Value of the optical coherence tomography in the diagnosis of unstable patients with non-significant coronary stenosis

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ABSTRACT

Introduction and objectives: The final diagnosis of a myocardial infarction with non-obstructive coronary arteries (MINOCA) is often hard to achieve. Angiographic findings may be suggestive of the presence of unstable plaques although it is common to discharge patients without an etiologic diagnosis. The high spatial resolution provided by the optical coherence tomography (OCT) allows the detection of vulnerable and unstable coronary plaques that are prone to rupture, erosion, and thrombi which may lead to more targeted individual therapies. The objective of this study is to assess the utility of OCT when achieving an etiologic diagnosis in selected patients with MINOCA and high clinical suspicion of atherosclerotic etiology.

Methods: Registry of 27 patients recruited between September 2015 and January 2020 admitted to a single tertiary hospital with acute coronary syndrome and non-significant stenosis in the coronary angiography who underwent OCT. The baseline data of the study population, the angiographic and OCT findings, treatment and follow-up information were all collected.

Results: The OCT imaging showed evidence of unstable plaques (thrombus, plaque erosion or plaque rupture) in 78% of patients, which lead to an etiologic diagnosis of MINOCA. Patients were predominantly males (89%), smokers (63%), middle-aged (median 53 years old) and with a low cardiovascular risk burden. The left anterior descending coronary artery was the most frequently compromised vessel (74%) and 95% of patients ended up receiving coronary stents. The mid-term follow-up was excellent.

Conclusions: In our study, OCT imaging proved to be a valuable tool to achieve an etiologic diagnosis in a large proportion of selected patients with MINOCA which, as a result could lead to more specific and individualized treatments.

Keywords: Optical coherence tomography. Myocardial infarction with non-obstructive coronary arteries. Unstable plaque. Vulnerable plaque.
INTRODUCTION

Patients admitted with a diagnosis of acute coronary syndrome (ACS) with coronary arteries without significant angiographic obstructions (considered as angiographic stenoses < 50% of the lumen of a major epicardial vessel) should be reassessed before re-planning their diagnosis. In general, differential diagnosis is required with other conditions that may trigger acute myocardial damage without an acute myocardial ischemia as the underlying cause (myocarditis, stress cardiomyopathy or other cardiomyopathies, pulmonary thromboembolism, etc.). Only when these are discarded or unlikely the diagnosis of acute myocardial infarction with non-obstructive coronary arteries, also known as MINOCA, can be established.

MINOCA amounts to between 5% and 7% of all acute myocardial infarctions, but even in some series its prevalence reaches 15% of the cases. The causes for MINOCA are varied: atherosclerotic plaque disruption (rupture or erosion), vasospasm, microvascular dysfunction, thrombus or coronary embolism, spontaneous coronary dissection or oxygen supply-demand imbalance (like in the tachyarrhythmia or anemia setting). For this reason, treatment varies significantly depending on each particular case. However, some studies have reported that in half of the patients no specific etiological diagnosis was established, which may lead to inappropriate treatments.

The optical coherence tomography (OCT) is an intravascular imaging modality based on the use of infrared light to acquire images with very good spatial resolution (approximately between 10 μm and 20 μm), even 10 times better resolution compared intravascular ultrasound (IVUS). For this reason, the OCT allows the detection of vulnerable plaques (those whose characteristics show a higher risk of destabilization) or findings suggestive that the plaque is already destabilized (Table 1). Therefore, it is a useful imaging modality to establish the etiological diagnosis of MINOCA, especially when there is clinical or electrocardiographic suspicion of ACS due to atherosclerosis and also in cases of spontaneous coronary dissection.

The objective of this study was to assess the utility of the OCT to establish the etiological diagnosis of patients with MINOCA and highly suspected ACS due to atherosclerosis, and describe the profile of the population studied.

Table 1. Pathologic findings on the optical coherence tomography

<table>
<thead>
<tr>
<th>Vulnerable plaque</th>
<th>Unstable plaque</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of plaque</td>
<td>Thrombus</td>
</tr>
<tr>
<td>Macrophages</td>
<td>Rupture of plaque</td>
</tr>
<tr>
<td>Neovessels</td>
<td>Erosion of the plaque</td>
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<tr>
<td>Cholesterol microcrystals</td>
<td>Protruding calcium nodule with presence of thrombus or plaque disruption</td>
</tr>
</tbody>
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METHODS

Study population

This was a prospective registry of selected cases of MINOCA in the reference center of an autonomous community between September 2015 and January 2020 with the following characteristics: a) admission with a diagnosis of ACS or recovered sudden death with suspected ACS as the underlying cause; b) angiographic coronary stenoses < 50%, and c) performance of an OCT on the possible culprit artery causing the event due to suspected angiographic imaging or ECG or segmental alterations on the echocardiogram. When in doubt on which the infarct-related culprit artery was, the vessels considered in each case were assessed using the OCT.

