http www.aimjournal.ir

Original Article



Coronary CT Angiography and Dual-Energy Computed Tomography in Ischemic Heart Disease Suspected Patients

Ali Mohammadzadeh, MD¹; Mehdi Farzaneh, MD²; Ali Zahedmehr, MD³; Reza Kiani, MD³; Madjid Shakiba, MD⁴; Ali Borhani, MD⁴; Mostafa Rouzitalab, MD²; Samaneh Ahmadi, MD²; Maryam Mohammadzadeh, MD^{5*}

¹Department of Radiology, Rajaie Cardiovascular and Medical Research Center, Iran University of Medical Sciences, Tehran, Iran ²Rajaie Cardiovascular and Medical Research Center, Iran University of Medical Sciences, Tehran, Iran

³Department of Interventional Cardiology, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran

⁴Advanced Diagnostic and Interventional Radiology Research Center, Tehran University of Medical Sciences, Tehran, Iran ⁵Department of Radiology, Amiralalm Hospital, Tehran University of Medical Sciences, Tehran, Iran (C. O)

Abstract

Background: Advanced computed tomography (CT) scanners enable concurrent assessment of coronary artery anatomy and myocardial perfusion. The purpose of this study was to assess dual-energy CT images in a group of patients suspected for ischemic heart disease and to evaluate agreement of cardiac computed tomography perfusion (CTP) images with CT angiography results in a single dual-energy computed tomography (DECT) acquisition.

Methods: Thirty patients (mean age: 53.8 ± 12.9 years, 60% male) with angina pectoris or atypical chest pain, suspected for ischemic heart disease, were investigated using a 384-row detector CT scanner in dual-energy mode (DECT). Firstly, resting CTP images were acquired, and then from the same raw data, computed tomography angiography (CTA) studies were reconstructed for stenosis detection. CT-based dipyridamole-stress myocardial perfusion imaging was then performed in patients who exhibited coronary stenosis >50% or had myocardial bridge (MB). A color-coded iodine map was used for evaluation of myocardial perfusion defects using the 17-segment model. Two independent blinded readers analyzed all images for stenosis and myocardial perfusion defects. Different myocardial iodine content (mg/mL) was calculated by parametric tests. The kappa agreement was calculated between results of two methods in cardiac scans.

Results: All 30 CT angiograms were evaluated and assessment ability was 100% for combined CTA/CTP. According to the combined CT examination, 17 patients (56.7%) exhibited significant coronary stenosis and/or deep MB (DMB). A total of 510 myocardial segments and 90 vascular territories were analyzed. Coronary CTA demonstrated significant stenosis in 22 vessels (24.4% of all main coronary arteries) among 12 patients (40%), DMB in 6 vessels (6.7% of all main coronary arteries) in 17 out of 30 patients (56.7%). Twenty-eight out of 90 vascular territories (31.1%) and 41 out of 510 segments (8%) showed reversible perfusion defects on stress DECT. Kappa agreement between CTA and CTP results in whole heart was 0.79 (95% confidence interval=0.57–1). There were significant differences in mean iodine concentration between ischemic (0.59 \pm 0.07 mg/mL) and normal segments (2.2 \pm 0.15) with *P* < 0.001.

Conclusion: Agreement of CTA and CTP in whole heart and in LAD considering DMB and significant CAD together were good to excellent; however, considering sole pathologies, most of the agreements were weak (<0.5). DECT with iodine quantification may provide a valuable method in comparison with previous methods for identifying both coronary stenosis and myocardial ischemia. **Keywords:** Coronary CT angiography, CT perfusion imaging, Dipyridamole, Dual-energy CT

Cite this article as: Mohammadzadeh A, Farzaneh M, Zahedmehr A, Kiani R, Shakiba M, Borhani A, et al. Coronary CT angiography and dual-energy computed tomography in ischemic heart disease suspected patients. Arch Iran Med. 2019;22(7):376–383.

Received: July 11, 2018, Accepted: December 24, 2018, ePublished: July 1, 2019

Introduction

Integration of cardiac anatomical and functional imaging is required for complete assessment and effective treatment of coronary artery diseases (CAD). Recently, computed tomography angiography (CTA) has been shown to reliably rule out coronary artery stenosis compared to invasive coronary angiography as the clinical reference method. However, it does not provide information about the hemodynamic relevance of coronary artery stenosis.¹ Therefore, concomitant assessment of myocardial perfusion in order to provide information about the functional significance of vessel stenosis has an important discriminatory role.¹ Static stress CT myocardial perfusion (CTP) imaging combined with coronary CTA has high diagnostic accuracy in detecting myocardial ischemia related to stenotic coronary lesions.²

