

Comparison of Radiation-Induced DNA Damage between Conventional and Computed Tomography Coronary Angiography

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Research Article

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Abstract

Purpose: Conventional coronary angiography (CCA) and coronary computed tomography angiography (CCTA) are the most frequently used imaging modalities to diagnose coronary artery disease (CAD). The amount of radiation and genotoxic damages of these imaging methods showed variation with the improved technology. Thus we sought to compare the ionizing radiation doses and radiation-induced DNA damage in patients who were performed CCA and CCTA.

Methods: 76 patients (39 in CCA group, 37 in CCTA group) were enrolled. Patients undergoing CCTA were grouped according to the use of flash technique (22 patients with CCTA-flash, 15 patients with CCTA-other). The effective radiation dose was recorded. Genotoxicity was compared with chromosome aberration test before and after imaging methods.

Results: There was a significant difference between the groups in effective radiation doses given to patients. Radiation was lowest in the CCTA-flash group, followed by CCA, and non-flash CCTA group. There was no change in chromosome aberration rate after CCTA-flash group ($p = 0.479$). There was a significant increase in chromosome aberration rates after CCA and CCTA-other groups (CCA: $p = 0.001$; CCTA-other: $p = 0.01$).

Conclusions: CTA which was taken with flash technique in dual-energy CT devices delivers lower dose radiation compared to other groups. Due to this significant difference, radiation-induced genetic damage was significantly less in patients with CCTA undergoing flash technique.

Introduction

Coronary artery disease (CAD) is the leading cause of morbidity and mortality in the world with an increasing prevalence regardless of the development status of the countries (1, 2). Although different modalities have been proposed for the diagnosis of coronary artery disease, conventional coronary angiography (CCA) and coronary computed tomography angiography (CCTA) are the tools commonly used for the diagnosis of CAD (3). CCA remains as the gold standard method for the diagnosis due to its high spatial and temporal resolution. However, it has several disadvantages such as need for hospitalization, risk of complications and high cost (4,5). However, CCTA is a noninvasive alternative, especially in the population with low and moderate risk of CAD (6,7). Recently novel developments in CCTA made it available to provide better anatomical details of coronary arteries by leading to useful information for the diagnosis of CAD (8,9). The commonality of both imaging methods is using ionizing radiation, which could have mutagenous effects (5,10). The radiation dose, which was previously reported to be higher in CCTA than CCA, decreased significantly with dual-energy technology (11). Using the flash technique an option presented in devices with recent technology, has also reduced the radiation dose to its minimum (11-13).

Ionizing radiation has many somatic and genetic effects on tissues. The increase in cancer risk, which is the most feared effect, has previously been demonstrated in observational studies, especially in people

exposed to radiation (14). The most important factor is DNA damage for the risk of cancer due to radiation exposure. There are several methods for detecting radiation-induced genotoxic damage. Chromosome aberration test (CAT) is a standard method commonly used to detect various structural chromosomal abnormalities induced by mutagens (15-17).

Thus, we sought to compare ionizing radiation doses of CCA and CCTA and radiation-induced DNA damage by chromosome aberration test caused by these imaging techniques.

Methods

Study Population

A total of 76 patients over 18 years, followed in XXX Cardiology Department and Radiology Departments were included. Thirty-nine patients underwent CCA and 37 patients underwent CCTA for diagnosis of CAD. Patients who had a history of malignancy, chemo-radiotherapy, coronary artery anomaly and radiological procedures other than chest radiography in the last year and patients with signs of active infection were excluded. In addition, since we aimed to compare CCTA with diagnostic CCA, patients who were performed ventriculography percutaneous coronary intervention in the same session were excluded. Before their participation, patients were informed about the research and written consents were obtained. This study was approved by the local ethical committee (XXX Faculty of Medicine Clinical Research Ethics Committee on 11.09.2017).

