REVIEW ARTICLE—CARDIOVASCULAR IMAGING FOR NUCLEAR CARDIOLOGISTS

Plaque Imaging Using Coronary Computed Tomography Angiography

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Received: December 12, 2017/Accepted: December 28, 2017
J-STAGE Advance published: February 28, 2018

Abstract

Coronary computed tomography angiography (CCTA) is the most commonly used modality for noninvasive plaque imaging in clinical settings. Characteristics of rupture-prone vulnerable plaques include positive remodeling, low attenuation, and napkin-ring sign in CCTA. About 60% of all vulnerable plaques have these characteristics, and these coronary lesions often result in plaque rupture. Identification of such groupings of coronary artery characteristics has been used to predict cardiovascular events.
Keywords: Comprehensive plaque imaging, Coronary computed tomography angiography, Vulnerable plaque
Ann Nucl Cardiol 2018; 4 (1): 132−136

Accurate risk stratification of future cardiovascular events may help prevent cardiovascular events and contribute to the development of a treatment strategy. To date, however, detecting vulnerable coronary arterial plaque remains a challenge. Currently in clinical settings, there is no established method of detecting vulnerable plaque that may lead to acute coronary syndrome (ACS). Braunwald addressed the limitations of the Framingham risk score for risk stratification of ACS in primary prevention. Cardiac imaging should be able to identify those at very high risk (15% or higher per year) of ACS (1). The pathological findings of ACS include plaque rupture (in 55-60% of patients), erosion (in 30-35%), and calcified nodule (in 3-7%) (2). About 60% of vulnerable plaque is associated with thin-capped fibroatheroma (TCFA) causing plaque rupture. The characteristics of arterial plaque also include positive vascular remodeling and a large necrotic core. Vulnerable plaque also has new blood vessel (vasa vasorum) formation. Characteristics of vulnerable plaque include fibrous capsule thickness of less than 65μ, macrophage infiltration of the fibrous capsule, and matrix metalloproteinase expression (3).

Current status of plaque imaging using coronary CT angiography

The most advanced research tool for noninvasive imaging of vulnerable plaque is currently coronary computed tomography angiography (CCTA) because of its versatility and its high image resolution. CCTA can provide data on several factors including positive remodeling of coronary arteries, plaque burden, and severity of coronary arterial stenosis. CCTA also provides information regarding necrotic core regions, in which the density of the lipid pool can be assessed based on the CT data. Lesions related to ACS have significant spotty calcification, positive remodeling (remodeling index >1.1), and low-attenuation plaque (CT<30 HU) as found in CCTA (Fig. 1a, Table 1) (4). Plaques with these characteristics are now referred to as having the napkin-ring sign (NRS). NRS is associated with a large necrotic core. This is a characteristic of vulnerable plaque (5-7) (Fig. 1b). The specificity of this NRS for detecting vulnerable plaque is relatively high based on autopsy studies but the sensitivity of this sign is low (6). Several studies have reported the prognostic value of vulnerable plaque identification through CCTA imaging.

doi: 10.17996/anc.18-00051

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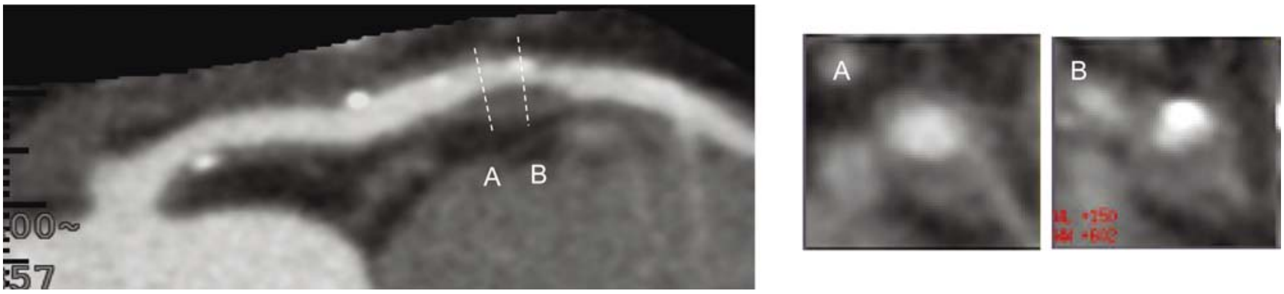


a

b

Fig. 1 Coronary CT-verified vulnerable plaque.
a: Plaque with positive remodeling, low attenuation and spotty calcification is regarded as vulnerable plaque in coronary CT angiography.
b: The napkin-ring sign can be defined as the presence of two features: a central area of low CT attenuation that is apparently in contact with the lumen and a ring-like higher-attenuation plaque tissue surrounding this central area.

