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Diagnostic value of coronary transluminal attenuation gradient in coronary CT Angiography to assess the severity of stenosis

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ABSTRACT

Background: Despite vast technological improvement in recent years, accurate determination of severity of coronary artery stenosis by Coronary CT angiography (CTA) is challenging especially in the case of complex or calcified coronary lesions. Transluminal attenuation gradient (TAG) is a recently developed process which can determine the severity of coronary artery stenosis by measurement of contrast attenuation drop-off along the length of coronary artery. Given the relative paucity of studies in this area,

and possible considerable effect on clinical practice, we aimed to evaluate the accuracy of TAG method for determining stenosis severity of coronary arteries in Iranian population. *Material and Methods:* 82 consecutive patients suspected of having coronary artery disease who underwent 64-slice MSCT coronary angiography and conventional angiography were recruited. Then TAG determined from the change in Hounsfield unit (HU) per 5-mm length of coronary artery and defined as the linear regression coefficient between intra-HU and length from the ostium (millimeters). The diagnostic performance of TAG for detection of significant stenosis was determined and compared by the area under the receiver operating characteristic (ROC) curve. *Result:* Of the 82 patients; 49 (60%) were male and 33 (40%) were female. The mean age of the study population was 56.4 years old. The average value of TAG was -2.87. The TAG was significantly different between patients with significant, and non-significant coronary stenosis (PV<0.0001). The study revealed that all patients with TAG value of lower than -5.55 have significant coronary stenosis. The cut off value was determined -3.56. There was not significant relationship between severity of stenosis and the composition of plaques. There was no significant difference in performance of TAG between patients with soft and calcified plaques (PV=0.260). *Conclusion:* The present study confirms that TAG is the accurate and noninvasive functional method to determine the significant coronary artery stenosis and appears to be able to contribute to improved classification of coronary artery stenosis severity, especially in severely calcified lesions.

Keywords: Transluminal attenuation gradient, coronary CT angiography, Hounsfield unit, region of interest, multislice computed tomography.

1. INTRODUCTION

Cardiovascular disease is the epidemic medical problem of our time and is the most common cause of death in most countries of the world, including Iran, and the most important cause of disablement. The imaging does not last a few minutes and provides very useful information about the anatomy and the state of the heart's internal structures, congenital anomalies, and cardiac arrhythmias (Hendel et al., 2006 and Budoff et al., 2006). Although conventional angiography is a golden standard test to diagnosing coronary artery disease (Hendel et al., 2006; Budoff et al., 2006 and Mollet et al., 2005), but due to some complications and problems and also anxieties that some patients have undergone angiography (Leschka et al., 2005), many attempts have been made, and in the short period the coronary CTA as a noninvasive test replaced as the initial and alternative modality in the clinical evaluation of patients suspected of having coronary artery stenosis (Gallagher et al., 2007; Pugliese et al., 2006 and Muhlenbruch et al., 2007). Currently, the interpretation of coronary CTA is based on the percentage reduction in the diameter or the area of the coronary artery lumen and the severity of the stenosis is divided into significant (more than 50%) or no significant (less than 50%) stenosis (Budoff et al., 2006).

Due to limited spatial resolution and artifacts (caused by calcification or movement) this method is usually challenging and reduces the specificity of determining the severity of stenosis (Ko et al., 2012). So other methods have been considered. Transluminal attenuation gradient has been suggested as a method to evaluate the hemodynamic consequences of a coronary lesion and to enhance the diagnostic performance of coronary CTA alone. In some studies, it was correlation between the TAG and diameter stenosis (Koo et al., 2011 and Choi et al., 2011 and Chow et al., 2011).

The purpose of this study was to determine of TAG of epicardial coronary arteries in patients with coronary artery disease (CAD) and compared it with the stenosis severity measured by diameter stenosis in coronary CTA and also assess the effect of type of plaque (soft or calcified) on our analysis and also try to obtain the TAG cutoff.

