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THE ROLE OF IVUS AND OCT IN THE PATIENTS WITH MYOCARDIAL INFARCTION WITH NON-OBSTRUCTIVE CORONARY ARTERIES (MINOCA)

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ABSTRACT

The work presented describes what is meant by the term MINOCA and the causes that lead to the onset of this acute event, responsible for myocardial ischemic necrosis.
Diagnosis with coronary angiography alone cannot be made since MINOCA is characterized in half of cases by the absence of hemodynamically significant lesions and therefore invasive coronary imaging performed through IVUS and OCT plays an important role.
The two imaging techniques have peculiar characteristics that differentiate them from each other.
IVUS uses ultrasound while OCT uses infrared light, but they are also distinguished in terms of spatial resolution, which is greater for OCT thus allowing better tissue characterization, and tissue penetration capacity which is greater for IVUS.
In MINOCA patients, coronary artery imaging could help identify pathological changes that are not visible by coronary angiography such as plaque rupture, coronary dissection, coronary thromboembolism, coronary spasm, and coronary artery disease in patients presenting with Takotsubo syndrome.
The use of intracoronary imaging (IVUS or OCT) can give us important information regarding the diagnosis and optimization of the treatment of patients with MINOCA, improving their prognosis.
The medical radiology technician, within the Hemodynamics Team, must have a role of responsibility in the management of diagnostic images.

INTRODUCTION

The term Myocardial infarction with non-obstructive coronary arteries (MINOCA) is defined as a syndrome caused by different factors and it is responsible of myocardial ischemic necrosis.
The MINOCA is characterised by the absence of significant lesions of the coronary arteries (stenosis <50%) when a coronary angiogram is performed.
The coronary angiography has some limitations in the diagnosis of the atherosclerosis as a cause for MINOCA and therefore the use of invasive coronary imaging like the intravascular ultrasound (IVUS) and the optical coherence tomography (OCT), has shown to have a higher diagnostic potential.
With this article we want to evaluate the fundamental role of the intra-coronary imaging in the diagnosis of MINOCA.

METHODOLOGY AND MATERIALS

In the most recent studies, among the patients affected by acute coronary syndrome (ACS) and subjected to a coronary angiogram, approximately 5% - 25% have normal or non-significant stenotic coronary arteries (<50%), with 2/3 of the MINOCA having an ECG pattern indicating myocardial infarction without ST segment elevation (NSTEMI) while the rest of them shows a pattern indicating a myocardial infarction with ST segment elevation (STEMI).
Acute myocardial infarction (Acute MI), according to the 4th universal definition, is defined by the evidence of acute myocardial damage accompanied by clinical data suggesting acute ischemia as a relevant symptomatology, new ischemic ECG changes, new evidences of vital myocardial loss when investigated with imaging or by the identification of a coronary thrombus. The detection of cardiac troponin values (I or T, even at high sensitivity) drawing a curve going either up or down characterized by at least one upper determination at the 99th percentile of the normal reference values, represents a damage of the myocardial cells. (Figure 1) The cases of MINOCA represent 5% - 20% of the cases of type 1 Acute MI (characterized by spontaneous intracoronary obstruction, even if not detectable at the time of coronary angiogram) and a

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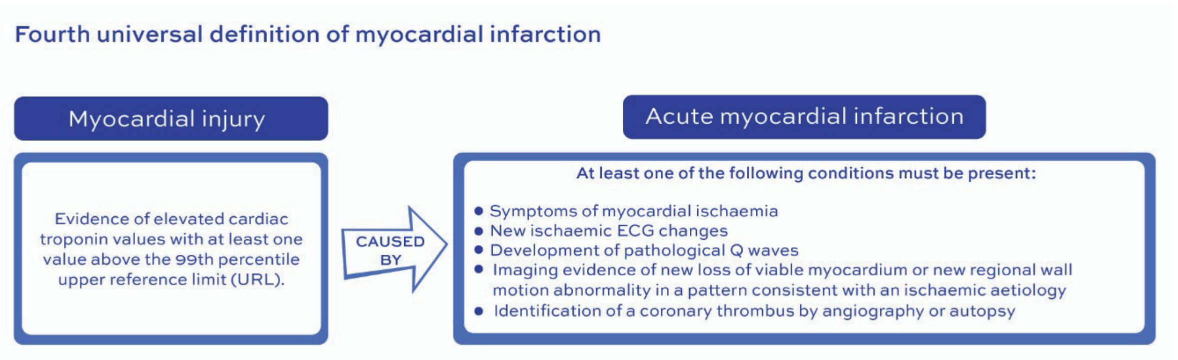