State-of-the-art 320-detector row systems have improved spatial and temporal resolution and z-axis coverage while reducing scan times and radiation exposure.³ In fact, along with the increasing number of detectors per scanner, the specificity and sensitivity of CTA for the diagnosis of significant stenosis have increased.⁴ Recently, dual-source CT with two X-ray tubes and two arrays mounted at 90° from each other in the same gantry operating at different

*Corresponding Author: Maryam Mohammadzadeh, MD; Department of Radiology, Amiralalm Hospital, Tehran University of Medical Sciences, Tehran, Iran (C.O). Email: mm1361@yahoo.com; m-mohammadzadeh@sina.tums.ac.ir

kilovolts (so-called "dual-energy CT") has become available. The usefulness of this technique in performing contrast medium enhanced CT angiography for the comprehensive analysis of coronary artery morphology as well as changes in myocardial perfusion has recently been demonstrated.⁵

The purpose of this study was to assess dual-energy images in a group of patients suspected of having ischemic heart disease and to evaluate agreement of cardiac CTP images with CT angiography results in a single dualenergy computed tomography (DECT) acquisition.

Materials and Methods

This study was a single-institution, prospective review of cardiac DECT images. Thirty patients with angina pectoris, suspected to have CAD, were enrolled into the study. Institutional review board and research ethics committee approval were obtained before enrollment into this study. All participants received explanations about the study protocol and signed an informed consent form.

Inclusion criteria were: age greater than 18 years and angina pectoris that is indicated for further assessment and exclusion criteria were: age >80 years; pregnancy; tachycardia (heart rate >100/min); allergy to iodinated contrast; chronic renal dysfunction or failure; and patients who required an emergent procedure.

Image Acquisition: Comprehensive CT Protocol

All patients who met the inclusion criteria were examined using a 384-detectors dual-source CT (DSCT) scanner in dual-energy mode (Siemens, SOMATOM Force, 384 detectors, Germany) with a gantry rotation time of 330 ms. DSCT system is composed of two detectors and two X-ray tubes operating independently with regard to their kilovoltage and milliamperage settings. For DECT acquisition, the tube voltages were set at 150 kVp (tube A adjusted to 50 mAs) and 90 kVp (tube B adjusted to 200 mAs).

On arrival to the CT room, two intravenous lines were inserted in the right and left antecubital veins (18 gauge for contrast delivery; 20 gauge for dipyridamole infusion). The stress CTP was initiated 4 min after the end of dipyridamole infusion (0.56 mg/kg body weight IV over 4–6 minutes). The heart rate, blood pressure, and ECG were monitored before CT and during dipyridamole infusion. The contrast medium (Omnipaque 350 [io-hexol]; Schening, Berlin, Germany;) delivered with a total injection time of 10 seconds or less followed by 50 mL saline chaser. The radiation exposure calculations are based on the individual CT parameters in each patient.

Figure 1 shows Myocardial CTP protocol involving the rest and stress acquisitions. The stress CT scan was performed after the resting state CT scan. The time interval between the two CT scans was 20 minutes to allow for washout of contrast medium from the myocardium.

From the DECT datasets, CT raw data were reconstructed for angiographic analysis. In patients with coronary stenosis \geq 50% or myocardial bridge (MB), CT-based dipyridamole-stress myocardial perfusion imaging was performed after resting state scan.

In order to reduce the overall radiation dose, only for 3 patients who agreed to additional imaging, coronary catheterization was performed. In other patients, due to high sensitivity and negative predictive value of CTA and the ethical issues in radiation protection, CTA was used as the final reference standard for validating myocardial perfusion defects on DECT.

Visual analysis of CTA based on the 19-segment model and CTP on the 17-segment model were done separately. For vessel perfusion analysis, segmental data were consolidated into three territories. Obstructive CAD was defined as stenosis \geq 50% with a corresponding myocardial hypoperfusion on CTP.⁶ To create a final vessel-territory result, it was considered positive if there were \geq 50% stenosis (CTA) + downstream myocardial perfusion defect (CTP) and it was considered negative if there were \geq 50% stenosis (CTA) + unrelated myocardial perfusion defect (CTP).

