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Noninvasive Functional Characterization of Coronary Plaques by Coronary Computed Tomography – Beyond the Morphology of Vulnerable Plaques

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ABSTRACT

Coronary computed tomography angiography (CCTA) is a reliable screening method of patients with coronary artery disease (CAD). CCTA is capable of both assessment of coronary stenosis and plaque morphology, but does not provides hemodynamic characterization of the coronary lesions. However the severity of coronary stenosis does not always reflect the hemodynamic significance of plaque. Invasive fractional flow reserve (FFR) is considered as gold standard for the functional evaluation of a potential ischemia-causing stenosis. FFR derived from CCTA (FFR-CT) is a new non-invasive diagnostic tool, using a typically acquired CCTA, without the need for any further radiation or medication. Additional functional assessment of the coronary lesions permit a more complex characterization of CAD patients. Based on the of FFR-CT examination, those patients who need invasive coronary intervention can be selected more precisely, and a more personalized and optimized treatment can be provided.

Keywords: coronary computed tomography angiography, coronary artery disease, invasive fractional flow reserve

INTRODUCTION

Cardiovascular diseases are the number one cause of death and long term disability in industrialized countries, mainly due to coronary artery disease (CAD). Despite the new improved screening methods (coronary computed tomography angiography – CCTA, inflammatory biomarkers) and therapeutic modalities, morbidity and mortality caused by CAD have shown increasing rates in the last decades, and several prospective studies suggest that this tendency will continue globally.[1] In addition, only in the USA the CAD morbidity is predicted

to increase with 8.6% by 2030.[2] In the majority of the affected population acute myocardial infarction (AMI) and sudden cardiac death represent the first manifestation of CAD, which means that half of the population at risk does not experience any symptoms before the major coronary event occurs.[3]

Effective prevention and treatment of CAD could reduce the prevalence of acute coronary events and ameliorate morbidity and mortality rates.[4] Noninvasive assessment of the coronary arteries could play an important role in patients risk stratification, however selecting patients at risk for acute coronary events remains an important challenge in cardiovascular imaging. Currently the coronary angiography is considered as a gold standard for the assessment of the integrity of the coronary arteries and able to identify luminal narrowing lesions above 20–30%, but does not provide information about the features of plaque morphology. Current strategies do not focus sufficiently on the characterization of coronary atherosclerotic plaques, but mostly on the detection of myocardial ischemia and hemodynamically significant stenosis, though in many cases due to positive remodeling of the plaques that are prone to rupture do not cause significant luminal narrowing on the coronary angiography.[5] The recent guidelines of the European Society of Cardiology (ESC) strongly recommend the use of CCTA as a first line noninvasive functional assessment of myocardial ischemia in patients with angina-like symptoms that might me caused by obstructive CAD.[3]

ROLE OF CCTA AS A NONINVASIVE EVALUATION OF CARDIOVASCULAR RISK

CCTA is a widely used diagnostic method, which demonstrated its reliability in the screening of patients with suspected obstructive CAD. The advantage of this imaging technique is that it is capable of both assessment of coronary stenosis severity and plaque morphology.[6] Based on CCTA exams, it was demonstrated that plaques that are prone to rupture have different morphological structure than stable plaques. According to these findings, CCTA helps to define those lesions that need invasive coronary intervention, preventing and these adverse coronary events.[7] Recently published studies evidenced that characterization by morphological structure and the atherosclerotic plaque burden determined by CCTA was superior in the prediction of major coronary events compared to conventional coronary angiography.[8]

Based on CCTA imaging, by comparing the morphological features, coronary plaques can be defined as stable or vulnerable ones. Vulnerable plaques are larger in size than stable lesions, respectively exhibit a large lipid rich necrotic core with a low CT attenuation (<30 Hounsfield Units). Spotty calcification is another characteristic feature of vulnerability, defined as a small dense plaque parts surrounded by non-calcified plaque tissue. Positive remodeling often occurs in cause if instable plaques, which consists of compensatory enlargement of the affected vessel, as the size of the lesion increases resulting in preservation of the vascular lumen, without causing significant stenosis on coronary angiogram.[9] Napkin-ring sign is a relatively recent discovery, a qualitative plaque feature, described as a central low CT attenuation area supposedly in contact with the vascular lumen, surrounded with higher CT attenuation plaque tissue.[10]

However, CCTA is able to provide a complex characterization and risk stratification based on the morphological characteristics of the coronary lesions, compared to ICA, functional assessment of these plaques is necessary in order the determine the hemodynamic significance and their of role in causing ischemia.