Fig. 1 - *Fourth universal definition of myocardial infarction*

conspicuous part of the forms of type 2 Acute MI. Patients with MINOCA are generally younger (average age 48), more often females with a tendency of fewer traditional cardiovascular risk factors compared to patients affected by Acute MI due to obstructive coronary artery disease (MI-CAD); even if these patients were less likely to have hyperlipidaemia, a similar distribution was observed with regard to hypertension, diabetes, cigarette's smokers and a family history of premature coronary artery disease.
The main mechanism of myocardial injury related to MINOCA is ischemic disease, therefore we can also include the Takotsubo syndrome (TTS) in the MINOCA subgroup. There are other conditions that can cause elevated troponin levels but those are not causing damage the heart muscle.
In this group we can include the myocarditis and the pulmonary embolisms which are not considered responsible for MINOCA.

IVUS AND OCT
OCT is an innovative method of endovascular imaging that provides real-time tomographic sections of the coronary arteries with high axial resolution (10-15 pM) and high sampling frequency. The OCT uses an infrared light carried by an optical fibre within a catheter (2.4-2.8 F). The light that illuminates the inside of the vessel rotates rapidly and this allows a longitudinal scans of the coronary artery (7.5-15 cm) in a few seconds (2-3.5 s). The use of contrast medium (3-4.5 ml / s depending on the size of the coronary) during the scan, allows the light to interact with the surrounding vascular structures without interference.
Vessels and surrounding tissues, are reflecting and absorbing the light in a different way and this is based on their structural composition. In the context of acute coronary syndromes, the OCT is used to detect the presence of thrombi, to evaluate the rupture or the erosion of the plaque, nodular calcifications, hematomas and spontaneous coronary dissection, to measure the coating thickness of potentially vulnerable plaques.
All of these information is used to evaluate the exact therapeutic approach based on the triggering cause.
In our cath-lab, we use the *Dragon Fly Optis Abbot Vascular* catheter. This catheter shows a distal radiopaque marker placed at 4mm from the tip followed by second marker at 23mm and distally another marker at 50mm. Between these two last markers there is the optical fibre that generates the light signal. During the acquisition, the lesion must be between the lens marker (23mm) and the distal marker (50mm). The catheter is connected to a computer which is used to process the signal generating images of the internal vessels wall.
The software used for the image processing is the Jude Optis Integrated. (Figure 2)

The IVUS (wavelength 40 uM to 40 MHz) is a scanning technique that uses ultrasounds to obtain information about the vessels lumen and it is able to collect information regarding the characteristics and the structure of the plaque. It uses miniaturized catheters to reach the coronary arteries. Not long ago, the IVUS images were only produced in a grey scale form. This limit has been overcome by the use of a software that