Cardiac CT Angiography: Cardiac CT images were evaluated by two different experienced observers (one radiologist and one cardiologist) and whenever they disagreed, a consensus had to be reached. CTA for stenosis detection and grading was analyzed using a dedicated software (Siemens, SYNGO) based on a combination of transverse sections and automatically generated curved multiplanar reformats of the target vessels. If there were





multiple lesions, the corresponding segment was classified by the worst lesion. Coronary arteries and lesions were classified into 3 major coronary vessels: the left anterior descending artery (LAD), the left circumflex artery (LCX), and the right coronary artery (RCA). A ramus intermedius was classified in the LCX, if present.⁷

Dual-energy CT perfusion: The same two observers that evaluated CTA images (one radiologist and one cardiologist) also evaluated the dual-energy based iodine maps for myocardial perfusion defects. The images were presented to observers without label and in a random order to ascertain that the observers are blinded to the CTA results. Dual-energy iodine maps were displayed using the dedicated dual-energy image post-processing software (Syngo Multi-Modality Workplace, Siemens).

The principle of DECT is based on different attenuation at different energy levels. Accordingly, a "color-coded iodine map" can show myocardial perfusion status by analyzing the iodine content within the myocardium on the basis of the unique X-ray absorption characteristics of this element at different kilovolt settings.⁸ With DECT color-coded iodine maps, myocardial iodine content (mg/mL) was calculated using a commercially available software (Syngo Dual Energy, Siemens Healthcare, Forchheim, Germany). Different iodine concentrations between normal and ischemic segments were calculated using parametric tests.

Statistical Analysis

The agreement of DECT and CTA for the demonstration of CAD was analyzed using the kappa statistic between the coronary artery lesions and the hypoperfused territories. The kappa result was interpreted as follows: values ≤ 0 as no agreement and 0.01-0.20 as none to slight, 0.21-0.40 as fair, 0.41-0.60 as moderate, 0.61-0.80 as substantial, and 0.81-1.00 as almost perfect agreement.9 Data were presented as mean ± SD or Number (%). In addition, percentage of patients with hypoperfusion in CTP versus percentage of patients with significant coronary stenosis and/or deep MB (DMB) in CTA was performed by McNemar test. All of analyses were performed in each main coronary arteries and in whole heart separately. Statistical analysis was performed using SPSS software (version 18). A statistically significant difference was defined as a Pvalue less than 0.05.

Results

Totally, 30 patients were enrolled in the study. Mean age of patients was 53.8 ± 12.9 years (35–78). Eighteen patients were male (%60). Mean BMI was 28 ± 3 kg/m² (20–35.85). Clinical symptoms included stable angina in 19 patients (%63.3) and unstable angina and atypical chest pain each one in 5 patients (%16.7). Details of the patients' coronary risk factors and previous medical history are summarized in Table 1.

 Table 1. Risk Factors among Patients

N	30
Age (y)	54 ± 13
Male/female	18/12 (60/40%)
BMI (kg/m ²)	27.8 ± 3
Heart rate	64 ± 4
Hypertension	13 (43.3%)
Dyslipidemia	13 (43.3%)
Diabetes mellitus	6 (20%)
Cerebrovascular disease	1(3.3%)
Current smoker	8(26.7%)
Family history	14(46.7%)

Different degrees of the coronary artery stenosis (including main coronary trunks and their branches) were assessed by CTA carefully and for each one, the significant stenosis (patients with at least moderate stenosis) were determined. In addition, the data of MBs were determined in main arterial segments. All of the data have been mentioned in Table 2. Significant stenosis (at least moderate) was seen in LAD among 11 patients, in LCX among 6 patients and in RCA among 5 patients. Whole heart significant arterial stenosis was seen in 12 patients. In addition, DMB was seen in 6 patients that all of them were seen in LAD (Table 2). One patient had LAD severe stenosis and DMB; thus we had totally 17 patients with significant arterial stenosis, MB or both of them.

In addition, the data of perfusion defects in 17 left ventricular segments were assessed. Hypoperfusion in LAD, LCX, RCA and Whole heart was seen in 17, 8, 3 and 20 patients respectively (Table 3).

For assessment of correlation and agreement between arterial anatomical defects (significant stenosis or DMB), we analyzed the data based on a vessel specific approach and also in whole heart. In each instance, we calculated the Kappa coefficient of agreement between arterial stenosis and CTP and between DMB and CTP. Then we integrated the data of significant stenosis and DMB and calculated the agreement again. This was only proposed for whole heart and LAD (as LCX and RCA did not show DMB). In LAD and whole heart, presence of significant stenosis or DMB considered as one positive factor for compromising perfusion; in this situation, we had 11 patients with significant stenosis in LAD and 6 DMBs in LAD and totally 16 patients with significant LAD stenosis, DMB in LAD or both. For assessment of agreement in vessel specific approach, we considered segments perfused by LAD together, segments perfused by LCX together and segments perfused by RCA together (The details have been mentioned in Table 3). Kappa coefficient of hypoperfusion in CTP and significant stenosis in LAD was 0.49 while it was 0.32 for CTP and DMB in this artery. When we Combined all anatomical data of LAD yielded by CTA and calculated the kappa, the coefficient was raised to 0.8

