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REVIEW

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Imaging Techniques for the Assessment of Coronary Arteries in Diabetic Patients Undergoing PCI with Bioresorbable Vascular Scaffolds

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ABSTRACT

Patients who suffer from diabetes mellitus and present coronary artery disease are at a higher risk of cardiovascular events. The coronary arteries of diabetic patients present a diffuse process of atherosclerosis with frequent distal involvement, being prone to acute cardiovascular events. Diabetics present an increased rate of developing coronary artery remodeling, negative remodeling being representative for this class of patients; this process is characterized by vessel shrinkage and an increased rate of coronary calcium accumulation that is a predictor for cardiovascular risk. Currently, it is desired to improve the treatment of diabetic patients with bioresorbable vascular scaffolds (BVS), because of their reduced risk of restenosis and the ability to restore coronary function, including vasomotion, adaptive shear stress, and expansive remodeling. Optical coherence tomography, intravascular ultrasound and multi-slice computed tomography are imaging techniques used for a high accuracy of diagnosis in coronary artery disease. This manuscript is a review that aims to highlight imaging techniques used for evaluating the functional impact of coronary lesions in diabetic patients who underwent coronary PCI with bioresorbable scaffolds and to describe the functional markers that show the specificity for predicting coronary artery disease.

Keywords: diabetes mellitus, coronary artery disease, bioresorbable scaffold, multi-slice computed tomography, shear stress, optical coherence tomography, intravascular ultrasound

INTRODUCTION

Diabetes mellitus is a chronic disease that affects the secretion and action of insulin, leading to a chronic high level of glycaemia, which will affect the cardiovascular system in the majority of cases.[1]

The prevalence of coronary artery disease (CAD) in these patients shows an upward trend from 9.5% to 55% compared with the general population, where the prevalence is between 1.6–4.1%.[2] Diabetes specialists estimate that there will be a continuous global growth of CAD, the prevalence of which had been estimated to 6.4% in 2010 and is predicted to grow up to 7.7% until 2030.[1]

Nicholls *et al.* have shown that in diabetic patients the lumen volume is smaller on intravascular ultrasound (IVUS) compared to non-diabetic patients, and that diabetic patients have a high percentage of atherosclerosis with more distal involvement and are prone to acute coronary events more frequently.[3]

In the majority of cases, CAD has no symptoms, leading in time to major adverse cardiac events such as myocardial infarction and cardiac death. It was noticed that most adverse cardiac events are not undergoing revascularization procedures. The BARTOD trial showed that waiting for symptomatic events is associated with irreversible myocardial disease and with a high prevalence of complications related to revascularization, cardiovascular death, and the development of heart failure.[4]

CORONARY ARTERY REMODELING

Negative remodeling is called vessel shrinkage, and it is frequent in diabetic patients, while positive remodeling is defined by the outward expansion of the vessel wall. Negative remodeling may make the stenotic plaque more vulnerable to rupture. In case of negative remodeling, lesions can be associated with a higher degree of stenosis.[5]

Positive remodeling was shown to be related to acute coronary syndromes, and the external elastic membrane at the lesion site was larger compared with the reference segment; negative coronary remodeling is responsible for stenosis in patients with stable angina, and the external elastic membrane at the lesion site is much smaller compared to the reference segment.[6]

By using IVUS, it was discovered that vessel shrinkage is correlated with a more circumferential distribution of the atheromatous plaque. Shrinkage appears as a constricting adventitial fibrosis. Lesions showing vessel shrinkage present adventitial thinning and greater media of the vessel wall. One characteristic of coronary artery remodeling is that in negative remodeling the plaque distribution is circumferential, while in positive remodeling the distribution of the plaque is mostly excentric.[5]

In IVUS studies, the negative remodeling index was under 0.95, compared with positive remodeling where the remodeling index was below 1.05. Plaque calcium appears with shadowing and hyperechoic. A thrombus is defined as an intraluminal mass with a lobulated appearance.[6]

Vessel shrinkage is characterized by post-interventional restenosis and an apparent disparity between the relatively low rate of death that follows the intervention despite the rate of recurrent morbidity. In this type of remodeling, identifying the plaques at high risk of rupture could help us consider this a marker for intervention.[5]

CORONARY CALCIUM SCORING

Coronary atherosclerotic lesions consist of calcified components and could be determined using the Agatston method or computed tomography.[7] Approximately half of the obstructive lesions visualized by invasive coronary angiography or coronary computed tomography angiography (CCTA) are a major cause of ischemia. This process is independent of the degree of luminal stenosis in case of necrotic core, positive remodeling, or spotty calcifications revealed by IVUS and CCTA.[8]

Several cross-sectional studies have revealed that patients suffering from diabetes have a higher rate and a higher extent of coronary calcifications compared with non-diabetic subjects.[9]

Raggi *et al.* have documented that coronary calcium is a predictor of all-cause mortality in diabetics who underwent fast coronary CT scanning.[10] A recent study found that the Coronary Calcium Score could be a predictor for silent cardiac ischemia. As the Adult Treatment Panel III Guidelines state, diabetics are considered high cardiovascular risk patients.[9]