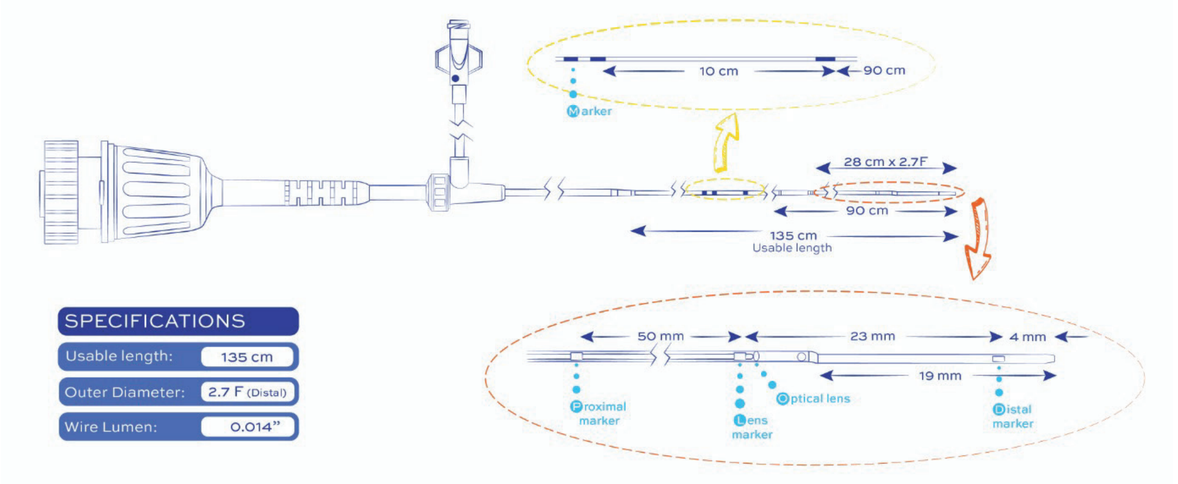

Fig. 2 - *Dragon Fly Optis Abbot Vascular catheter diagram*

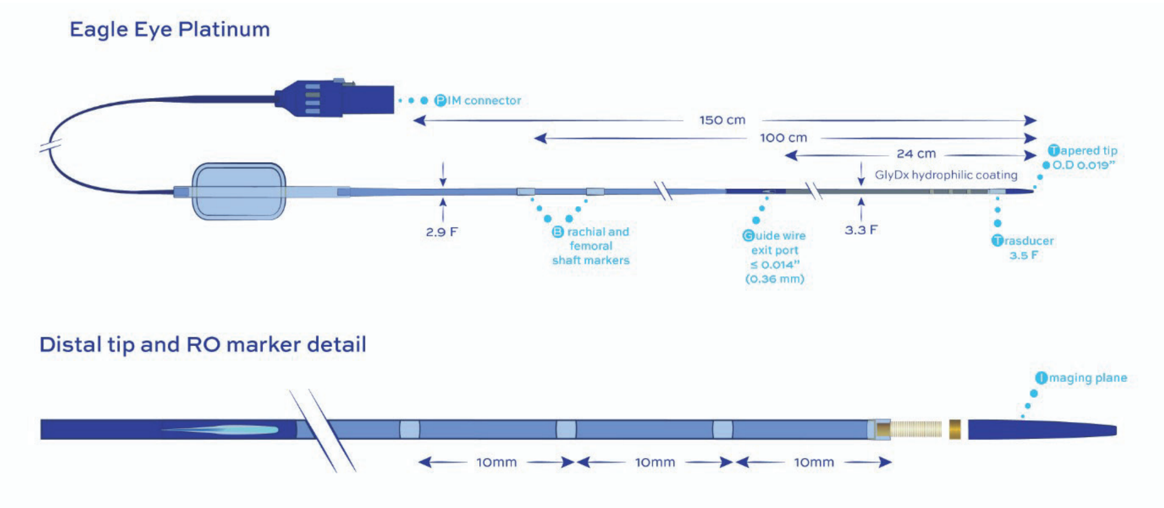

Fig. 3 - *Philips Healthcare Eagle Eye Platinum Catheter Diagram*

processes the signals as colour images and creates the so-called Virtual Histology (VH-IVUS). The images have different colours depending on the type of tissue. The fibrotic tissue appears green, the necrotic core appears red and the lipids appear yellow.
In this way we can have a quantitative but also qualitative analysis of the vessels wall.
In our cath lab we use the *Philips Healthcare Eagle Eye Platinum* catheter*;* the tapered distal catheter tip and the hydrophilic coating GlyDx are providing an increased lubrication and durability during use. In addition, there are 3 radiopaque markers10mm apart to facilitate the operator in estimating the length.

Both imaging techniques therefore allow us to obtain images from the inside the coronary arteries but they show substantial differences. OCT has a 10 times higher spatial resolution than IVUS, allowing an improved tissue characterization, thrombus detection and the identification of lesions responsible of ACS. The IVUS has a greater penetration of soft tissues (5-6 mm) than OCT (1-2 mm) allowing a full-thickness view of the vessels wall. The OCT requires increased use of contrast medium for imaging and is not indicated in patients with chronic renal failure in whom IVUS is preferred. The aorto-ostial lesions, are not clearly visible through OCT and IVUS is preferred. This is due to the difficulties to obtain an adequate proximal blood flow.
The differences between IVUS and OCT are summarized in Figure 4.