2. MATERIAL AND METHODS

We examined 82 consecutive patients with suspected CAD who underwent 64-slice CTA from January 2017 to December 2017 in department of radiology of al-zahrah University Medical Center (Isfahan, Iran). We excluded patients with previous myocardial infarction, previous percutaneous coronary intervention or coronary bypass surgery, unstable angina, and stable angina with 3-vessel disease.

Scanning was performed on 82 consecutive patients; using a 64-slice CT scanner (Aquilion 64; Light Speed VCT; GE Healthcare, Waukesha, WI, USA). The Aquilion 64 is a 64 * 0.5 mm collimation scanner with a gantry rotation speed of 350 ms per rotation. Scanning was performed at 80-140 kV and 800 mAs, and the table feed was 10.6 mm per gantry rotation with a beam pitch of 0.2. Cardiovascular medications were ceased before CCTA apart from beta-blockers. On arrival, an 18-gauge intravenous line was inserted in the right antecubital vein for administration of contrast. The scan was acquired during injection of 55 ml of 100% Omnipaque 350 ml at 5 ml/s, followed by 20 ml of a 30:70 mixture of contrast and saline, followed by 30 ml of saline. Scanning was

triggered in the arterial phase using automated contrast bolus test with the region of interest (ROI) placed in the descending aorta and automatically triggered at 300 HU (Choi et al., 2011).

CT angiographic images were analyzed on a dedicated workstation (GE workstation 4.4) by 2 experienced CT angiographers (a radiologist and a cardiologist). The CT angiographers read independently of each other. Each coronary vessel was analyzed for the composition of plaque and degree of luminal stenosis. Plaque composition was classified as soft (non-calcified) and calcified plaque according to the presence of calcific component (130 Hounsfield units [HU]) in the plaque. Then each coronary vessel visually assessed for degree of luminal stenosis, and a vessel was classified significant if there was more than 50% diameter stenosis and no significant if less than 50% diameter luminal stenosis.

For Transluminal attenuation gradient; Cross-sectional images perpendicular to the vessel centerline; that examined; were reconstructed and the contour of the ROI and the vessel centerline were manually corrected if necessary. The ROI contour was positioned in the center of the cross-sectional images and the wall of the vessel is included. The mean Hounsfield unit at a 5-millimeter distance was measured, where the cross-sectional vessel was visible (from the ostium to a distal level). Soft or calcified plaque if it was on the site of the area of interest, may measure. The below factors from the ostium to the distal level were measured at a 5-millimeter distance: Intraluminal attenuation (HU) and distance from ostium (mm), TAG was determined from the change in Hounsfield unit per 5-millimeter length of CA and defined as the linear regression coefficient between intra-Hounsfield unit and length from the ostium (mm).

Statistical analysis

We consider multilevel random intercept model with two nested levels patient ID and distance, which severity regarded as binary outcome and, type of plaque and TAG as independent variables. The ROC curve used to display the cutoff point of TAG. The Pearson correlation of density between any pair of distances calculated. MLwiN (Centre for Multilevel Modelling, University of Bristol), the statistical software package for fitting multilevel models and also SPSS 22.0 (SPSS Inc., Chicago, Illinois) had been used. P value 0.05 was considered statistically significant.

Ethical Consideration

The institutional ethics committee approved the research protocols, and all patients gave informed consent. The ethical committee code is IR.MUI.REC.1396.3.456.

3. RESULTS

Patient Characteristics

The study group consist 82 patients; 49 (60%) patients were male and 33 (40%) patients were female. The mean (S.D) age of the study population was 56. We divided the patient in two groups: on group were the patients with significant stenosis (n=37) and other the patients with no significant stenosis (n=45) based on "diameter percentage of stenosis" (cut off of 50%) on Coronary CT Angiography. Also we compared our knowledge with coronary conventional angiography as a gold standard test. The percentage chance that the "diameter percentage of stenosis on Coronary CT Angiography" correctly identify a person who actually has the significant stenosis by coronary conventional angiography as a gold standard test in this study; is equal to 92.3%, 95% Bootstrapping Confidence Interval (BCI) (82.9%-100%). The percentage of patients without significant stenosis that receive a similar result is equal to 93.8%, 95% BCI (77.8%-100%). Positive and negative predictive values are 97.2%, 95% BCI (90.7%-100%) and 93.3% with 95% BCI (64.0%-100%) respectively (Table1).