Study Protocol

Patients who were performed CCTA were divided into two groups according to being scanned with prospective ECG-triggered high-pitch spiral technique with dual-energy CT device (CT-flash). Thus, three patient groups were formed at last; CCA, CCTA-flash and CCTA-other. Baseline characteristics and effective radiation doses obtained from imaging tools were calculated and recorded. Blood samples were taken immediately before and one hour after imaging protocol.

Conventional Coronary Angiography

Conventional coronary angiography procedures were performed on the Innova IGS 320, General Electric Healthcare (Milwaukee, USA) device by physicians experienced in interventional cardiology. The number of images was left to the initiative of the interventional cardiologist, provided that all coronary imaging were performed (Figure 1).

Coronary Computer Tomography Angiograph

384 sections (192x2), dual energy, 3rd generation tomography device Somatom Force CT, Siemens Healthcare (Siemens AG, Erlangen, Germany) was used for CCTA. All patients had coronary calcium scoring before angiography procedure. No negative chronotropic agents were given to patients to reduce pre-procedure pulse. The imaging protocol was determined by the radiologist according to the pulse rate

of the patients during the procedure (Figure 2). Flash mode shooting (prospective ECG-triggered high-pitch spiral technique with dual-energy) was performed for eligible patients.

Radiation Dose Measurements

There are different parameters to calculate the radiation doses of the patients. In our study, we used the effective dose (ED) which is more frequently used among these parameters. The dose-area product (DAP) values of the patients who underwent CCA automatically measured by the device after the procedure and were converted to ED unit (mSv) by multiplying the converting factor for diagnostic CCA by 0.12 mSv / Gy.cm². In CCTA, the dose-length product (DLP) values given by the device were converted to ED by multiplying the conversion factor 0.014 mSv x (mGy x cm) ⁻¹ for the chest region.

Chromosome Aberration Test

CAT is a standard method commonly used to detect various structural and numerical chromosomal abnormalities induced by mutagens. Chromosome aberration frequency determined in circulating lymphocytes is a biomarker of cancer risk and reflects both early biological effects and individual sensitivity of exposure to genotoxic carcinogens (17). Chromosomal aberration analysis of human lymphocytes on metaphase is still accepted as the gold standard method for radiation biodosimeter (18). In our study, standard procedures were applied to the blood samples taken from patients before and after the imaging procedures for CAT. After lymphocytes were kept at the metaphase stage and spread to the slides, 100 metaphases were examined by experienced researchers for each individual (Figure 3). In our study, the structural aberration types, chromosome-chromatid gap, chromosome-chromatid fracture, ring chromosome, dicentric and acentric chromosomes were determined and total aberration rate was calculated before and after procedure for each patient. The relative change in chromosome aberration rates was accepted as the genotoxic effect of radiation.

Statistical Analysis

Statistical analyzes were performed using IBM SPSS (IBM, Chicago, IL, USA) for Windows Version 19.0 package program. Numerical variables were summarized with mean ± standard deviation or median [interquartile range]. Categorical variables were represented by numbers and percentages. The normality of numerical variables was examined by Shapiro Wilks test. The difference between the numerical values before and after imaging was examined by using T test in dependent groups in case of parametric test assumptions and Wilcoxon test in case of lack of parametric test assumptions. Differences between categorical variables were evaluated by chi-square test. Differences between groups were analyzed by one-way analysis of variance if parametric test assumptions were met, and Kruskal Walli's test if parametric test assumptions were not met. Bonferroni correction was applied for post-hoc tests. Changes in the parameters of genetic damage assessment before and after imaging were calculated as a percentage. Significance level was accepted as p <0.05.

Results

Totally 76 patients were included in the study and CCA group consisted of 39 patients. The patients who underwent CCTA were divided into two groups according to the flash mode of the device. Of the 37 patients who underwent CCTA, 22 (59.5%) were in the CCTA-flash group and 15 (40.5%) were in the CCTA-other group. The baseline demographic and clinical characteristics of the participants are shown in Table 1. The mean age of the patients was 56.9 ± 10.8 years. Basal characteristics of the groups were similar except heart rate and age. The mean age of the CCTA-other group was higher compared to others.