Table 1 Parameters and signs of coronary plaque with CCTA

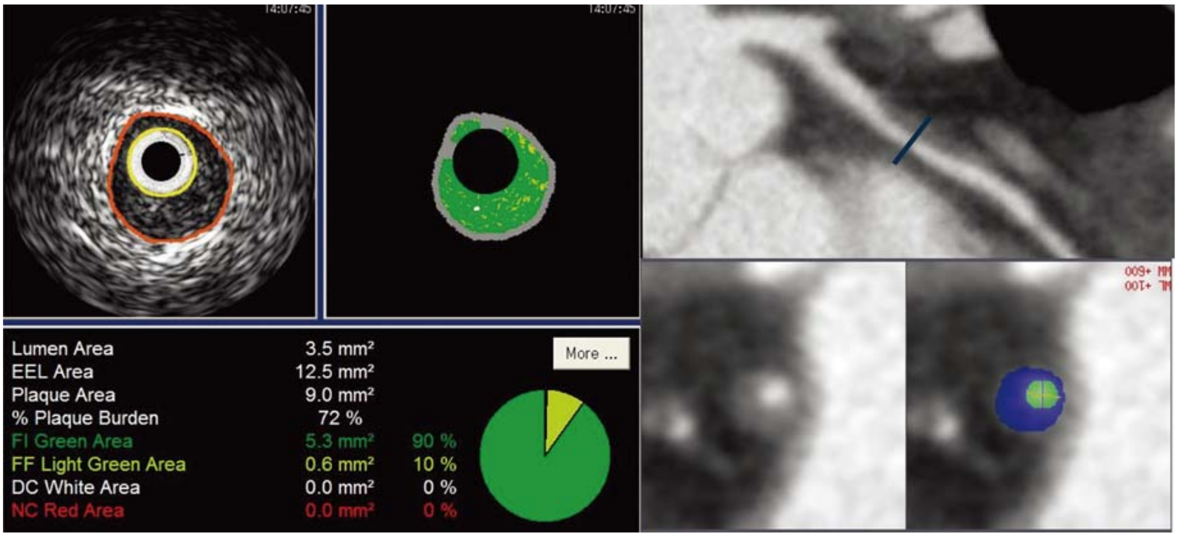
Parameter	Description and definitions
Positive remodeling	Ratio of outer vessel diameter at the site of plaque divided by the average outer diameter of the proximal and distal vessel greater than 1.1, or Av/[(Ap þ Ad)/2] >1.1
Napkin-ring sign	Central low-attenuation plaque with a peripheral rim of higher CT attenuation
Low-attenuation plaque	Non-calcified plaque with internal attenuation less than 30 HU
Spotty calcification	Punctate calcium within a plaque

Prognostic value of coronary plaque identification through CCTA

Motoyama et al. noted specific characteristics of coronary plaque, identified through CCTA, such as positive remodeling (remodeling index >1.1) and low attenuation (CT<30HU). Coronary plaque meeting one of these 2 conditions is referred to as 1-feature positive plaque (1FPP). Motoyama et al. observed the outcomes of patients with these coronary plaques for a period of 2 years. During the observational period, 10 (22.2%) of 45 cases with 2FPP had ACS. In contrast, only one (3.7%) of 27 cases with 1FPP, and only 4 (0.5%) of 820 patients without any features associated with positive plaque had ACS (8). Otsuka et al. evaluated 1,174 plaques in 12,727 segments in 895 subjects (mean: 2.3±0.8 years follow-up period). As were several CT findings, such as positive remodeling and low-attenuation plaque, the napkin-ring sign was an independent predictor for acute coronary syndrome (9).

Relationship between anatomical coronary stenosis and plaque vulnerability

The relationship between the severity of coronary stenosis, plaque burden, and vulnerability of plaque has been noted. Narula et al. investigated 295 coronary arterial lesions in 213 autopsy cases of sudden cardiac death. In contrast to previous studies, their findings for cases of ACS of the vascular cross-sectional area showed ruptured plaque in 70% of coronary lesions. Only 5% of lesions at rupture sites had <50% stenosis. In addition, in its precursor lesion, TCFA, about 40% showed >75% stenosis of the vascular cross-sectional area, and only about 10% showed <50% cross-sectional stenosis. This finding may indicate the importance of plaque burden and severity of coronary arterial lumen stenosis for identification of vulnerable plaque (10). Rapidly growing plaque with characteristics of TCFA may indicate higher risk for ACS onset (11). Therefore, vulnerable plaque with more severe coronary arterial lumen stenosis is associated with higher