CCTA-BASED FUNCTIONAL PLAQUE CHARACTERIZATION

General atherogenic risk factors (smoking, arterial hypertension, diabetes mellitus etc.) are affecting all the segments of the coronary systems, even so the luminal narrowing coronary lesions appear only in some section of coronary arteries, such as outer walls of bifurcation, the inner curve of arteries, or in side branches. Hemodynamic factors (endothelial shear stress – ESS) are considered to play an important role in the development and localization of coronary atherosclerotic plaques.[11] Persistently low EES induces cell apoptosis and inflammatory process with local oxidative stress and increased LDL uptake, initiating thereby an atherogenic process. Furthermore the majority of vulnerable plaques are localized in low ESS segments. At the same time high ESS facilitates plaque destabilization by regression of fibrous tissue and expansion of the necrotic core.[12]

Detection of hemodynamically coronary stenoses is essential in treatment of patients with CAD. A number of large clinical trials demonstrated that revascularization of a non-significant coronary artery stenosis affects the functional status and clinical outcome of the patient and it is not superior to optimal medical therapy.[13–15]

Invasive fractional flow reserve (FFR) is considered as gold standard for the functional evaluation of a potential ischemia-causing stenosis, as well as improves the diagnostic accuracy, and effects on therapy and clinical outcome.[13]

FFR represents the rate between the pressure determined distal to the coronary stenosis and the aortic pressure, measured after administration of a hyperemic agent (e.g., 100–200 mcg of Adenosine depending on the selected vessel, Papaverine, Nitroprusside, Nicorandil) causing maximal hyperemia of the coronary vessels. FFR was established as a diagnostic tool to assess the functional impact of intermediate stabile coronary plaque. As determined by invasive FFR measurement, only half of the intermediate stenoses (between 50–75% diameter stenosis determined by ICA) lead to significant hemodynamic changes.[15] The a large number of patients are presenting multiple atherosclerotic coronary lesions and FFR measurements is able to detect the ischemia causing culprit lesion. It was reported that intermediate lesions with modified FFR and abnormal ESS tend to transform into a rupture-prone lesions. FFR guided PCI is associated with lower events and incidence of urgent revascularization Studies showed that only less than 1% of patients with intermediate lesions with normal FFR (>0.8) presented with myocardial infarction within 5 years. Based on the results published by Muller et al. non ischemia – causing lesions determined by invasive FFR measurements should be treated with conservative medical treatment instead of invasive coronary approach, as this group of patients exhibited better outcomes in terms of long term mortality.[16]

Computational fluid dynamics technology permits the calculation of coronary blood flow and pressure, as well as noninvasive FFR calculation without need for further additional investigations, image acquisition and medications or even modification of CCTA protocol being necessary. FFR-CT can be calculated from a typically acquired CCTA exam. CCTA itself can assess accurately and identify vulnerable coronary plaque prone to rupture, but cannot identify accurately the functionally significant stenosis. Adding the additional computational fluid dynamics to the conventional CCTA images, the ischemia causing lesions can be localized, that are prior to invasive cardiac intervention. Re-calculation of coronary blood flow and FFR from CCTA scans can be used to predict the hemodynamic effects of stent implantation in a lesion specific manner, hereby predicts the therapeutic benefits of coronary revascularization.[17] In the Diagnosis of Ischemia-Causing Stenoses Obtained Via Noninvasive Fractional Flow Reserve (DISCOVER-FLOW) trial, they compared FFR-CT with invasive FFR, having a per-vessel accuracy of 84.3%, sensitivity of 87.9%, and specificity of 82.2%.[18] In addition, Investigators in the Determination of Fractional Flow Reserve by Anatomic Computed Tomographic Angiography (DeFACTO) trial, which was a multicenter international study, with the scope of evaluating the diagnostic performance of FFR-CT, they enrolled 252 patients. Their results showed FFR-CT was effective tool to identify ischemic lesions than CCTA in identifying ischemic lesions (having a higher accuracy of 73% while CCTA has just 64%; in case of sensitivity FFR-CT has 90% while CCTA only 84%; the same findings with the specificity 54%, 42% respectively).[19]

DISCUSSION

CCTA has the ability to assess noninvasively the coronary vessels, to identify and localize the lumen narrowing lesions, it can also be used to obtain an accurate characterization and risk stratification of the coronary lesions. As a result of technological development, with substantial decrease in radiation doses, CCTA provides an optimal noninvasive tool for reliable for screening of obstructive CAD. In addition, CCTA can provide important morphological data, therefore it is capable of the morphological characterization of the atherosclerotic lesions, it can indicate the calcification level of the coronary system, plaque composition, lipid content, as well as it can identify the vulnerable markers of coronary plaque such as the Napkin-ring sign, spotty calcification, positive vessel remodeling, low CT attenuation zones with large necrotic core respectively.[10] CCTA can also be used to assess the coronary plaques functionally, using FFR-CT and ESS, identifying the ischemia-causing stenosis, hereby relieve the lesion selection, and with "virtual stenting" of the coronary lesions, it can predict the hemodynamic effects of the coronary revascularization.[17] Modified FFR-CT or ESS provides additional information on risk stratification of the lesion. Functional characteristics added to CCTA images, lead to a better characterization of the coronary lesion, and permit new opportunities for the noninvasive detection of vulnerable plaques.

CONCLUSION

FFR-CT and ESS can play an important role in the selection of therapeutic choice and in the assessment of the plaque evolution, as well as the mapping of the hemodynamic changes following the percutaneous coronary intervention. Novel imaging techniques allow both morphological and functional noninvasive assessment of coronary artery plaques, which provides essential information for proper follow-up and treatment for patients with CAD.

CONFLICT OF INTEREST

None declared.

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