Main Arteries, Their Branches and Whole Heart		Arterial Stenosis						Myocardial Bridge		
		No	Mild	Moderate	Severe	Complete	No	Superficial	Deep	
LM	LM	26	4	0	0	0	28	2	0	
	Proximal LAD	20	7	1	1	1	21	4	5	
	Middle LAD	20	4	4	1	1	24	5	1	
	Distal LAD	27	2	1	0	0	_	_	_	
	Ramus Intermedius	13	4		1		_	_	_	
LAD	D1 LAD	16	10	2			_	_	_	
	D2 LAD	9	5	1		1	_	_	_	
	D3 LAD	3	4				_	_	_	
	Whole LAD	10	9	6	3	2	15	9	6	
	Proximal LCX	21	8	0	1	0	30	0	0	
	Middle LCX	21	9	0	0	0	29	1	0	
	Distal LCX	21	8				30	0	0	
	OM1 LCX	19	5	4	2	0	_	_	_	
LCX	OM2 LCX	14	1		1		_	_	_	
	OM3 LCX	6					_	_	_	
	PLV LCX	5	1				_	_	_	
	PDA LCX	5					_	_	_	
	Whole LCX	16	8	3	2	1	29	1	0	
	Proximal RCA	23	5	1	1	0	0	0	0	
	Middle RCA	22	6	2	0	0	0	0	0	
	Distal RCA	23	7	0	0	0	0	0	0	
RCA	RV RCA	30	0	0	0	0	_	_	_	
	PDA RCA	22	4		1		_	_	_	
	PLV RCA	25	1				_	_	_	
	Whole RCA	18	7	3	2	0	30	0	0	
Whole He	eart	8	10	6	4	2	2 14 10 6		6	

Table 2. Distribution of Arterial Stenosis and Myocardial Bridge in Each Main Coronary Arteries and Their Branches

LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery.

for this main artery. Kappa coefficient between CTP and CTA in LCX and RCA was 0.63 and 0.43. In whole heart, Kappa agreement between CTP and significant stenosis was 0.5 and it was 0.22 for CTP and DMB while when we combined the data of stenosis and DMB, the coefficient raised to 0.79 (Table 4).

We summed the total number of myocardial regions with defect in CTP. This variable varied among patients from 0-6. Zero number means normal CTP and 6 means the patient showed totally 6 myocardial regions with CTP defect. As it can be seen in Table 4, three patients had abnormal CTP without any significant stenosis in coronary arteries and DMB. All patients with abnormal CTA [including significant stenosis or DMB or both] showed abnormal CTP. There was only one patient with both DMB and significant coronary stenosis. This patient had 2 abnormal CTP regions. In 5 other patients with DMB, only one myocardial region showed abnormal CTP while, among 11 patients with significant coronary stenosis, mean number of myocardial regions with abnormal CTP was 2.6 ± 2.2 [range: 1-6]. Among other 11 patients with at least one significant coronary stenosis, the details of myocardial region number with abnormal CTP and their corresponding CTA results have been mentioned in Table 5.

Spearman correlation coefficient of sum myocardial

regions showing abnormal CTP with coronary stenosis severity among all 30 patients were 0.75 (P value < 0.001). This coefficient was 0.62 among 11 patients with significant coronary stenosis without DMB (P value = 0.042). In addition, spearman correlation coefficient of total number of hypoprfused areas in CTP versus significant stenosis and DMB in CTA for LAD, LCX, RCA and whole heart were 0.73, 0.66, 0.45v and 0.77 respectively (all P values < 0.015).

Discussion

This study was performed using the latest 384-row detector CT scanner for the comprehensive analysis of coronary artery morphology and myocardial ischemia with a single CT acquisition and for measuring agreement between coronary angiography and myocardial stress perfusion with dipyridamole. We have demonstrated that DECT was able to identify reversible myocardial perfusion defects in patients with significant stenosis or deep muscle bridge. There was an acceptable amount of radiation exposure and admissible duration of exam.