Table 1 Distribution of Significant and no significant Stenosis in CT Angiography in Cross with Conventional Angiography as A Golden Test

		Conventional Angiography	
		Significant Stenosis	Non-Significant Stenosis
CT Angiography	Significant Stenosis	36(43.9%)	1(1.2%)
	Non-Significant Stenosis	3(3.65%)	42(51.2%)
	PPV=97.2%, NPV=93.3%		

According to multilevel random intercept model, Component of variance (effect size (S.E): 3.675(0.629)) in random intercept reduced model was statistically significant (PV<0.0001). As can see in table 2 there isn't significant relationship between severity and type of plaque, but the decreasing one unit of TAG, increase 1.51 times odds of significant stenosis.

Table 2 Coefficient of Multilevel Random Intercept Model

	Coefficients	S.E	Odds Ratio(95% CI*)
Intercept	2.668	0.589	-
TAG**	0.922	0.156	2.51(1.85-3.41)
Type of Plaque(Ref: soft)	0.221	0.935	1.24(0.199-7.79)
Variance(S.E***) of Random Intercept(9.019(1.59))			

*Confidence Interval

** Transluminal Attenuation Gradient

***Effect Size

The ROC curve display the cutoff point -3.56 for TAG, AUC= 0.877 (95%CI: (0.851-0.903)); the Sensitivity plus Specificity are 1.66 (Fig 1-5). The data shows when the TAG is lower than -5.55 all of patient can achieve to significant stenosis. Total mean (S.E) of TAG is -2.87(0.28), the TAG is significantly different (PV<0.0001) in patients with significant stenosis -4.71(0.36) in compare with no significant stenosis -1.30(0.23), but our finding doesn't represent differences between patients with soft -3.01(0.32) and calcified 2.18(0.53) type of plaque (PV=0.260).

The multilevel regression model represents the density (dependent variable) with each 5mm distance from the ostium decrease about 3.17 HU. The Pearson correlation of density between any pair of distances with early arteries reported in table 3 &4 and figure 1. The correlation coefficients are smaller when the distances are bigger.

Table 3 The Correlation Coefficient of Density According to Distance from Ostium

	5mm Distance	10mm Distance	15mm Distance	20mm Distance	25mm Distance	30mm Distance	35mm Distance	40mm Distance	45mm Distance	50mm Distance	55mm Distance	60mm Distance
Early Arteries	.924**	.892**	.854**	.819**	.751**	.703**	.658**	.619**	.572**	.479**	.167	-.333
N	82	82	82	82	82	82	82	82	77	60	26	10

** P. value <0.001,

Table 4 The Correlation Coefficient of Density According to Distance from Early Arteries Split by Severity

	5mm Distance	10mm Distance	15mm Distance	20mm Distance	25mm Distance	30mm Distance	35mm Distance	40mm Distance	45mm Distance
Significant Stenosis (N=37)									
Ostium	.941**	.827**	.556**	.721**	.737**	.586**	.701**	.677**	.682**
Non-significant Stenosis (N=45)									
Ostium	.774**	.577**	.346*	.525**	.623**	.474**	.590**	.640**	.701**