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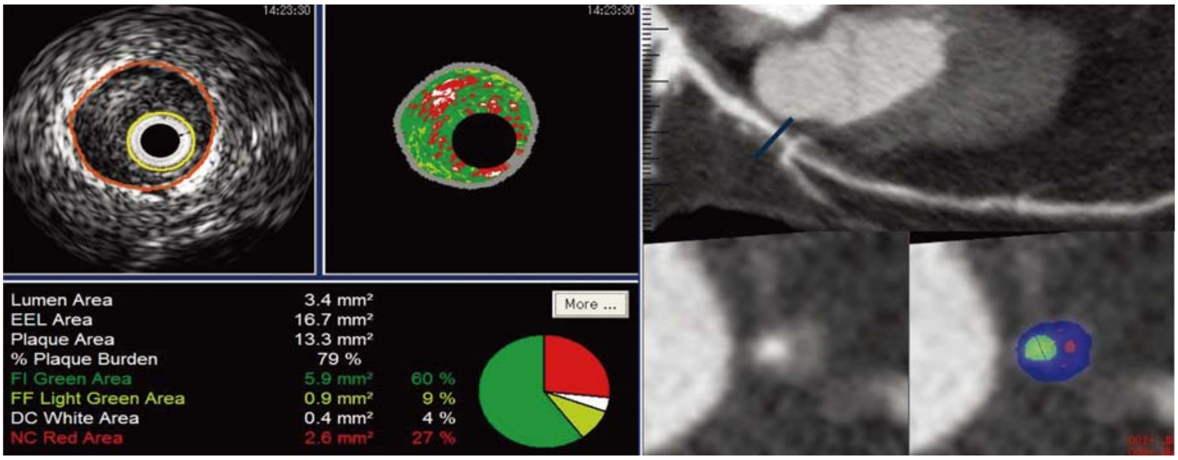

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Fig. 2 Plaque morphology analysis by the labeling method and by VH-IVUS.
Properties of fibrous plaque (**a**) and plaque accompanied by a necrotic core area (**b**) on VH-IVUS were similarly analyzed objectively and quantitatively through coronary arterial CT using the labeling method.
VH-IVUS: virtual histology intravascular ultrasound

cardiac event risk. The characteristics of vulnerable plaque, as identified through CCTA, and rapid plaque progression have been reported to be strong predictors for cardiovascular events (12). CCTA can be used to accurately evaluate plaque burden and coronary arterial lumen stenosis. Meta-analysis of 42 studies revealed that sensitivity and specificity of coronary CTA to detect any plaque and that of intravascular ultrasound were 93% and 92%, respectively, with an area under the receiver-operating curve of 0.97 (13).

Problem of plaque imaging by coronary CT angiography

The usefulness of plaque evaluation through CCTA has been reported as described above. However, there are also problems associated with plaque detection through CCTA. Although coronary artery calcium score, the severity of stenosis of the lesion, and number of diseased vessels have been recognized as strong predictors of cardiovascular events identified through CCTA (14, 15), limited studies have demonstrated the incremental prognostic value of plaque evaluation using CCTA (16). Moreover, few studies have evaluated incremental prognostic value of CCTA plaque estimation in either primary prevention or secondary prevention. It is also not clear whether CCTA plaque estimation has incremental prognostic value over conventional risk assessment such as the Framingham risk score (16).

Another problem is the lack of objective assessments for plaque severity. To date, necrotic core area, fibrous area, and level of calcification of the plaque have been quantitatively evaluated based on CT numbers. However, various factors, such as the contrast-medium concentration in the coronary arterial lumen, the severity of stenosis of coronary arterial lesions, artifact for calcification, and tube voltage, can influence CT numbers. Meta-analysis of literature reporting on 36 studies involving CT number-based plaque properties analysis revealed large variations in the CT numbers of lipid-rich and fibrous plaque. Many problems remain to be solved before this method can be determined suitable for clinical settings (17). For example, plaque property analysis corrected through contrast attenuation is required (18). As well, subjective plaque tissue characteristics analysis (labeling method) through the addition of 3-dimensional distribution, and noise-employing clustering analysis would be needed (19) (Fig. 2). Further investigations and development of a standardized index would also be necessary prior to any clinical application of this method.