Procedure and analysis

The OCT was performed using the Dragonfly Optis catheter (Abbott, United States) over a pullback length of 55 mm or 75 mm in the segment of interest. The OCT study was performed in the same Ilumien Optis OCT console (Abbott). The angiographic study was performed using the Stenosis Analysis 1.6 software package (GE Healthcare, Advantage Workstation 4.5, United States). The offline analyses of the angiographic and OCT findings were performed by the same operator while the interventional procedure was being performed. This operator made the therapeutic decisions too. Afterwards, 2 expert operators performed an independent, thorough, and retrospective analysis of the angiographic and OCT images in a first reading and, simultaneously, in a second reading to achieve consensus when in the presence of suspected cases or possible discrepancies.
Regarding the OCT findings, the median minimum lumen area was in any of the patients. In 2 and 3 cases, respectively. No thromboaspiration was performed did not show any signs indicative of an unstable plaque. The coronary artery (74%). In most patients the angiographic imaging was normal (Thrombolysis in Myocardial Infarction [TIMI] grade 3). The vessel most often damaged was the left anterior descending coronary artery was the vessel more commonly 20 of the 21 patients (95%) with data of the plaque, ruptured plaque, and protruding calcium nodule. Unstable plaque is defined as a plaque with a thrombus, ruptured plaque, erosion of the plaque or protruding calcium nodule with thrombus or plaque disruption as seen on the OCT. Quantitative analysis was performed for every 1 mm interval while the software automatically calculated luminal dimension. The results of patients treated with a stent and those who underwent a new OCT after the implant were confirmed by verifying the adequate position, expansion, and lack of large dissections of the borders of the stent.

**Statistical analysis**

Quantitative variables with a normal distribution were expressed as mean and standard deviation. Those without a normal distribution were expressed as median and interquartile range [IQR]. Finally, qualitative variables were expressed using percentages as the frequency measure.

**RESULTS**

The registry included 27 patients. A total of 28 arteries through 38 OCT pullbacks were studied. Results are shown on table 2.

The patients’ mean age was 53 years [45-64]. Most of them were males (89%). Smoking was the main cardiovascular risk factor (64%). The most common indication for the coronary angiography was non-ST-segment elevation ACS (63%).

The median angiographic stenosis obtained through visual analysis was 40% [30-40]. In 5 cases the stenosis assessed through visual estimation was between 50% to 60%; according to the quantitative coronary angiography the median stenosis was 41.2% [35.5-48.8]. The quantitative coronary angiography showed a 50% to 60% stenosis in 2 cases only. In all of the patients the initial TIMI flow was normal [Thrombolysis in Myocardial Infarction [TIMI] grade 3]. The vessel most often damaged was the left anterior descending coronary artery (74%). In most patients the angiographic imaging did not show any signs indicative of an unstable plaque. The angiographic imaging was suggestive of a thrombus and an ulcer in 2 and 3 cases, respectively. No thromboaspiration was performed in any of the patients.

Regarding the OCT findings, the median minimum lumen area was 3.2 mm² [2.5-4.9]. In most of the cases different types of vulnerable plaque were found in the form of a TCFA (67%), macrophages (59%), and neovessels (56%). The OCT showed signs of unstable plaque in 21 cases (78%) with thrombus in 70% of the patients. The erosion of the plaque was the main cause for plaque instability (41%) followed by the rupture of the plaque (30%). A decision was made to implant a stent in 20 of the 21 patients (95%) with data of unstable plaque as seen on the OCT. One patient with plaque erosion received medical therapy. The 6 patients without data of unstable plaque on the OCT received medical therapy too. In 75% of the cases with stenting the outcomes were assessed using the OCT; 5 out of the 20 cases were postdated and an additional overlapping stent was implanted in 1 out of the 20 cases.