Diabetic patients with no evidence of coronary calcium have a similar survival rate to non-diabetic subjects with zero calcium score at a five-year follow-up.[10] Regrouping these results suggests that coronary calcium can be helpful in short-term risk stratification in diabetic subjects.[9]

SHEAR STRESS

Endothelial shear stress (ESS) represent a measure of tangential friction force accomplished by blood flow at the level of the vessel wall and is proportional with fluid velocity and viscosity (the constant related to hematocrit).[11]

The unsteady nature of arterial blood flow determines the endothelial shear stress in combination with the geometric vessel configuration, being characterized by direction and magnitude. In regions with irregular geometry, a disturbed laminar flow appears, and the pulsatile flow shows oscillatory endothelial shear stress. In arterial segments with a right direction, endothelial shear stress is unidirectional and pulsatile, the magnitude being between 15 to 70 dyne/cm^2 during the cardiac cycle.[12]

An important parameter in the localization of early atherosclerosis is the flow that induces wall shear stress.

A frequently applied technique that is used to appreciate time-average wall shear stress distribution that appears in human coronary artery, is computational fluid dynamics.[13]

Caro *et al*. were the first who described the evidence regarding endothelial shear stress in the localization of atherosclerosis about 40 years ago. The clinical significance of atherosclerotic plaques is mostly dependent on the formation and development of atherosclerosis and on the vascular remodeling response. If the arteries are normal, the low value of endothelial shear stress causes a response that is adaptive at the level of the arterial wall, leading to constrictive remodeling.[12]

The implantation of rigid stents determines alterations in the arterial geometry and induces irregularities associated with strut protrusion. The focal in-stent endothelial shear stress distribution is altered by these vascular deformities that modify flow velocity profiles all along the length of the stent, reducing the post-implantation endothelial shear stress.[14]

Multi-slice computed tomography (MSCT) represents a non-invasive coronary angiography technique that can visualize the coronary artery, the complete arterial tree, and the bifurcation regions. In the future, development of increased resolution methods is expected, such as 3D lumen reconstruction for a precise endothelial shear stress computation. MSCT can provide the geometrical data necessary to calculate wall shear stress near bifurcations.[13]

BIORESORBABLE VASCULAR SCAFFOLDS

New techniques are continuously developed regarding the interventional treatment of CAD. Bioresorbable vascular scaffolds (BVS) are developing as a promising technology that responds to the inconveniences of previously developed stents. BVS assure early temporary scaffolding, and after a period this structure disappears. BVS enable the restoration of coronary artery functions, including expansive remodeling, adaptive shear stress, and vasomotion. This device liberates the vessel from being treated with a permanent metallic cage.[15]

The first BVS used in humans was the Igaki-Tamai stent, which was self-expandable when heated. The development of these stents was interrupted, and there are other types of scaffolds currently available, because of two limitations: the heated contrast dye could cause vessel wall injury, and the implantation requires 8 French guiding catheters.[16]

Using the results of the ABSORB trial cohort A and cohort B, the scaffold named Absorb BVS was the first device that became available in Europe for clinical use. During the five-year follow-up, the collected data demonstrated sustained efficacy of this device, the results being evaluated using multimodality imaging.[17]

BVS showed important results regarding the emergency revascularization of coronary artery plaques and revealed a low rate of major adverse cardiac events. Because no foreign structure remains in the vessel, the risk of late stent thrombosis was reduced and sometimes eliminated, the process being dependent of resorption duration.[16]

IVUS and OCT are the main imaging methods used to show late lumen enlargement in subjects who underwent PCI with the Absorb BVS, as well as the DeSolve BVS, another type of scaffold that is frequently used.[16]

IVUS has an important limitation, because it can visualize neo-intimal tissue inside the stented segment with limited axial resolution, which rules out the determination of neointimal coverage of each individual stent. OCT resolves this problem, allowing the evaluation of vascular healing after stenting, besides providing information about morphometric stent performance. OCT allows detailed characterization of the neointimal tissue and may facilitate the visualization process of neoatherosclerosis at a tissular level.[18]

Diabetic patients undergoing percutaneous intervention present an increased risk of stent thrombosis and restenosis. The incidence rate of device-oriented composite end-point and probable stent thrombosis was favorable in patients treated with BVS.[19]

BVS are more convenient than metal scaffolds for non-invasive imaging such as magnetic resonance imaging and computed tomography. These scaffolds do not cause artifacts and allow medical follow-up with these imaging techniques. Another important point is that the implantation of BVS may allow surgeons to carry out coronary artery bypass grafting, and it will be useful for patients who might require multiple interventions, because it will not interfere with previously implanted stents.[16]

Considerable progress is being made regarding the use of BVS in the interventional treatment of CAD. Some restrictions exist, and future finesses are required.[19] In patients with BVS, the incidence of target lesion failure (TLF), cardiac death, myocardial infarction (MI), and ischemia-driven target lesion revascularization (ID-TLR) was numerically lower in patients with diabetes (3.7%) compared with patients without (5.1%).[20]