IVUS	OCT
Ultrasound-based technology	Infrared light-based technology
Higher tissue penetration	Higher spatial resolution
Better for vessel remodelling assessment	Better for tissue characterization, plaque rupture, and thrombus identification
Lower doses of contrast are needed (better for patients with CKD)	Need for additional contrast
Better for aorto-ostial lesion evaluation	Difficult to obtain in aorto-ostial lesion
More extensive researches	Easier to interpret

Fig. 4 - *Differences between IVUS and OCT*

DISCUSSION

Pathophysiology

The ischemic damage can be the consequence of a problem that involves both the epicardial coronaries and the microcirculation. Anamnesis, electrocardiogram, cardiac enzymes, echocardiography, coronary angiography, ventriculography represent the first diagnostic level in identifying the causes of MINOCA. Following this pathophysiological concept, the causes of MINOCA are classified into epicardial and microvascular. When the damage is limited to the territory supplied by a single coronary artery it is defined as epicardial, it is defined as microvascular when the alterations of the kinesis of the heart wall are linked to a territory supplied by several coronary arteries.
The epicardial causes that determine the onset of MINOCA are the rupture and/or erosion of an atheromatous plaque, dissections and vasospasm. The microvascular causes of MINOCA are coronary thromboembolism, Takotsubo syndrome and the coronary microcirculation dysfunction.
Coronary angiography alone in most cases does not allow to reach a precise etiological diagnosis and the introduction of intracoronary imaging such as IVUS and OCT has increased the identification of the underlying mechanisms especially in the epicardial causes of MINOCA.

Rupture and / or erosion of coronary plaque

Many atherosclerotic plaques are characterized by a lipid body and a thin fibrotic cap, making them extremely vulnerable to rupture. The thrombotic process that leads to the rupture of these plaques can create peripheral thromboembolism and/or vasospasm and it is followed by a spontaneous thrombolytic process, which is why complete vascular occlusion is no longer appreciable during the angiograph. On the other hand, when an area of “haziness” is found on coronary angiography after the administration of contrast media, it is a sign that indicates the presence of a re-canalized plaque break. In these cases, the use