** P. V<0.001, * P. V<0.05,

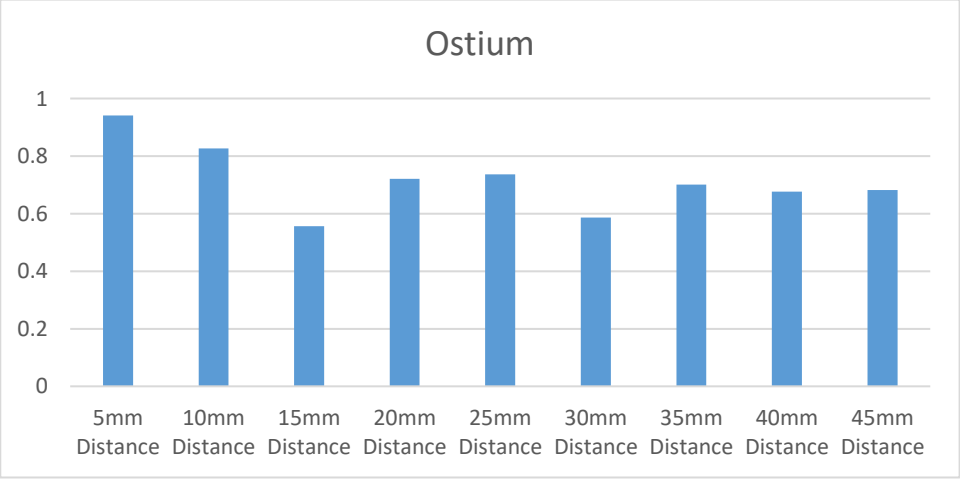

Figure 1 The Correlation Coefficient of Density According to Distance from Early Arteries Split by Severity

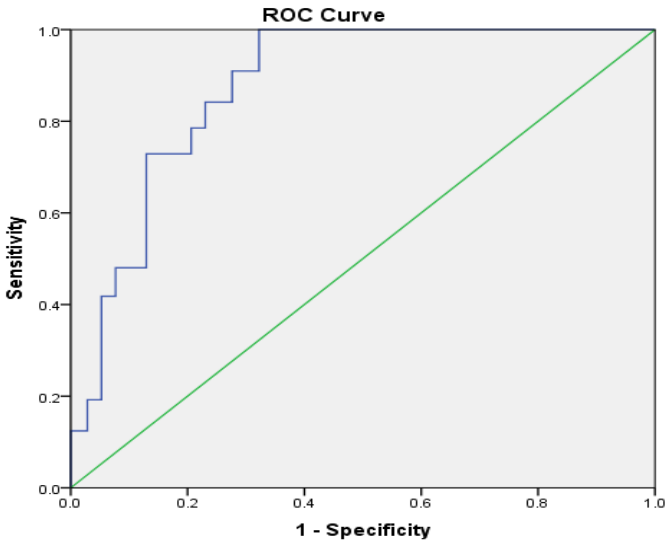

Figure 2 ROC Curve for Predict Severity by TAG

Figure 3 Coronary CT Angiography, Posterior Lateral Branch

4. DISCUSSION

The current study was directed to evaluate the potential of TAG to assess the severity of coronary stenosis diagnosed by coronary CTA compared with routine assessment by diameter stenotic percentage (cutoff of 50%). The results demonstrate that TAG does improve the diagnostic accuracy over 64-slice coronary CTA alone to diagnose severity-significant lesions.

Current method to analysis of severity of coronary stenosis is to determine the percentage of occlusion in diameter in cross section of vessel in site of stenosis. Using a diameter stenosis threshold of 50% of coronary CTA displayed an excellent sensitivity and negative predictive value (Hendel et al., 2006; Budoff et al., 2006 and Mollet et al., 2005) So if the plaque is more than 50% occupied the cross section of vessel lumen, it classified as significant stenosis (Min et al., 2007). But multiple pitfall and artifacts had cause to overestimate or underestimate of severity of stenosis. Multiple additional methods were assessed that be help to rise our confidence of severity assessment. For instance, some studies have assessed combined coronary CTA and CT perfusion as a method to provide both anatomic and functional assessment of coronary stenosis (Danad et al., 2014 and Choi et al., 2012). But TAG is one of the new methods that describe recently. Wong et al. (Wong et al., 2013) and Choi et al. (Choi et al., 2011) and Stuijfzand et al.

(Stuijfzand et al., 2014) compared Transluminal Attenuation Gradient of Coronary CTA by conventional angiography. Although the data was conflicting, but most of them support the TAG as the useful method (Choi et al., 2011 and Stuijfzand et al., 2014).