INTRAVASCULAR ULTRASOUND

Intravascular ultrasound is an invasive imaging technique that uses a catheter and provides two-dimensional cross-sectional images of the entire arterial wall. This technique has a high accuracy in measuring the plaque, lumen, and vessel area and has the ability to localize and quantify plaque burden using 40 MHz detectors. Lipid-rich plaques, which appear like echo-lucent areas, unstable plaques in coronary arteries that may be visualized by quantifying the necrotic nucleus, can be identified by IVUS.[21] IVUS can also accurately identify calcium, but it is unable to quantify its thickness.[22]

The raw signals appearing from the reflection of ultrasound waves present a color-coded structure of plaque characteristics. In the last years, IVUS was frequently used and validated. With this technique, it is possible to determine plaque components such as fibrous tissue, necrotic core, lipids, and calcification.

Virtual histology intravascular ultrasound (VH-IVUS) appears to be the next promising tool for the characterization of vulnerable plaque.[23]

In patients with acute coronary syndromes or stable coronary artery disease, IVUS detects the thin-cap fibroatheroma that appears like a morphological plaque associated with a critical risk of acute coronary syndrome.[24]

OPTICAL COHERENCE TOMOGRAPHY

Optical coherence tomography is an invasive imaging modality, analogue to ultrasound, using light conversion of sound. There are two types of technologies that show OCT images: frequency domain and time domain.[25]

OCT provides cross-sectional images of the coronary arteries and facilitates the identification of intimal hyperplasia, the external elastic laminae and the internal elastic laminae as echo-lucent regions, as opposed to IVUS that cannot provide this information. It can identify the key features of vulnerable plaque such as large lipid pools or thin fibrous caps.[23]

The main obstacle in the decision to undergo OCT imaging in clinical practice is that this technique cannot acquire images through a blood field, and it needs the blood to be cleared from the lumen. The acquisition of an OCT image requires a contrast media that is injected via the guiding catheter. The acquisition rate can be set up in a series between 5 and 40 mm/s.[22]

The applied energies in OCT are low and do not cause damage at the level of structural or functional tissue. OCT can penetrate calcium deposits that are located superficially, but penetration through superficial necrotic lipid pools is known to be less than through fibrous tissue or through calcified tissue. OCT has the potential to detect angiogenesis.[25]

For bioresorbable stents, the evaluation of the entire thickness it is now possible, because light can penetrate non-metallic structures. It is important to know that the degradation process is characterized by empty spaces that replace the stent column; however, this phenomenon was described in the first generation of bioresorbable stents, and in the second-generation model the degradation process was not visible.[22]

OCT is indicated for evaluating vague angiographic lesions and focal vessel spasm. It has the ability to identify coronary thrombosis in the presence of haziness on the angiography. OCT imaging catheters are smaller in size compared to IVUS catheters, providing a reason to choose OCT over IVUS, because it may reduce coronary spasm or catheter wedging. The main limitation of OCT consists in the inability to measure plaque burden.[25]

MULTI-SLICE COMPUTED TOMOGRAPHY

This technique allows the acquisition of images of the entire heart in a single gantry rotation. The expansion of MSCT from 64 to 128, followed by 256 to 320 slices, allows a highly accurate study of atherosclerotic plaque composition and stenosis severity.[26]

Coronary plaques can be classified into three types using CT attenuation: calcified-plaques that are lesions with a higher density than contrast enhancement in the coronary lumen, non-calcified plaques that are lesions with a radio-density greater than soft tissue, and mixed plaques within a single lesion or within a segment of the coronary artery. This noninvasive method can detect plaque components, allowing the differentiation of stable from unstable plaques and the measurement of atherosclerotic plaques.[27]

MSCT has the ability to provide a complete assessment of the coronary tree with a high level of diagnostic accuracy. The radiation dose that is associated with CT imaging has increased substantially in the last period, with the development of MSCT.[26] Multi-detector CTA cannot be used as a substitute for angiography because of its negative predictive value of 83%.[23]

CONCLUSIONS

Diabetic patients have a higher risk of developing coronary artery disease, and in case of percutaneous coronary angioplasty, they are more prone of developing in-stent thrombosis and restenosis. Furthermore, the CT coronary artery Calcium Score is correlated with higher all-cause mortality in patients with CAD and diabetes. Patients with diabetes mellitus have a higher rate of negative vessel remodeling compared to non-diabetics who show a greater prevalence of positive vascular remodeling.

Considerable progress is being made providing bioresorbable vascular scaffolds for the interventional treatment of coronary artery disease. The development of bioresorbable vascular scaffolds has allowed the preservation of vascular function and vasomotor properties, leading to better results after percutaneous coronary interventions when compared to traditional metallic stents, in case of diabetic patients. IVUS, OCT and MSCT are invasive and noninvasive imaging techniques that allow the accurate identification of plaque components and can be very useful tools for risk prediction in case of vulnerable coronary plaques.

CONFLICT OF INTEREST

Nothing to declare.

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