The mean effective radiation dose given to all participants was 4.6 ± 2.9 mSv. The mean dose of radiation administered was significantly different between the groups (Figure 4). The highest radiation was observed in the CCTA-other group with an ED of 7.2 ± 2.4 mSv. The least radiation was seen in the CCTA-flash technique and the mean ED was 1.1 ± 0.2 mSv.

Total chromosome aberration rates measured by CAT before and after imaging methods are shown in Table 2. In the CCTA-flash group with the lowest radiation dose, there was no change in chromosome aberration rate after the study. Chromosome aberration rates increased significantly after imaging protocols for patients in the CCA and CCTA-other groups. The increase in these two groups was found to be similar ($p = 0.366$).

Discussion

In our study; we aimed to compare genotoxic damage due to ionizing radiation by assessing CAT in patients who underwent CCA and CCTA. Radiation dose was significantly lower in CCTA-flash group compared to other groups. While chromosomal aberration rate was not increased for CCTA-Flash group, chromosome aberrations were observed in CCTA-Other and CCA groups.

Coronary artery disease is one of the most important health problems worldwide due to its negative consequences and frequency (1,2,19). Although CCA still appears to be the gold standard in diagnosis; use of CCTA has increased considerably with the latest technological advances (10,20). There are two important reasons for this increase: firstly it provides very good anatomical detail in the visualization of coronary arteries with the increase in the number of sections with three-dimensional isometric imaging feature (8,9). Secondly high radiation doses previously feared in CT have been reduced by techniques in the new generation CT devices (11,21,34). The number of patients being scanned by CCA or CCTA is increasing due to higher admissions to hospitals with increased sensitivity to CAD. Moreover, access to mentioned imaging tools has become easier. This makes it more necessary to know the effects of ionizing radiation used in imaging method. Current guidelines emphasize that CCTA should be preferred for the diagnosis of CAD (22). However, adequate protocols should be followed to achieve low radiation doses to prevent radiation-induced comorbidities.

Radiation doses in CCA and CCTA have been compared many times and previous studies observed that patients are exposed to more radiation in CCTA (23,24). However, with the development of CT technology, especially with the emergence of dual energy CT systems, the radiation dose decreased in CCTA scans (25). Flash mode in dual-energy CCTA devices transmits low dose in a single pulse during a certain period

of the cardiac cycle (12,13,26). In our study, it was observed that the patients had very low dose of radiation, such as 1.1 ± 0.2 mSv, on flash mode. This result was found to be consistent with previous studies (12,27,33). In order to use flash mode in dual-energy CT devices, patients' heart rates should be low (28,29). Therefore, in our study, it is expected that the heart rates of patients with CCTA-flash group are lower than the other groups. The average ED calculated in the CCA group was found to be similar to previous studies (29).

Genotoxicity of ionizing radiation in CCTA has been shown in several studies (30,31). However, there is a few studies comparing CCA and CCTA in this respect (5). Our study provided clinically important results by comparing two methods that expose radiation and whose prevalence is increasing day by day. Chromosomal damage has an important role as a biological indicator of genotoxic carcinogen exposure such as ionizing radiation. Determining the frequency of chromosomal aberration in cultured peripheral blood lymphocytes is one of the most widely used methods in evaluating the biological effects of genotoxic carcinogen exposure (32). In our study, we preferred the CAT because it shows genotoxicity effectively by being reliable for many years. There is no study comparing dual-energy CCTA and CCA using the CAT for the genotoxic effects of radiation.

Our results revealed that chromosome aberration increase was lowest in the CCTA-flash group, which has a significantly lower mean radiation dose received. However, the increase in chromosome aberration rate was not higher in CCTA-other group which has the the highest mean radiation dose received compared to CCA group ($p = 0.366$). It could be explained that the number of patients is not enough to provide a statistically significant difference and genotoxic effect may depend not only on radiation dose but also on individual sensitivity. Therefore larger prospective studies should be performed.