Finally, no sudden deaths were reported during the index event. At the median 4-month follow-up only 1 death due to cardiovascular causes was reported.

**DISCUSSION**

In some series of patients with MINOCA it has been reported that in up to 50% to 70% of the cases no etiological diagnosis is established. This means that these patients may end up receiving unspecific treatment for their MINOCA. For this reason, diagnostic algorithms have been designed by expert consensus including intravascular imaging techniques as useful tools to establish the etiological diagnosis of MINOCA. Regarding the use of the OCT specifically for these patients, the studies have proven its capacity to detect the mechanism of the infarction in some of MINOCAs. However, although its use has been reported in some series of patients with MINOCA it has been only in those with 0.08% in some registries. This may be due to the fact that its wide use in this type of patients has not been fully established or to the different availability and training capabilities of each center.

According to different expert consensuses in our center OCTs are performed on this type of patients [suspected atherosclerotic cause]. This registry was started back in 2015 to later study and assess the utility of OCT in these cases since scientific evidence available on this regard is scarce in part due to its low use. Also, it would be advisable to establish a protocol to perform OCTs in most cases of MINOCA even in the absence of suspected atherosclerotic etiology; thanks to its high spatial resolution, the OCT also allows us to detect other causes for MINOCA like thromboembolisms, vasospasms or spontaneous coronary dissections. This was also confirmed by our study that identified 2 cases of hematoma/spontaneous coronary dissection [table 2, figure 3].

The characteristics of this registry were those of a young population of patients [median age, 53 years], which is consistent with what has been reported by former studies. However, most of the patients included were males (89%), which varies significantly from other previous registries or reviews where over half of the patients with MINOCA were women. Our interpretation of these data is that our registry studied highly selected cases of MINOCA with a high clinical suspicion of atherosclerotic ACS due, which is more common in males. This would be consistent with the characteristics of the series of ACS previously reported. Also, when the different causes for MINOCA were analyzed, some studies have reported that when it is due to the disruption of the plaque there is a higher prevalence of male sex. However, in the occurrence of MINOCAs due to other causes, female sex is still predominant.

According to several studies, the main clinical presentation of these patients was non-ST-elevation ACS (63%). However, there was a larger number of sudden deaths with MINOCA as the early presentation, which would be indicative of the utility of OCT for the etiological study of recovered sudden death.

Regarding the coronary angiography findings, although the atherosclerotic cause for MINOCA was suspected, the angiography imaging were inconclusive (non-significant stenosis and scarce cases of images suggestive of plaque instability). This totally justified performing the OCT in all of the cases. The left anterior descending coronary artery was the vessel more commonly damaged, which is consistent with the results reported by other studies.

The OCT findings show that the median minimum lumen area of the patients was 3.2 mm². Former studies conducted with IVUS have reported on the minimum lumen area as suggestive of
non-significant stenosis for which medical therapy is, therefore, preferred. The study conducted by Gonzalo et al., that studied the value of OCT to establish the severity of intermediate angiographic stenoses (40% to 70% as seen on the quantitative coronary angiography) in patients with stable coronary artery disease revealed that the minimum lumen area as seen on the OCT to establish the concept of a functionally significant stenosis (fractional flow reserve ≤ 0.80) was 1.95 mm². Therefore, our patients showed stenoses on the OCT without compromised coronary flows, which is consistent with the angiographic results that showed non-significant stenoses (median of 40% by visual estimation and 41.2% on the quantitative coronary angiography). However, the OCT detected the instability of the plaque in 78% of registry patients, which is why although no significant stenosis was seen (on the angiography or OCT) a decision was made to implant a stent in 95% of the cases with an unstable plaque as seen on the OCT. There is not enough evidence to support this therapeutic strategy over pharmacological treatment only.

The EROSION trial studied conservative management (pharmacological) in cases of ACS with residual angiographic stenosis < 70% after the aspiration of a thrombus and the erosion of the plaque as the infarction mechanism. At the 1-year follow-up, 92.5% of the patients were still free from any major cardiovascular events. Therefore, conservative treatment may have been an option for a larger percentage of patients from our series. We should mention that the OCT avoided stent implantation in 6 patients in whom no unstable plaque was detected or in whom a different cause for MINOCA was found [hematoma/coronary dissection]. It would be advisable to conduct randomized, prospective clinical trials to assess the possible benefit of percutaneous
coronary intervention compared to pharmacological medical therapy for the management of patients with plaque disruption as the cause for MINOCA.