CTA, as a noninvasive procedure, can be used to reduce the number of invasive coronary angiographies and also provide additional information on anatomy in order to plan revascularization; however, not all anatomical lesions are functionally significant.¹⁰ This is where myocardial

Table 3. Patient Information

	LAD			LCX			RCA		
Patient No.	Number and Location of Significant Stenosis Areas in CTA	Number and Location of DMB Areas	Number and Location of Hypoperfusion Areas in CTP	Number and Location of Significant Stenosis Areas in CTA	Number and Location of DMB Areas	Number and Location of Hypoperfusion Areas in CTP	Number and Location of Significant Stenosis Areas in CTA	Number and Location of DMB Areas	Number and Location of Hypoperfusion Areas in CTP
1	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0
3	1 [mid.]	0	1 [1-ap. ant.]	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0
5	1 [ram. Int.]	1 [mid]	1 [1-ap. sep.]	2 [OM1, OM2]	0	1 [1-mid. inf. lat.]	0	0	0
6	0	0	2 [1-mid. ant. sep., 2-ap. Sep.]	0	0	0	0	0	1 [1-mid. inf.]
7	0	0	0	0	0	1 [1-ap. lat.]	0	0	0
8	1 [mid.]	0	1 [1-mid ant.]	0	0	0	0	0	0
9	2 [prox.,D1]	0	1 [1-mid. ant. sep.]	1 [OM1]	0	0	1 [prox.]	0	0
10	2 [prox., D1]	0	6 [1-bas. ant., 2-bas. ant. sep., 3-mid. ant., 4-mid. ant. sep., 5-ap. ant., 6-ap. sep.]	0	0	0	1 [prox.]	0	0
11	1 [mid.]	0	1 [1-mid. ant. sept.]	0	0	1 [1-mid. ant. lat.]	0	0	0
12	0	0	0	0	0	0	0	0	0
13	0	1 [dis.]	1 [1-ap. sep.]	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0
15	2 [mid., D2]	0	1 [1-mid. ant. sep.]	1 [OM1]	0	1 [1-mid. inf. lat.]	1 [mid.]	0	0
16	2 [prox., mid.]	0	2 [1-ap., 2-mid. ant. sep.]	1 [OM1]	0	3 [1-bas. inf. lat., 2-mid. inf. lat., 3-ap. lat.]	1 [PDA]	0	1 [1-mid. inf.]
17	1 [mid.]	0	3 [1-ap., 2-mid. ant. sep., 3-mid. ant.]	2 [prox., OM1]	0	2 [1-ap. lat., 2-mid. inf. lat.]	1 [mid.]	0	1 [1-mid. inf.]
18	0	0	0	0	0	0	0	0	0
19	1 [D2]	0	0	0	0	2 [1-ap. lat., 2-mid. ant. lat.]	0	0	0
20	0	0	0	1 [OM1]	0	1 [1-mid. inf. lat.]	0	0	0
21	0	0	0	0	0	0	0	0	0
22	1 [dis.]	0	1 [1-ap.sSep.]	0	0	0	0	0	0
23	0	1 [mid]	1 [1-ap. sep.]	0	0	0	0	0	0
24	0	0	1 [1-ap. sep.]	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0
26	0	1 [mid]	1 [1-ap. sep.]	0	0	0	0	0	0
27	0	1 [mid]	1 [1-mid. ant. sep.]	0	0	0	0	0	0
28	0	1 [mid]	1 [1-ap. sep.]	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0
30	0	0	U	U	U	0	0	U	0

* mid, middle, ap, apical; prox, proximal; dis, distal; ram. Int., ramus intermedius; OM, obtuse marginal; sep, septal; ant, anterior; bas, basal; inf, inferior; lat, lateral; PDA, posterior descending artery; DMB, deep myocardial bridge; CTA, CT angiography; CTP, CT perfusion.

perfusion imaging as a principal diagnostic tool for the assessment of extent and severity of myocardial ischemia is additive to CTA.¹¹ The clinical use of CTP is supported in the investigation of patients with suspected CAD when CTA identified heavily calcified vessels or if the functional

severity of stenosis is uncertain.6

Although some studies have suggested that rest perfusion images alone are sufficient for detecting coronary stenosis,¹² our data did not support this, as rest imaging alone was not sufficient for differentiation between significant and

Table 4. Compa	rison and Agreeme	nt of CTP and CTA ir	Different Coronary	y Arteries and the	e Whole Heart ^{a,b,c}
----------------	-------------------	----------------------	--------------------	--------------------	--------------------------------