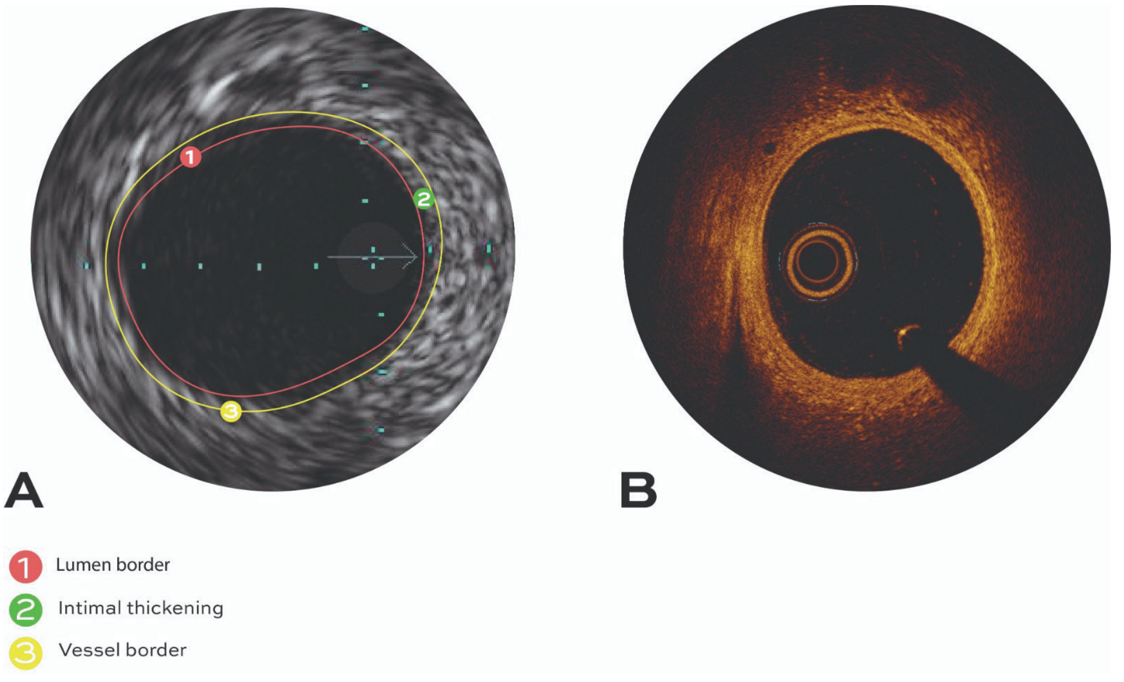

Fig.5 - *Image (A) IVUS and (B) OCT of a coronary artery free from stenosis*

of OCT allows to document the rupture and/or erosion of a plaque and the associated presence of intraluminal thrombus (Figure 6). The OCT is preferred to IVUS for the higher spatial resolution. On imaging, the plaques are divided into fibrous plaques (region with high homogeneous signal) and lipid plaques (region with low signal with poorly delineated edges).

Coronary dissection

Spontaneous coronary artery dissection (SCAD) represent a significant cause of ACS mostly in young and middle-aged women with most cases not related to recent pregnancy. Pregnancy, the peripartum period, fertility hormones, and preeclampsia can increase the risks.

The distal coronary segments and the anterior ascending artery are typically involved. There are two mechanisms that lead to the formation of the false lumen: the most probable "outside" model, in which a primary destruction of a micro-vessel determines a haemorrhage directly into the middle layer; and the "inside-out" model where the random event is the development of an endothelial and intimal discontinuity, followed by the passage of blood in the elastic internal lamina and accumulation in the middle layer. The OCT is able to give us detailed information on the true lumen including the presence of thrombus, the size, nature and extent of the false lumen, the relationship between false lumen and lateral branches. Accurate measurements of the thickness of the intima-medial membrane and the area of the true compressed lumen can be made. It is important to recognize that the attenuation of the light by the false lumen is highly variable. Alternatively, IVUS has a low axial resolution but is able to give a better visualisation of the vessel walls, even in those patients with intraluminal red thrombus or ectatic arteries.

Coronary Thromboembolism

Coronary thromboembolism can be related to inherited or acquired thrombotic disorders, but it can also be linked to the rupture of an atheromatous plaque or vasospasm. It represents a rare cause of ACS, about 3%, and thromboembolic episodes are divided into three groups: iatrogenic when they occur following interventional procedures, usually valve replacement and angioplasty, direct when thrombi originate from the left atrium, left ventricle, aortic or mitral valve, or primary when the thrombi origin of the coronary district. The embolic tissue can be a thrombus, valve material, or rarely even neoplasms. Paradoxical emboli pass through patent foramen ovale, atrial defect or arteriovenous malformation from the venous circulation in the coronary district.

In this case, IVUS or OCT could be used to evaluate the vessel and identify the potential embolic origin linked to an erosion of an isolated plaque. Direct emboli are the main cause (73%) but cardiomyopathies or valve diseases are also common. (Figure 8)

A boy was admitted to our operating unit for myocardial infarction with ST -segment elevation (STEMI) and coronary angiography shows occlusion of the anterior descending artery and remaining vessels devoid of lesions. (A) OCT highlights the presence of thrombus without the presence of atherosclerotic disease. (B) Subsequently he was placed on transesophageal ultrasound and cardiac magnetic resonance and we evaluated a bicuspid valve with small vegetation endocarditis as an embolic source.

