.2 ± 11.3	0.11

CAD = coronary artery disease; CCTA = computed tomographic coronary angiography

Data are presented as mean ± SD or as number and percentage. *P* <0.05 was considered statistically significant.

Clinical Outcomes and Survival Analysis

During a mean follow-up duration of 2.4 ± 0.9 years, MACE occurred in 32 patients (3.5%): 11 cardiac deaths, 15 late revascularization procedures (10 PCI and 5 CABG), and 6 nonfatal MIs. The occurrence of MACE was similar for both groups (RG, 3.8%; vs PG, 2.6%; $P=0.42$), as was the occurrence for each type of event: cardiac death (RG, 1.4%; vs PG, 0.5%; $P=0.32$), late revascularization (RG, 2.1%; vs PG, 1.5%; $P=0.63$), and nonfatal MI (RG, 0.7%; vs PG, 0.5%; $P=0.78$).

Overall, patients with obstructive CAD had the highest annualized MACE rate, followed by those with non-obstructive CAD; the rate was less than 0.5% per year in those with normal arteries. The rates between the RG and PG groups in each category were not significantly different (Fig. 2).

Kaplan-Meier analysis revealed no significant difference in MACE-free survival between the RG and PG groups (Fig. 3). In comparison of overall MACE-free survival by extent of CAD at 4 years after CCTA, the rate was higher in patients with nonobstructive CAD than in those with obstructive CAD, and it was highest in patients with normal arteries ($P < 0.0001$) (Fig. 4).

Predictors of Major Adverse Cardiac Events

On univariate Cox regression analysis, age ($P < 0.001$), diabetes mellitus ($P=0.015$), nonobstructive CAD ($P=0.005$), and obstructive CAD ($P < 0.001$) were associated with MACE (Table III). After adjustment in

the multivariate model, nonobstructive CAD ($P=0.015$) and obstructive CAD ($P < 0.001$) each remained independently associated with MACE. The use of PG was not associated with higher rates of MACE in either the univariate or multivariate model.

Effective Radiation Dose

The mean effective radiation dose in the PG group (4 ± 2 mSv) was significantly lower than that in the RG group (12 ± 4 mSv; $P < 0.01$) (Fig. 5).

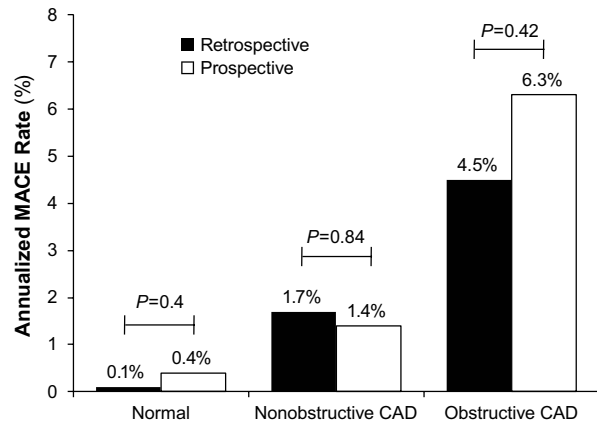


Fig. 2 Annualized major adverse cardiac event (MACE) rates according to severity of coronary artery disease (CAD) detected by retrospective and prospective electrocardiographic-gated coronary computed tomography angiography.

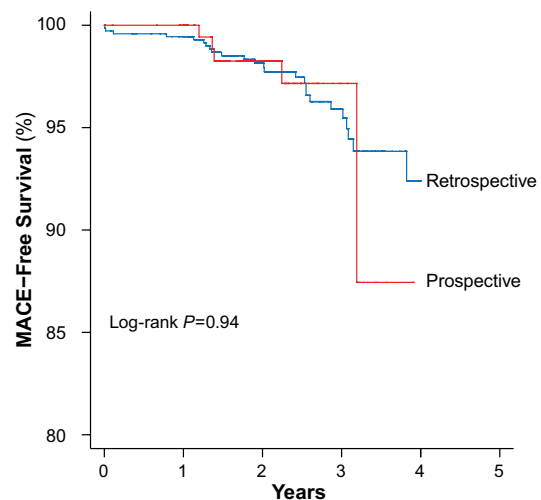
$P < 0.05$ was considered statistically significant.

TABLE II. Comparison of Severity of Coronary Artery Disease Detected on CCTA

Grade	Gating		P Value
	Retrospective (n=720)	Prospective (n=195)	
Normal	282 (39)	108 (55)	<0.001
Nonobstructive CAD	310 (43)	72 (37)	0.14
1-vessel	101	32	—
2-vessel	57	13	—
3-vessel	77	12	—
LMCA	75	15	—
Obstructive CAD	128 (18)	15 (8)	<0.001
1-vessel	76	13	—
2-vessel	31	2	—
3-vessel	12	0	—
LMCA	9	0	—

CAD = coronary artery disease; CCTA = computed tomographic coronary angiography; LMCA = left main coronary artery

Data are presented as number and percentage.