		Concordant No.		Discordant No.						
Artery or Whole Heart	Anatomical Defect in CTA	CTP Abnormal and CTA Showing Significant CAD and/or DMB	CTP and CTA Normal	CTP Normal and CTA Showing Significant CAD and/or DMB	CTP Abnormal and CTA Normal	Concordance Percent	Discordance Percent	Карра [95% CI]	ICC [95% CI]	P Value [Kappa, McNemar test]
	Stenosis*	10	12	1	7	73.3	26.7	0.49 [0.2– 0.77]	0.51 [0.19– 0.73]	0.004, 0.07
LAD	DMB	6	13	0	11	63.3	36.7	0.32 [0.09– 0.56]	0.033 [-0.33–0.38]	0.017, 0.001
	Stenosis or DMB	15	12	1	2	90	10	0.8 [0.58–1]	0.53 [0.23–0.74]	<0.001, 0.99
LCX	Stenosis	5	21	1	3	86.7	13.3	0.63 [0.30– 0.96]	0.58 [0.28– 0.77]	<0.001, 0.63
RCA	Stenosis	2	24	3	1	86.7	13.3	0.43 [0–0.89]	0.44 [0.1– 0.69]	0.014, 0.63
	Stenosis	12	10	0	8	73.3	26.7	0.5 [0.24– 0.76]	0.71 [0.48– 0.85]	0.002, 0.008
Whole Heart	DMB	6	10	0	14	53.3	46.7	0.22 [0.04– 0.41]	-0.03 [-0.38–0.33]	0.053, <0.001
	Stenosis or DMB	17	10	0	3	90	10	0.79 [0.57–1]	0.7 [0.46- 0.84]	<0.001, 0.25

Abbreviations: LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; DMB, deep myocardial bridge; CTA, CT angiography; CTP. CT perfusion: ICC, intraclass correlation coefficient.

Stenosis means significant stenosis.

^b ICCs have been calculated between number of significant stenosis or/plus deep myocardial bridges versus number of hypoperfusions in CTP. ^c Significant stenosis in CTA, deep myocardial bridge and hypoperfusion in CTP have been considered for individual vessels and in whole heart.

Table 5. Distribution of Myocardial Regions with Abnormal CTP in Patients with Significant Coronary Stenosis

Number Myocardial Regions with Abnormal CTP	LAD	LCX	RCA
1.00	Moderate stenosis	Narrowing	Narrowing
1.00	No stenosis	Moderate stenosis	Narrowing
1.00	Moderate stenosis	No stenosis	No stenosis
1.00	Severe stenosis	Mild stenosis	Mild stenosis
1.00	Moderate stenosis	Moderate stenosis	Moderate stenosis
2.00	Moderate stenosis	No stenosis	Narrowing
2.00	Moderate stenosis	Mild stenosis	Mild stenosis
2.00	Complete stenosis	Complete stenosis	Moderate stenosis
6.00	Severe stenosis	Moderate stenosis	Severe stenosis
6.00	Complete stenosis	Mild stenosis	Severe stenosis
6.00	Moderate stenosis	Severe stenosis	Moderate stenosis

Abbreviations: LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; CTP, CT perfusion.

non-significant stenotic lesions. Previous studies with CT adenosine stress demonstrated that combination of CTA and CTP by 64 slice, 256 slice and dual-source scanners can detect atherosclerosis causing perfusion abnormalities when compared with the combination of quantitative coronary angiography and SPECT.13 Moreover, a recent study showed that dipyridamole-stress CTP by 320-detector CT in patients with LBBB can be an alternative strategy for assessing myocardial ischemia.¹⁴

As it was previously mentioned that significant (50% or greater) stenosis is associated with functional significance, our findings showed that all stenosis >50% are associated with myocardial hypoperfusion. This finding demonstrated excellent agreement between coronary artery stenosis and the region of myocardium affected by ischemia. Moreover, it has been shown that the perfusion defects in individuals with stenosis <50% by CTA were most likely caused by superficial MB. Therefore, a 50% stenosis threshold on CTA is suggested to be a cutoff value below which ischemia could be ruled out.¹⁵

Recently, dual-source CT with two X-ray tubes at different kV levels (DECT) has become available.¹⁶ Ruzsics et al were among the first to evaluate the accuracy of DECT in comparison with SPECT for detection of myocardial ischemia. DECT had sensitivity, specificity and accuracy of 91% for detecting any type of myocardial ischemia on a segmental basis.⁵ Compared with single-energy CT, DECT iodine maps had the highest sensitivity, negative predictive value, and accuracy of 91%, 97% and 93% for the detection of mixed and fixed perfusion defects.¹⁷

Our findings showed that the defects in perfusion maps have moderate agreement with significant coronary stenosis in LAD and whole heart. This is due to cases of DMB as DMB could impair the perfusion that increases



Figure 2. An Example of Stress-Induced Ischemia in a 78-Year-Old Female with a Post Stent Significant Stenosis in the Mid Portion of the LAD with Multiple Calcified Plaques. Rest (A) and stress (B) CTP showing a reversible perfusion defect in this same patient in the apical anterior wall.