Limitations of the Study

The most important limitation of our study was the limited number of patients, however, we believe to explicit relevant results. Another limitation is that evaluation of chromosome aberration can be subjective. Therefore, it was evaluated by the only experienced researchers.

The results of this study indicate that coronary imaging with CCTA- flash mode in dual - produces less radiation and radiation-induced genotoxicity than non-flash mode CT scans and CCA. Further studies with a larger patient population are necessary to confirm the results of our study.

Main Points

- Coronary computed tomography angiography with flash mode in dual energy devices produces less radiation
- Coronary computed tomography angiography with flash mode in dual energy devices results less radiation induced genotoxicity assessed by chromosome aberration.

- Conventional coronary angiography and coronary computed tomography angiography with non-flash mode result similar radiation-induced genotoxicity assessed by chromosome aberration.

Declarations

Funding

Not applicable

Conflicts of interest/Competing interests

All authors report no relationships that could be construed as a conflict of interest.

Ethics approval

The study was approved by the Gazi University Faculty of Medicine ethics committee.

Consent to participate

All subjects gave written informed consent prior to inclusion

Consent for publication

Not applicable

Availability of data and material

Data available on request due to privacy/ethical restrictions

Code availability

Not applicable

Authors' contributions

The listed authors contributed to the manuscript, in the following manner:

Conception and design of the study or analysis and interpretation of data, or both (GG, SÜ);

Manuscript drafting or critical revision for important intellectual content (GG, SÜ, AE, AY, BK);

Final approval of the manuscript submitted (SÜ, MC, GE, NBB)

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Tables

Table 1. Baseline characteristics of the participants.

Variables	Total (n = 76)	CCA (n = 39)	*¥#CCTA (n=37)		P
			CCTA-Flash (n=22)	CCTA-Other (n=15)	
Age (year)	56.9 ± 10.8	59.2 ± 11.1#	54.5 ± 10.0		0.057
			54 ± 9.5	50.3 ± 10.7#	0.016
Gender (female)	31 (40.8%)	16 (%41)	15 (40.5%)		0.460
			6 (27.3%)	9 (60.0%)	0.138
SBP	133.8 ± 12.9	135.1 ± 13.1	132.3 ± 12.7		0.342
			133.2 ± 10.5	131 ± 15.7	0.563
DBP	80.7 ± 7.7	79.9 ± 7.8	81.5 ± 7.3		0.363
			81.4 ± 6.9	81.7 ± 8.6	0.658
HR	71.6 ± 10.1	72.7 ± 10.4*	70.3 ± 9.75		0.304
			63 ± 2.8*¥	81.1 ± 4.9¥	<0.001
Lenght (cm)	167 ± 10.4	167 ± 10.4	166.3 ± 8.1		0.770
			168 ± 8.1	164 ± 8.0	0.455
Weight (kg)	77.7 ± 13.9	76.9 ± 15.6	78.5 ± 12.1		0.610
			80.6 ± 12.4	75.5 ± 11.3	0.493
BMI (kg/m ²)	28.2 ± 4.3	27.5 ± 4.2	28.8 ± 4.4		0.182
			28.9 ± 4	28.8 ± 5.1	0.413
Diabetes mellitus	18 (23.7%)	13 (33.3%)	5 (13.6%)		0.059
			3 (13.6%)	2 (13.3%)	0.127
Hypertension	36 (47.4%)	21 (53.8%)	15 (40.5%)		0.262
			9 (40.9%)	6 (40%)	0.508
Hyperlipidemia	29 (38.2%)	18 (46.5%)	11(29.7%)		0.163
			8 (36.4%)	3 (20%)	0.204
Smoking			21 (56.8%)		0.786
	42 (55.3%)	21 (53.8%)	13 (59.1%)	8 (53.3%)	0.104
Alcohol			9 (24.3%)		0.821

	17 (22.4%)	8 (20.5%)	4 (18.2%)	5 (33.3%)	0.512
CKD	5 (6.6%)	4 (10.2%)	1 (2.7%)		0.359
			0 (0%)	1(6.7%)	0.300

BMI: Body mass index, CCA: Conventional Coronary Angiography, CCTA: Coronary Computed Tomography Angiography, CKD: Chronic kidney disease, DBP: Diastolic blood pressure, HR: Heart rate, SBP: Systolic blood pressure

Table 2. Total chromosome aberration rates before and after imaging.