	0	1	2	3	4	5
Retrospective	720	703	481	218	19	
Prospective	195	188	118	21	0	

Fig. 3 Kaplan-Meier curve of MACE-free survival according to scan mode.

$P < 0.05$ was considered statistically significant.

MACE = major adverse cardiac events

Discussion

Recent advances in CT technology have enabled much faster image acquisition with a lower radiation dose, while preserving or improving diagnostic accuracy. Scanning in PG mode is one of the methods that considerably decreases the radiation dose needed for cardiac CT. Investigators¹⁴ from the Prospective Multicenter Study on Radiation Dose Estimates of Cardiac CT Angiography I study, which sampled 64-MDCT CCTA reports from 47 international sites, reported a median radiation dose of 11.2 mSv for RG, compared with 3.6 mSv for PG.

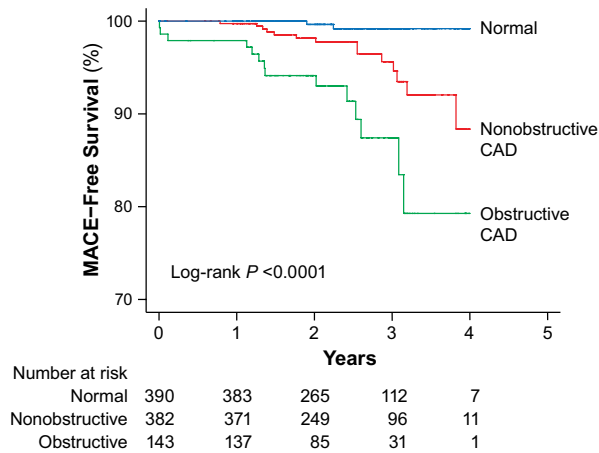


Fig. 4 Kaplan-Meier curve of MACE-free survival according to severity of coronary artery disease.

$P < 0.05$ was considered statistically significant.

CAD = coronary artery disease; MACE = major adverse cardiac event

Even though PG does not capture data throughout the cardiac cycle, it is well established that CCTA image quality and diagnostic accuracy with PG are comparable to that with RG.⁶⁻¹⁰ Our study is one of the first to compare the prognostic value of CCTA with PG and RG, and our results indicate that the predictive values for both scan modes are similar. We found that the presence of coronary lesions on CCTA was an independent predictor of MACE, but the scan modes were not. A normal CCTA result was associated with an excellent prognosis, regardless of scan mode. Furthermore, an abnormal CCTA result was predictive for MACE in both the RG and PG groups. These findings suggest that PG is at least as effective as RG for prognosticating MACE in patients suspected of having CAD.

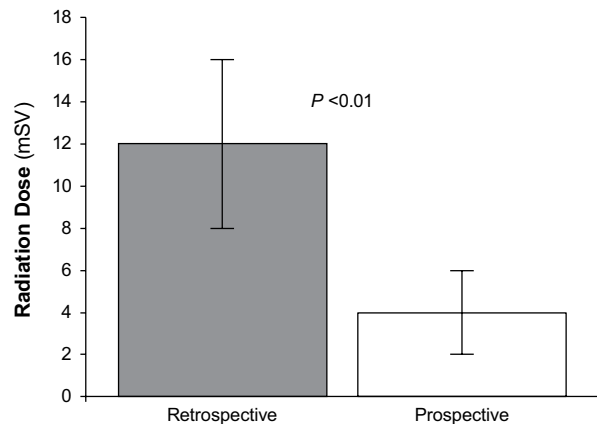


Fig. 5 Comparison of the mean effective radiation dose (mSv) in the retrospective and prospective electrocardiographic-gated groups.

$P < 0.05$ was considered statistically significant.

TABLE III. Predictors of Major Adverse Cardiac Events

Variable	Univariate Model			Multivariate Model*		
	HR	95% CI	P Value	HR	95% CI	P Value
Age	1.05	1.02–1.08	<0.001	—	—	—
Male	1.24	0.61–2.52	0.55	—	—	—
Hypertension	1.39	0.68–2.81	0.92	—	—	—
Diabetes mellitus	2.54	1.20–5.37	0.015	—	—	—
Dyslipidemia	1.52	0.75–3.08	0.25	—	—	—
Smoking	1.6	0.74–3.47	0.23	—	—	—
Prospective gating	1.04	0.39–2.74	0.94	1.29	0.49–3.41	0.61
Nonobstructive CAD	8.16	1.87–35.71	0.005	6.61	1.44–30.25	0.015
Obstructive CAD	24.6	5.62–107.73	<0.001	17.39	3.53–85.74	<0.001

CAD = coronary artery disease; HR = hazard ratio

*Adjusted for age, sex, and cardiovascular risk factors

$P < 0.05$ was considered statistically significant.