Coronary vasospasm

Vasospasm is an overactive response of the smooth muscle component of the coronary wall to endogenous (vasospastic angina) or exogenous substances (e.g. drugs such as cocaine). The pathology can affect both the epicardial vessels and the microcirculation. In a study that included 69 patients, with vasospastic angina and undergoing OCT, the presence of

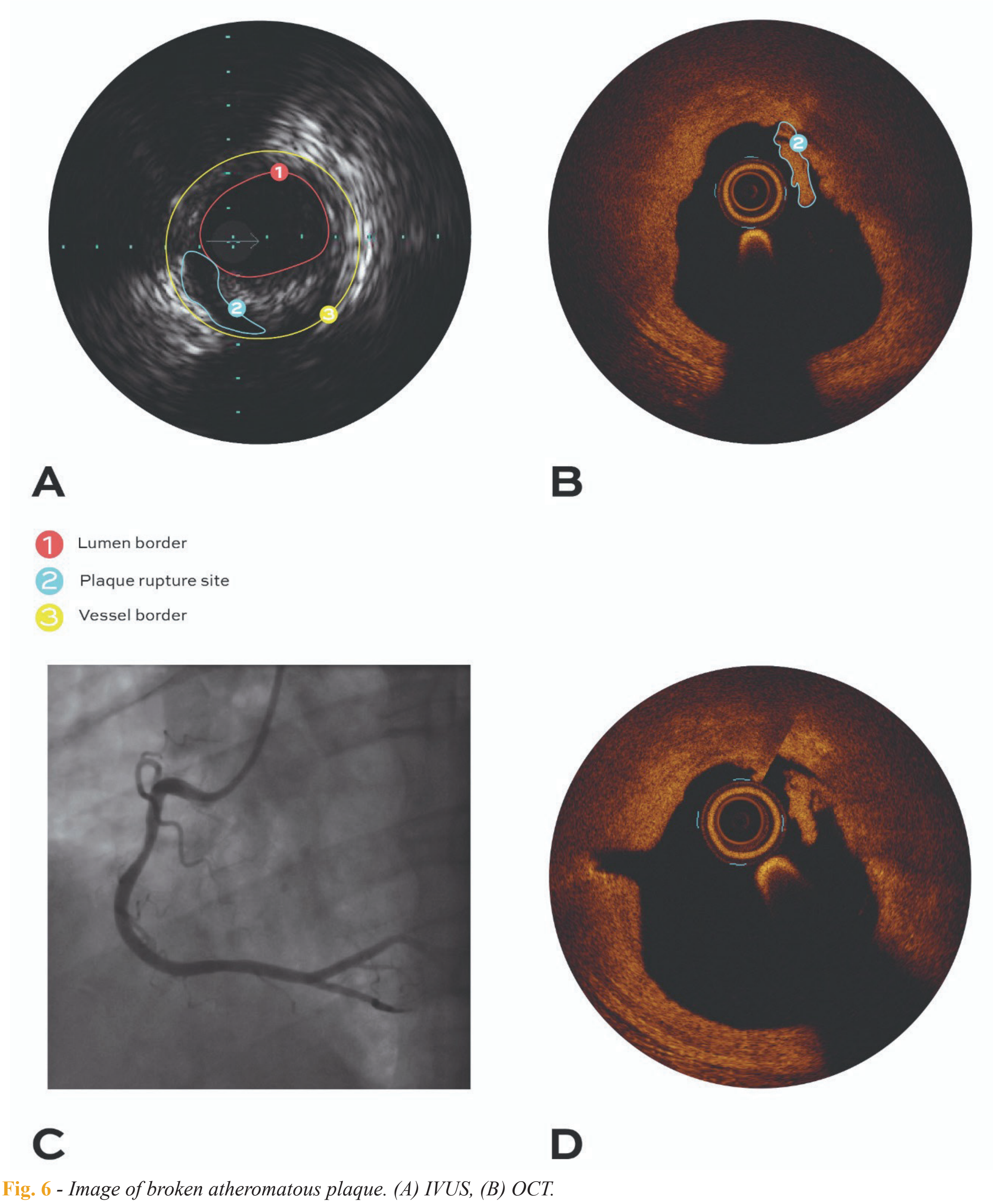

Fig. 6 - *Image of broken atheromatous plaque. (A) IVUS, (B) OCT.*
A middle-aged patient was admitted to our operating unit for posterior myocardial infarction with ST -segment elevation (STEMI). (C) Coronary angiography shows narrowing of the middle tract of the right coronary angiograph at regular margins. (D) OCT shows the presence of atheroma with plaque rupture and thrombotic apposition.