mismatched cases and decreases the agreement. This is observed when the data of significant stenosis and DMB are accumulated together, the agreement is increased to excellent values. When the data of these two lesions were combined together, the Kappa coefficients of agreement improved from 0.5 or lower to about 0.8 in LAD and whole heart. [In addition, in this case, *P*-value for comparisons in McNemar test change from significant to non-significant as could be seen in Table 4. This is due to lowering mismatch cases between significant CTA stenosis and CTP defects due to adding the DMB to significant CTA stenosis patients]. This shows that the perfusion defects could accurately predict presence of an important coronary stenosis or DMB that both require treatment plan and interventional considerations.

Our findings showed that there was a moderate agreement between RCA lesions and perfusion defects in the corresponding segments. This is due to superimposition of territories, mainly occurring between the LAD and the RCA at the inferoapical and inferoseptal regions.^{18,19}

Myocardial bridging (MB) is categorized as deep or superficial based on the thickness of the overlying myocardium. It can be very clearly depicted by CTA.²⁰ Although most cases of MB are clinically asymptomatic, it is sometimes associated with myocardial ischemia, myocardial infarction, arrhythmia, and sudden death.²¹ Hwang et al reported that LAD-MB rate using DSCT was 42%, with two-thirds of MB segments being the superficial type²¹ that is consistent with our results. In our patients, mostly the mid portion of the LAD (83%) was involved and LAD-DMB was associated with myocardial ischemia in septal segment.

In conclusion, agreement of CTA and CTP in whole heart and in LAD, considering DMB and significant CAD together, were good to excellent; however, considering sole pathologies, most of the agreements were weak (<0.5). Iodine perfusion maps allow visualization of myocardial perfusion and may facilitate the diagnosis of myocardial perfusion defects. Thus, a 384-row detector DSCT scanner could be an efficient and sensitive tool for the diagnosis of coronary stenosis combined with detection of myocardial ischemia in the same examination which would be beneficial for clinical decision-making. However, more studies are needed to further explore this approach for the integrative assessment of patients with known or suspected CAD based on a single, contrast enhanced CT acquisition as the first imaging investigation.

Authors' Contribution

AM: Study design; MF: Data gathering; AZ: Referring patients; RK: Referring patients; MS: Statistical analysis; AB: Major revisions; MR: Data gathering; SA: Data gathering.

Conflict of Interest Disclosures

The authors declare that there are no conflicts of interest.

Ethical Statement

This study was approved by research committee of Iran University of Medical Sciences (IR.IUMS.FMD.REC 1396.9211171024).

References

- Menke J, Kowalski J. Diagnostic accuracy and utility of coronary CT angiography with consideration of unevaluable results: a systematic review and multivariate Bayesian randomeffects meta-analysis with intention to diagnose. Eur Radiol. 2016;26(2):451-8. doi: 10.1007/s00330-015-3831-z.
- Sørgaard MH, Kofoed KF, Linde JJ, George RT, Rochitte CE, Feuchtner G, et al. Diagnostic accuracy of static CT perfusion for the detection of myocardial ischemia. A systematic review and meta-analysis. J Cardiovasc Comput Tomogr. 2016;10(6):450-457. doi: 10.1016/j.jcct.2016.09.003.
- Ko BS, Cameron JD, Defrance T, Seneviratne SK. CT stress myocardial perfusion imaging using multidetector CT—a review. J Cardiovasc Comput Tomogr. 2011;5(6):345-56. doi: 10.1016/j.jcct.2011.10.005.
- Khan A, Khosa F, Nasir K, Yassin A, Clouse ME. Comparison of radiation dose and image quality: 320-MDCT versus 64-MDCT coronary angiography. AJR Am J Roentgenol. 2011;197(1):163-8. doi: 10.2214/AJR.10.5250.
- 5. Ruzsics B, Lee H, Zwerner PL, Gebregziabher M, Costello

P, Schoepf UJ. Dual-energy CT of the heart for diagnosing coronary artery stenosis and myocardial ischemia-initial experience. Eur Radiol. 2008;18(11):2414-24. doi: 10.1007/ s00330-008-1022-x.