Groups	Total C. Aberration Rate (%) – Before	Total C. Aberration Rate (%) – After	P
CCA	4.3 ± 2.9	5.3 ± 2.9	0.001
CCTA – Flash	3.4 ± 2.4	3.2 ± 2.3	0.479
CCTA – Other	3.1 ± 2.4	4.7 ± 2.6	0.010

CCA: conventional coronary angiography, CCTA; coronary computer tomography angiography

Figures



Figure 1

Conventional coronary angiography image of a study patient.

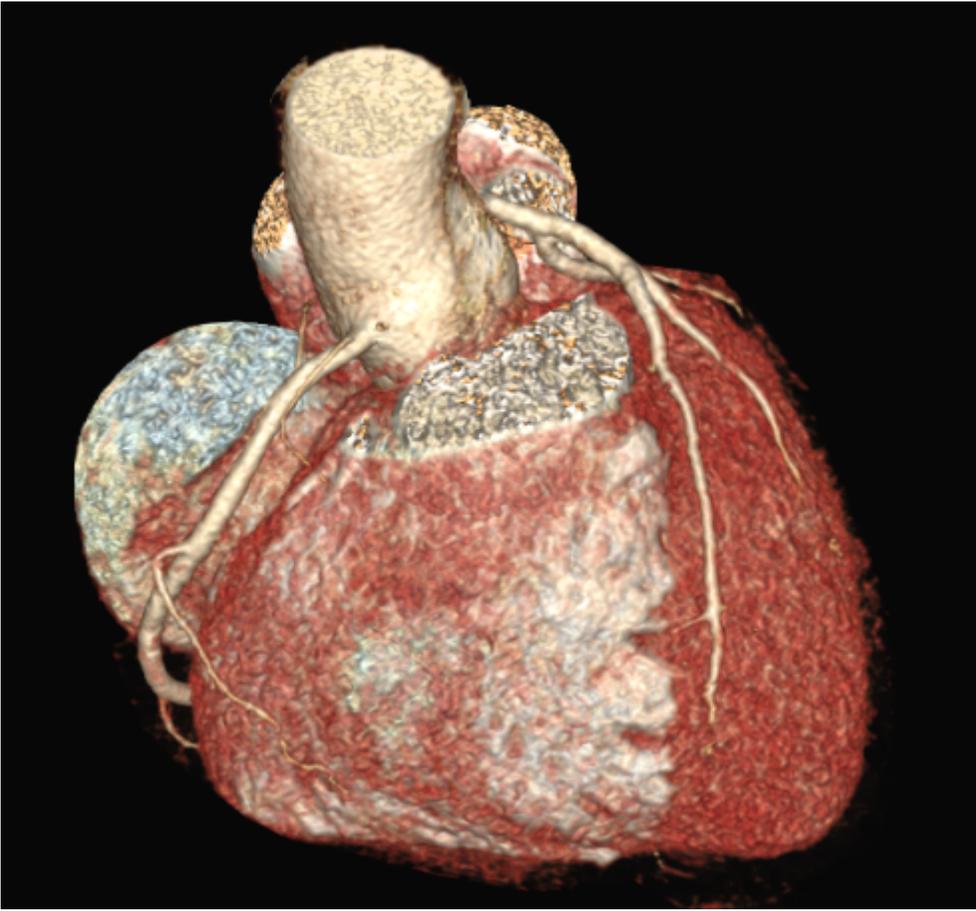


Figure 2

Coronary computed tomography angiography image of a study patient.