Figure 4 Coronary CT Angiography, Left Anterior Descending Artery

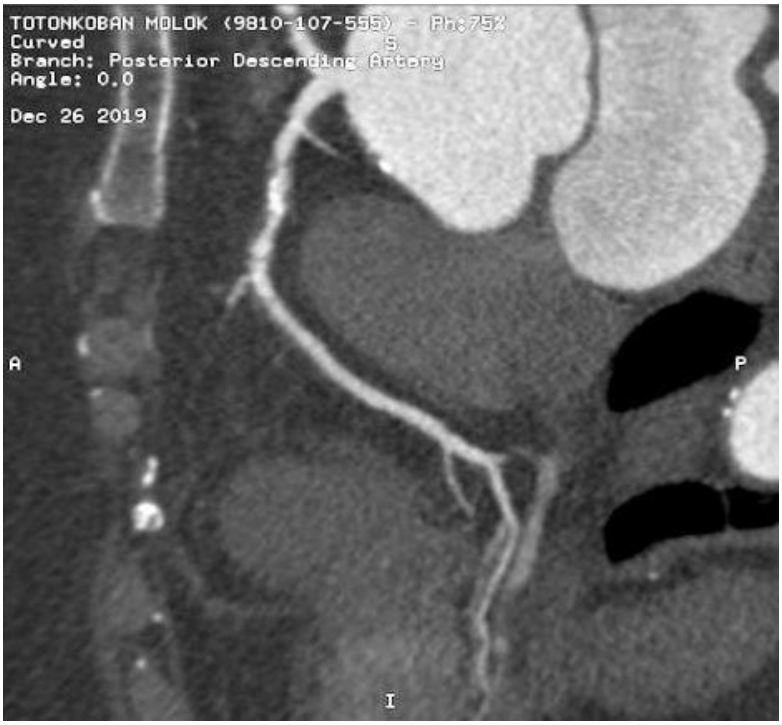

Figure 5 Coronary CT Angiography, Posterior Descending Artery

First we compare our CCTA analysis (determination of severity by diameter) by conventional angiography, and shows correctly identify severity of stenosis by CCTA (equal to 92.3%, 95% Bootstrapping CI (82.9%-100%)). Then we determined TAG of each vessel. TAG decreased significantly according to severity of stenosis that determined by CCTA (PV<0.0001). Other similar studies show different result; for example, Stuijfzand et al. (Stuijfzand et al., 2014) demonstrate that the TAG doesn't evidently improve the diagnostic accuracy of coronary CTA to diagnose severity of stenotic lesions. The sample size of the current study was relatively

small and also intracoronary adenosine administration was used to achieve vasodilation. So it may have effect on concentration of contrast material and consequently on the final result. Other studies compare the accuracy of TAG with conventional angiography and showed that TAG, which provides information on the functional significance of coronary artery stenosis by reflecting the gradient of intraluminal attenuation across the lesion, can refine the attenuation values, which are influenced by various signification of anatomic coronary CTA stenosis severity artifacts including partial volume effects, image compared with invasive coronary angiography as a reference standard (Ko et al., 2012 and Einstein, 2013).

But our study demonstrates a relationship between coronary stenosis severities assessed by 64-slice CTA in two different methods (compare severity in to method in only one study). We have also evaluated value of type of plaques in discriminating significant coronary arterial stenosis (effect of type of plaque (soft Vs calcified) to assess the severity). Our finding doesn't show any different between patients with soft and calcified type of plaque. Also our study demonstrates the TAG cutoff of -3.56. In sum; The current study examined the diagnostic accuracy of TAG and diameter stenosis, to determine the severity stenosis of coronary arteries (significant Vs no significant) and definition the cutoff point for TAG for better evaluation of severity.