- Williams MC, Mirsadraee S, Dweck MR, Weir NW, Fletcher A, Lucatelli C, et al. Computed tomography myocardial perfusion vs 15O-water positron emission tomography and fractional flow reserve. Eur Radiol. 2017;27(3):1114-1124. doi: 10.1007/s00330-016-4404-5.
- ido T, Watanabe K, Saeki H, Shigemi S, Matsuda T, Yamamoto M, et al. Adenosine triphosphate stress dual-source computed tomography to identify myocardial ischemia: comparison with invasive coronary angiography. Springerplus. 2014;3:75. doi: 10.1186/2193-1801-3-75. eCollection 2014.
- Kang MJ, Park CM, Lee CH, Goo JM, Lee HJ. Dualenergy CT: clinical applications in various pulmonary diseases. Radiographics. 2010;30(3):685-98. doi: 10.1148/ rg.303095101.
- 9. McHugh ML. Interrater reliability: the kappa statistic. Biochem Med (Zagreb). 2012;22(3):276-82.
- Meijboom WB, Van Mieghem CA, van Pelt N, Weustink A, Pugliese F, Mollet NR. Comprehensive assessment of coronary artery stenoses. J Am Coll Cardiol. 2008;52(8):636-43. doi: 10.1016/j.jacc.2008.05.024.
- Bettencourt N, Chiribiri A, Schuster A, Ferreira N, Sampaio F, Pires-Morais G, et al. Direct comparison of cardiac magnetic resonance and multidetector computed tomography stress-rest perfusion imaging for detection of coronary artery disease. J Am Coll Cardiol. 2013;61(10):1099-107. doi: 10.1016/j. jacc.2012.12.020.
- 12. Osawa K, Miyoshi T, Koyama Y, Hashimoto K, Sato S, Nakamura K, et al. Additional diagnostic value of first-pass myocardial perfusion imaging without stress when combined with 64-row detector coronary CT angiography in patients with coronary artery disease. Heart. 2014;100(13):1008-15. doi: 10.1136/heartjnl-2013-305468.
- George RT, Arbab-Zadeh A, Miller JM, Kitagawa K, Chang HJ, Bluemke DA, et al., Adenosine stress 64-and 256-row detector computed tomography angiography and perfusion imaging. Circ Cardiovasc Imaging. 2009 May;2(3):174-82.

doi: 10.1161/CIRCIMAGING.108.813766.

- Cabeda EV, Falcão AM, Soares J Jr, Rochitte CE, Nomura CH, Ávila LF, et al., Dipyridamole stress myocardial perfusion by computed tomography in patients with left bundle branch block. Arq Bras Cardiol. 2015;105(6):614-24. doi: 10.5935/ abc.20150117.
- Tamarappoo BK, Gutstein A, Cheng VY, Nakazato R, Gransar H, Dey D, et al. Assessment of the relationship between stenosis severity and distribution of coronary artery stenoses on multislice computed tomographic angiography and myocardial ischemia detected by single photon emission computed tomography. J Nucl Cardiol. 2010;17(5):791-802. doi: 10.1007/s12350-010-9230-6.
- Flohr TG, McCollough CH, Bruder H, Petersilka M, Gruber K, Süss C, et al. First performance evaluation of a dual-source CT (DSCT) system. Eur Radiol. 2006;16(2):256-68.
- Arnoldi E, Lee YS, Ruzsics B, Weininger M, Spears JR, Rowley CP, et al. CT detection of myocardial blood volume deficits: dual-energy CT compared with single-energy CT spectra. J Cardiovasc Comput Tomogr. 2011;5(6):421-9. doi: 10.1016/j. jcct.2011.10.007.
- Pereztol-Valdés O, Candell-Riera J, Santana-Boado C, Angel J, Aguadé-Bruix S, Castell-Conesa J, et al., Correspondence between left ventricular 17 myocardial segments and coronary arteries. Eur Heart J. 2005;26(24):2637-43. doi:10.1093/ eurheartj/ehi496.
- Donato P, Coelho P, Santos C, Bernardes A, Caseiro-Alves F. Correspondence between left ventricular 17 myocardial segments and coronary anatomy obtained by multi-detector computed tomography: an ex vivo contribution. Surg Radiol Anat. 2012;34(9):805-10. doi: 10.1007/s00276-012-0976-1.
- Bruschke AV, Veltman CE, de Graaf MA, Vliegen HW. Myocardial bridging: what have we learned in the past and will new diagnostic modalities provide new insights? Neth Heart J. 2013;21(1):6-13. doi: 10.1007/s12471-012-0355-x.
- 21. Hwang JH, Ko SM, Roh HG, Song MG, Shin JK, Chee HK, et al. Myocardial bridging of the left anterior descending coronary artery: depiction rate and morphologic features by dual-source CT coronary angiography. Korean J Radiol. 2010;11(5):514-21. doi:10.3348/kjr.2010.11.5.514.

© 2019 The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons. org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.