Our findings on the prognostic value of CCTA in patients with suspected CAD are consistent with other reports.^{2,3,15,16} The annualized MACE rate in our study was highest in the patients with obstructive CAD, followed by that in patients with nonobstructive CAD. Patients with normal arteries had excellent intermediate-term outcomes. In a study of 2,076 patients who had CCTA with RG and a mean follow-up duration of 16 ± 8 months, the MACE rates were similar to those in our RG patients with both nonobstructive CAD (0.8% vs 1.7%) and obstructive CAD (3.7% vs 4.5%).² Hulten and co-authors¹⁵ conducted a meta-analysis that included 18 studies to determine the prognostic value of CCTA in patients with suspected CAD. They also found that the MACE rate was higher in patients with obstructive CAD than in those with normal coronary arteries or nonobstructive CAD. The weighted average annualized MACE rate (death/MI) was higher in patients with scans positive for CAD (8.8% / 3.2%) than in those with negative scans (0.17% / 0.15%).

The focus of these large studies has been to validate the overall prognostic performance of CCTA, mostly with RG; they have not evaluated the role of scan modes. Buechel and colleagues¹⁶ have shown good prognostic performance of low-dose CCTA with PG: patients with normal coronary arteries had excellent event-free survival rates, followed by patients with nonobstructive CAD. Patients with obstructive CAD had the lowest event-free survival rates.¹⁶ The MACE rates in Buechel and colleagues' study were similar to those in our PG patients who had normal coronary arteries (0 vs 0.4%) or nonobstructive CAD (3% vs 1.4%). However, the MACE rate was much higher in their patients with obstructive CAD (26%) than in ours (6.3%), probably because they had a higher-risk patient population. They also included patients who had prior PCI or CABG, and we did not. However, they did not directly compare the prognostic value of PG and RG. Finally, they used a different MDCT system (64-slice GE Healthcare LightSpeed® VCT XT).

In our study, the mean effective radiation dose for PG was 4 ± 2 mSv, compared with 12 ± 4 mSv for RG. These doses are consistent with those in previously reported studies in which a similar generation of 64-slice MDCT was used. Hirai and colleagues¹⁰ showed a 79% reduction in radiation dose with use of PG; the mean effective dose was 4.1 ± 1.8 mSv in their PG group, compared with 20 ± 3.5 mSv in their RG group. This reduction in radiation dose with PG is also a greater reduction in radiation exposure than is seen when using dose modulation with RG.¹⁰ Sabarudin and associates¹⁷ reviewed 23 studies in which PG had been evaluated with use of several different detectors. Overall, the mean effective radiation dose was 3.6 mSv; for 64-slice scanners, it was 4.7 mSv. Advances in CT technology may enable even lower radiation doses with good diagnostic

accuracy. These approaches include fixed tube current modulation, iterative reconstruction, high-pitch helical dual-source scanning, and automatic attenuation for radiation dose optimization and padding reduction.^{4,5} However, the prognostic value of these newer radiation reduction strategies needs to be validated.

No guidelines have been established on which scan mode is optimal for particular clinical situations. Although PG is preferable to RG because it limits radiation exposure, the mode chosen ultimately depends on the patient's age, sex, heart rate, BMI, and calcium burden. Whereas PG may be suitable for younger patients and women, RG is preferred in patients with a higher BMI, a higher heart rate, and a greater calcium burden because more cardiac phases are obtained, enabling segments with artifact to be evaluated. Nevertheless, advances in software and hardware will continue to increase the usefulness of PG, and it may become the main scan mode for evaluating patients with suspected CAD. Our data show that the prognostic power of CCTA with PG is comparable to that of CCTA with RG.

Limitations

This is a single-center retrospective study, and the results need to be validated in a larger multicenter prospective study. Because PG scanning is newer than the older and more established RG technique, the PG group had fewer patients. In addition, there were a few differences between the 2 groups in terms of baseline characteristics; nevertheless, our patient population and event rates were similar to those in previously reported studies. We did not include ventricular function data, which was available for the RG group, because the value added to the coronary data would have been incremental. Finally, we did not evaluate image quality between the RG and PG groups because other studies have shown it is comparable.

Conclusion

Previous studies have established the diagnostic accuracy of PG, and our study goes a step further, supporting its prognostic usefulness. In selected patients, PG is preferable to RG because it reduces radiation exposure to the patient while preserving the clinical value of CCTA.

Acknowledgments

The authors thank Jennifer P. Connell, PhD, for her critical reading of the manuscript, and Jiaqiong Xu, PhD, for providing statistical support.

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