5. CONCLUSION

We assess two functional and anatomic methods and confirm that TAG is the accurate and noninvasive functional method to determine the significant coronary artery stenosis. Cut off point of -3.56 HU can increase our accuracy of diagnosis. Also the current study demonstrates that the type of plaque does not show any difference between two groups of soft and calcified plaques.

Study limitations

This is a descriptive study on a small sample that may lead to an inappropriate estimate of the CTA findings. In addition, the lack of a comparison group only pushed us to describe the findings. Larger studies are required to determine the diagnostic and prognostic value of combined TAG and diameter stenosis in coronary CTA assessment.

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Conflicts of Interest: The authors declare no conflict of interest.

Author's Contribution

MK: Study idea, study design, interpretation and contribution in writing the paper, Final approval of the version
PA: contributed in data collection and data analysis and preparation of paper (corresponding author)
MM: study design, contributed in interpretation of CTA, Final approval of the version
MF: revising paper for important intellectual content, Final approval of the version, contributed in interpretation of CTA
FA: revising paper for important intellectual content, Final approval of the version, contributed in interpretation of CTA

List of abbreviations

CTA: Computed tomography angiography.
TAG: Transluminal attenuation gradient.
HU: Hounsfield unit.
ROC: Receiver operating characteristic.
CAD: Coronary artery disease.

REFERENCE

1. Bamberg F, Becker A, Schwarz F, Marcus RP, Greif M, von Ziegler F, et al. Detection of hemodynamically significant coronary artery stenosis: incremental diagnostic value of dynamic CT-based myocardial perfusion imaging. Radiology 2011;260:689-98.
2. Becker A, Becker C. CT imaging of myocardial perfusion: possibilities and perspectives. J Nucl Cardiol 2013;20:289-96.
3. Budoff MJ, Achenbach S, Blumenthal RS, Carr JJ, Goldin JG, Greenland P, et al. Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from

the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. Circulation 2006;114:1761-91.