Conclusions

At present, CCTA is considered the most advanced modality for noninvasively detecting coronary plaque. However, it is necessary to establish quantitative approaches and evidences based on large-scale prospective multicenter clinical trials. Evaluation of not only the anatomy and morphology but also the physiology by CCTA has recently become possible. Comprehensive evaluation of these may facilitate plaque imaging with high accuracy for predicting cardiovascular events.

Acknowledgments

None.

Sources of funding

None.

Conflicts of interest

None.

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References

1. Braunwald E. Epilogue: what do clinicians expect from imagers? J Am Coll Cardiol 2006; 47 (8 Suppl): C101-3.
2. Virmani A, Burke AP, Farb A, et al. Pathology of the vulnerable plaque. J Am Coll Cardiol 2006; 47 (8 Suppl): C13-8.
3. Narula J, Finn AV, Demaria AN. Picking plaques that pop... J Am Coll Cardiol 2005; 45: 1970-3.
4. Motoyama S, Kondo T, Sarai M, et al. Multislice computed tomographic characteristics of coronary lesions in acute coronary syndromes. J Am Coll Cardiol 2007; 50: 319-26.
5. Maurovich-Horvat P, Hoffmann U, Vorpahl M, et al. The napkin-ring sign: CT signature of high-risk coronary plaques? JACC Cardiovasc Imaging 2010; 3: 440-4.
6. Maurovich-Horvat P, Schlett CL, Alkadhi H, et al. The napkin-ring sign indicates advanced atherosclerotic lesions in coronary CT angiography. JACC Cardiovasc Imaging 2012; 5: 1243-52.
7. Seifarth H, Schlett CL, Nakano M, et al. Histopathological correlates of the napkin-ring sign plaque in coronary CT angiography. Atherosclerosis 2012; 224: 90-6.
8. Motoyama S, Sarai M, Harigaya H, et al. Computed tomographic angiography characteristics of atherosclerotic plaques subsequently resulting in acute coronary syndrome. J Am Coll Cardiol 2009; 54: 49-57.
9. Otsuka K, Fukuda S, Tanaka A, et al. Napkin-ring sign on coronary CT angiography for the prediction of acute coronary syndrome. JACC Cardiovasc Imaging 2013; 6: 448-57.
10. Narula J, Nakano M, Virmani R, et al. Histopathologic characteristics of atherosclerotic coronary disease and implications of the findings for the invasive and noninvasive detection of vulnerable. J Am Coll Cardiol 2013; 61: 1041-51.
11. Ahmadi A, Leipsic J, Blankstein R, et al. Do plaque rapidly progress prior to myocardial infarction? The interplay between plaque vulnerability and progression. Cir Res 2015; 117: 99-104.
12. Motoyama S, Ito H, Sarai M, et al. Plaque characterization by coronary computed tomography angiography and the likelihood of acute coronary events in mid-term follow-up. J Am Coll Cardiol 2015; 66: 337-46.
13. Fischer C, Hulten E, Belur P, et al. Coronary CT angiography versus intravascular ultrasound for estimation of coronary stenosis and atherosclerotic plaque burden: a meta-analysis. J Cardiovasc Comput Tomogr 2013; 7: 256-66.
14. Min JK, Dunning A, Lin FY, et al. Age- and sex-related differences in all-cause mortality risk based on coronary computed tomography angiography findings results from the International Multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) of 23, 854 patients without known coronary artery disease. J Am Coll Cardiol 2011; 58: 849-60.
15. Greenland P, Bonow RO, Brundage BH, et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) developed in collaboration with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol 2007; 49: 378-402.
16. Fujimoto S, Kondo T, Takamura K, et al. Incremental prognostic value of coronary computed tomographic angiography high-risk plaque characteristics in newly symptomatic patients. J Cardiol 2016; 67: 538-44.
17. Kristanto W, van Ooijen PM, Jansen-van der Weide MC, et al. A meta analysis and hierarchical classification of HU-based atherosclerotic plaque characterization criteria. PLos One

2013; 8: e73460.

18. Obaid DR, Calvert PA, Gopalan D, et al. Atherosclerotic plaque composition and classification identified by coronary computed tomography: assessment of computed tomography-generated plaque maps compared with virtual histology intravascular ultrasound and histology. Circ Cardiovasc Imaging 2013; 6: 655-64.
19. Fujimoto S, Kondo T, Kodama T, et al. A novel method for non-invasive plaque morphology analysis by coronary computed tomography angiography. Int J Cardiovasc Imaging 2014; 30: 1373-82.