Figure 3

Chromosome aberration test of lymphocyte chromosomes at the metaphase stage with light microscopy.

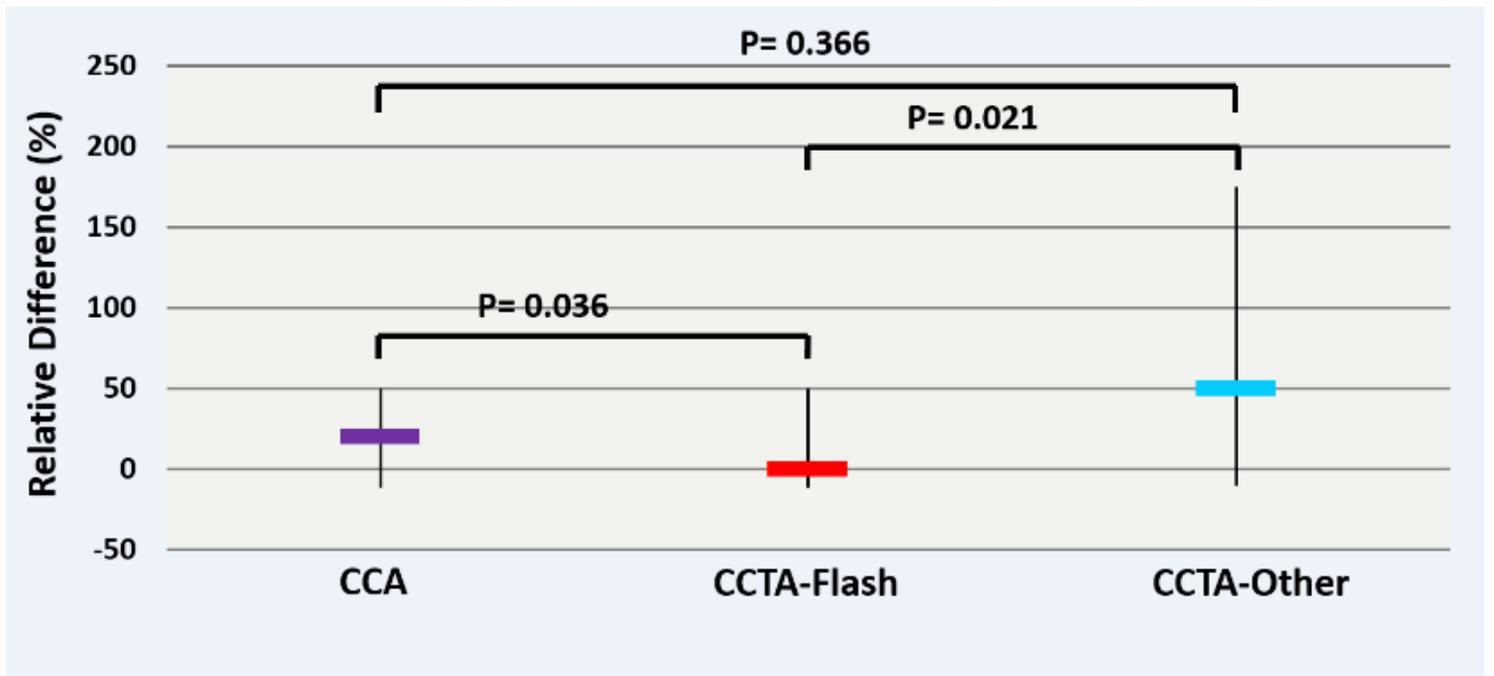


Figure 4

Comparison of mean effective radiation dose among study groups. ($P < 0.001$ with ANOVA, p values regarding post-hoc tests were presented on the bars) (CCA; conventional coronary angiography, CCTA-Flash; coronary computed tomographic angiography-flash, CCTA-Other; coronary computed tomographic angiography-other groups)