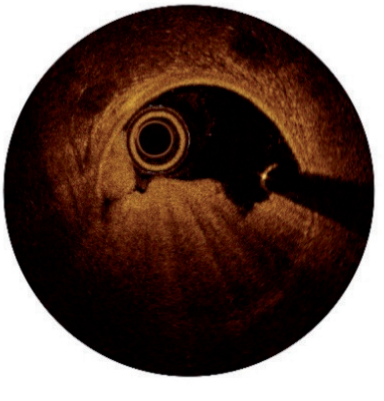

Fig. 7 - *Image of intracoronary thrombus highlighted by OCT*

thrombi was found in 28.8% of cases. OCT-defined erosion, identified as the concomitance of thrombus and intact fibrous hood, was common in patients with vasospastic angina (26%). Constricting endothelial damage can cause thrombus formation at the site of the spasm, followed by partial or total arterial occlusion at that site, especially if superimposed on pre-existing arteriosclerosis. Coronary vasospasm may develop after stent insertion. This happened in a 55-year-old patient who was admitted to our operating unit for myocardial infarction with ST segment elevation and who had 90% occlusion in the middle right coronary artery on coronary angiography. The lesion was treated with stent placement and post dilation with TREK balloon and after one day of observation he was discharged. After three days the patient is

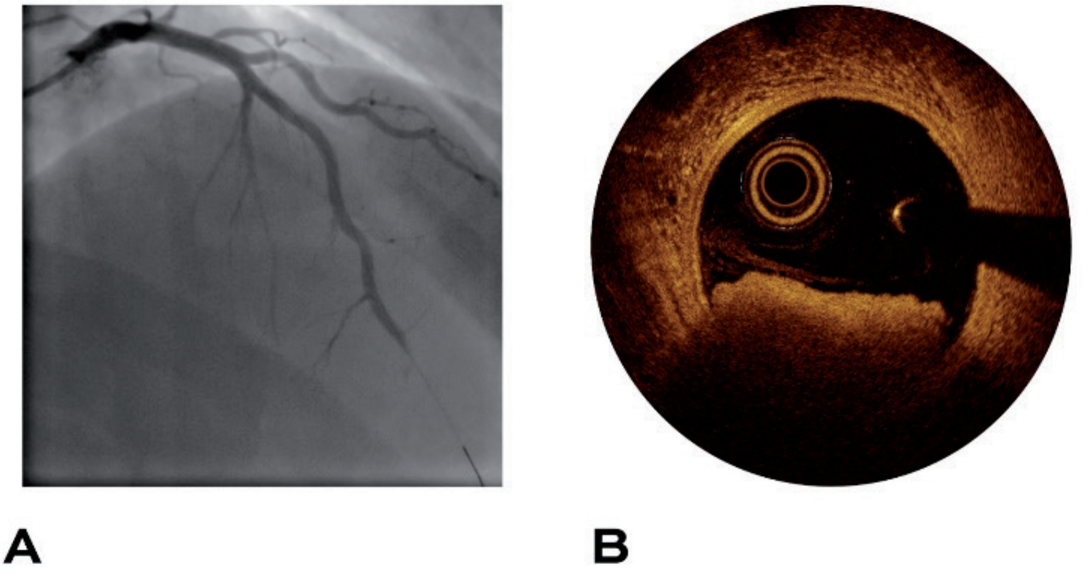

Fig. 8 - *Case report of a boy with coronary thromboembolism.*

admitted again with chest pain and ST segment elevation. Subjected to another coronary angiography, the patient was found to have severe vasospasm in the next part of the of the right coronary artery at the level of the proximal edge of the stent implanted. Following the administration of intra coronary nitro-glycerine the chest pain passed as well as the ECG changes. In patients with vasospasm-induced ACS, intimal laceration, intimal erosion and micro-thrombi are the main abnormal morphological findings of OCT compared to patients with chronic stable vasospastic angina.

Intrastent thrombosis

The elevation of the ST segment is now a rare complication with the latest generation DES insertion but it remains a serious complication with a high mortality rate and relapses.