4. Choi JH, Koo BK, Yoon YE, Min JK, Song YB, Hahn JY, et al. Diagnostic performance of intracoronary gradient-based methods by coronary computed tomography angiography for the evaluation of physiologically significant coronary artery stenoses: a validation study with fractional flow reserve. Eur Heart J Cardiovasc Imaging 2012;13:1001-7.
5. Choi JH, Min JK, Labounty TM, Lin FY, Mendoza DD, Shin DH, et al. Intracoronary transluminal attenuation gradient in coronary CT angiography for determining coronary artery stenosis. J Am oll Cardiol Img. 2011;4:1149 -57.
6. Chow BJ, Kass M, Gagné O, Chen L, Yam Y, Dick A, et al. Can differences in corrected coronary opacification measured with computed tomography predict resting coronary artery flow? J Am Coll Cardiol 2011;57:1280-8.
7. Danad I, Raijmakers PG, Harms HJ, van Kuijk C, van Royen N, Diamant M, et al. Effect of cardiac hybrid 15 O-water PET/CT imaging on downstream referral for invasive coronary angiography and revascularization rate. Eur Heart J Cardiovasc Imaging 2014;15:170-9.
8. Einstein AJ. TAG-is it it? Improving coronary computed tomography angiography with the isotemporal transluminal contrast attenuation gradient. J Am Coll Cardiol 2013;61:1280-2.
9. Gallagher MJ, Ross MA, Raff GL, Goldstein JA, O'Neill WW, O'Neil B. The diagnostic accuracy of 64-slice computed tomography coronary angiography compared with stress nuclear imaging in emergency department low risk chest pain patients. Ann Emerg Med 2007;49:125-36.
10. Hendel Rc, Patel Mr, Kramer Cm, Poon M, Hendel Rc, Carr Jc, et al. Accf/Acr/Scct/Scmr/Asnc/Nasci/Scai/Sir 2006 Appropriateness Criteria For Cardiac Computed Tomography And Cardiac Magnetic Resonance Imaging: A Report Of The American College Of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American College Of Radiology, Society Of Cardiovascular Computed Tomography, Society For Cardiovascular Magnetic Resonance, American Society Of Nuclear Cardiology, North American Society For Cardiac Imaging, Society For Cardiovascular Angiography And Interventions, And Society Of Interventional Radiology. J Am Coll Cardiol 2006;48:1475-97.
11. Ko BS, Cameron JD, Meredith IT, Leung M, Antonis PR, Nasis A, et al. Computed tomography stress myocardial perfusion imaging in patients considered for revascularization: a comparison with fractional flow reserve. ur eart J 2012;33:67-77.
12. Koo BK, Erglis A, Doh JH, Daniels DV, Jegere S, Kim HS, et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. Results from the prospective multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve) study. J Am coll cardiol 2011;58:1989-97.
13. Leschka S, Alkadhi H, Plass A, Desbiolles L, Grunenfelder J, Marincek B, et al. Accuracy of MSCT coronary angiography with 64-slice technology: first experience. Eur Heart J 2005;26:1482-7.
14. Min JK, Koo BK, Erglis A, Doh JH, Daniels DV, Jegere S, et al. Usefulness of noninvasive fractional flow reserve computed from coronary computed tomographic angiograms for intermediate stenoses confirmed by quantitative coronary angiography. Am J Cardiol 2012;110:971-6.
15. Min JK, Shaw LJ, Devereux RB, Okin PM, Weinsaft JW, Russo DJ, et al. Prognostic value of multi detector coronary computed tomographic angiography for prediction of all-cause mortality. J Am Coll Cardiol 2007;50:1161-70.
16. Mollet NR, Cademartiri F, Van Mieghem CA, Runza G, McFadden EP, Baks T, et al. High-resolution spiral computed tomography coronary angiography in patients referred for diagnostic conventional coronary angiography. Circulation 2005;112:2318-23.
17. Muhlenbruch G, Seyfarth T, Soo CS, Pregalathan N, Mahnken AH. Diagnostic value of 64-slice multi-detector row cardiac CTA in symptomatic patients. Eur Radiol 2007;17:603-9.
18. Pugliese F, Mollet NR, Runza G, van MC, Meijboom WB, Malagutti P, et al. Diagnostic accuracy of non-invasive 64slice CT coronary angiography in patients with stable angina pectoris. Eur Radiol 2006;16:575-82.
19. Sato A, Hiroe M, Tamura M, Ohigashi H, Nozato T, Hikita H, et al. Quantitative measures of coronary stenosis severity by 64-Slice CT angiography and relation to physiologic significance of perfusion in non obese patients: comparison with stress myocardial perfusion imaging. J Nucl Med 2008;49:564-72.
20. Schuijf JD, Wijns W, Jukema JW, Atsma DE, de Roos A, Lamb HJ, et al. Relationship between noninvasive coronary angiography with multislice computed tomography and myocardial perfusion imaging. J Am Coll Cardiol 2006;48:2508-14.
21. Shreibati JB, Baker LC, Hlatky MA. Association of coronary CT angiography or stress testing with subsequent utilization and spending among Medicare beneficiaries. JAMA 2011;306:2128-36.
22. Stuijfzand WJ, Danad I, Raijmakers PG, Marcu CB, Heymans MW, van Kuijk CC, et al. Additional value of transluminal attenuation gradient in CT angiography to predict

hemodynamic significance of coronary artery stenosis. JACC Cardiovasc Imaging 2014;7:374-86.

23. Tonino PA, Fearon WF, De Bruyne B, Oldroyd KG, Leesar MA, Ver Lee PN, et al. Angiographic versus functional severity of coronary artery stenoses in the FAME study fractional flow reserve versus angiography in multivessel evaluation. J Am Coll Cardiol 2010;55:2816-21.
24. Wong DT, Ko BS, Cameron JD, Nerlekar N, Leung MC, Malaiapan Y, et al. Transluminal attenuation gradient in coronary computed tomography angiographyisa novel noninvasive approach to the identification of functionally significant coronary artery stenosis: a comparison with fractional flow reserve. J Am Coll Cardiol 2013;61:1271-9.