The OCT allows to differentiate the thrombus from the tissue components, differentiating the mechanisms that are involved in ST elevation.

Among the possible causes there are the sub-expansion of the stent, the distribution of uncovered meshes wrongly placed and the presence of broken lipid plaques inside the stent.

In the European study PRESTIGE, the OCT evaluation is carried out immediately after the reopening of the stent (231 patients with acute, late or very late thrombosis and mostly with the use of last generation stents). The dominant aspects observed with OCT are different based to the time interval elapsed between the stent placement and the elevation of the ST section. The sub-expansion of the stents and uncoated meshes are the most common causes of acute/subacute thrombosis, while new atherosclerosis and uncovered strut are the most frequent mechanisms of late/very late ST elevation.

Takotsubo Syndrome

Growing evidence suggests that excess of catecholamine could play an important role in the pathophysiology of TTS.

The excess of catecholamine causes an increased sympathetic activity and a reduced coronary microcirculation.

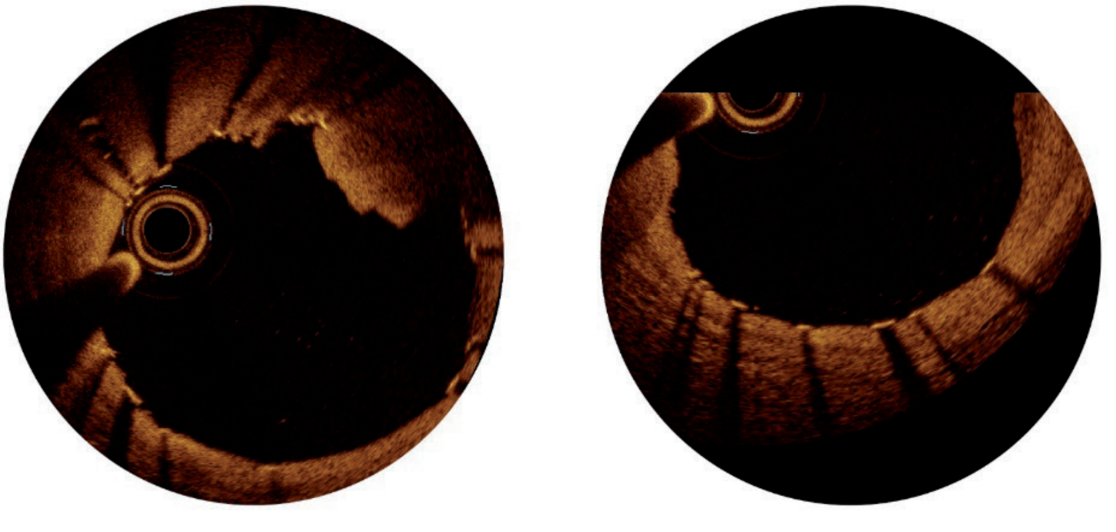

Fig. 9 - *OCT image of uncovered struts.*

For this reason, the Takotsubo syndrome is classified within the MINOCA group.
However, not all TTS patients show stressful triggers and elevated catecholamine levels.
In the Takotsubo International Registry there was a significant coexistence of coronary heart disease with a prevalence between 10% and 29%. Several alternative pathophysiological mechanisms have been proposed, including disrupted atherosclerotic plaques in the left anterior descending coronary artery causing myocardial infarction with spontaneous thrombus lysis. This was found in a small study where IVUS was used as intravascular imaging.
In a prospective study, atherosclerotic plaques were identified in 16 of 23 patients with TTS.
However, OCT can be further used to characterize CAD where present and eliminate the possibility of an acute plaque rupture and the causing lesion.

CONCLUSIONS

The term MINOCA indicates a heterogeneous group of pathologies that determine the onset of AMI and that on coronary angiography does not show the presence of significant lesions. In these cases, the intracoronary imaging (IVUS or OCT) plays a determinant role giving us important information about the diagnosis and subsequent management of patients with MINOCA in view of the significant risk of short, medium and long term events.
The radiographer plays a fundamental role within the team in cath-lab and he/she is responsible for the management of the diagnostic images. The radiographer assists the Hemodynamic Cardiologist in the success of the examination and in the interpretation of the images.

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