Mid-term patient progression was good and consistent with what has been reported by registries. Only 1 patient died of cardiovascular causes at the follow-up (a patient with multiple comorbidities and of an older age compared to the study median age, that is, a patient different from the population studied).

On the other hand, although this trial basically tries to identify the presence of unstable plaques on the OCT, the presence of vulnerable plaques was also studied since they are indicative of high cardiovascular risk. Thus, in most of the patients studied vulnerable plaques were found and they were often thin-cap fibroatheromas. TCFAs are considered as some of the most vulnerable plaques of all because they are made up of a lipid core [also known as lipid-rich necrotic core] covered by a very thin fibrous cap [< 65 μm] that makes them more prone to destabilization. Plaques with calcium nodules protruding towards the vessel lumen also have a higher risk of destabilization due to prospective plaque disruption, but in general they are less common. As a matter of fact, only 2 cases were found in our registry. Other findings of vulnerable plaque are the presence of macrophages [indicative of plaque inflammation], neovessels [they are immature, they can break, and cause intraplaque hemorrhage], and the size of the lipid core. all of these findings were present in over half of the study patients. Findings that are consistent with those reported by former studies.

Finally, we should mention that the registry included very few patients (27) over a 4.5-year period. The largest number of patients included happened over the last 2 years. This is due to the few OCTs performed in our center to this profile of patients at the beginning of the registry with a wider use of this imaging modality after its great utility was confirmed in selected cases (figure 1 of supplementary data). The follow-up of patient was short [median follow-up, 4 months] because over the last 6 months of the registry up to 9 patients (33%) were included and because 7 patients (26%) had a different nationality and were followed in their home countries; overall this amounts to 59% of the patients with a limited follow-up period.

CONCLUSIONS

The OCT is an intravascular imaging modality to establish etiological diagnosis in a large number of patients with MINOCA, which
Figure 2. Forty-year-old male patient admitted with an ST-segment elevation acute coronary syndrome. High-sensitivity troponin I peak levels of 5000 ng/L and normal left ventricular ejection fraction. The coronary angiography reveals the presence of a non-significant plaque (30%) in the distal right coronary artery. The optical coherence tomography reveals the presence of vulnerable plaques with the shape of a fibro-lipid plaque (green arrow) and neovessels (yellow arrow). Afterwards, it confirms the presence of a massive amount of thrombus, but the discontinuity of the intima layer cannot be identified (blue arrow) suggestive that it is plaque erosion.

Figure 3. Thirty-five-year-old male patient. He is a smoker who is admitted with a non-ST-segment elevation acute coronary syndrome, high-sensitivity troponin I peak levels of 2796 ng/L, and a normal left ventricular ejection fraction. The coronary angiography reveals angiographic diffuse thinning of the left anterior descending coronary. The optical coherence tomography reveals a very well-established low-signal region surrounding the vessel lumen (yellow arrow) suggestive of hematoma.
can lead to a better decision-making process with each particular case. Our study confirms the great accuracy of this imaging modality for the detection of unstable atherosclerotic plaques. Yet despite its proven utility and recommendation from expert consensuses, the use of this imaging modality in this type of patients is still scarce. This means that it will be necessary to establish algorithm of common actions in patients with MINOCA to avoid misdiagnosing its different etiologies.

CONFLICTS OF INTEREST

None reported.

WHAT IS KNOWN ABOUT THE TOPIC?

- MINOCAs amount to 5% to 7% of all myocardial infarctions. Different causes can trigger MINOCAs and treatment is different in each of them.

- Although there are different imaging modalities available (magnetic resonance imaging, OCT, IVUS, etc.) and their utility has been proven in the diagnosis of MINOCA, in over half of the patients the etiological diagnosis is never established.

WHAT DOES THIS STUDY ADD?

- In part this is due to a scarce use of these imaging modalities, although expert consensuses recommend their use.

- This study shows the utility of OCT to establish the etiological diagnosis of MINOCA, which reinforces the idea of a wider use of this imaging modality.

- We should mention that OCT findings can change the therapeutic approach.

- The need to conduct more specific studies to assess the best therapeutic strategy for the management of patients with MINOCA and plaque disruption.

SUPPLEMENTARY DATA

Supplementary data associated with this article can be found in the online version available at https://doi.org/10.24875/RECICE.M20000117.
REFERENCES


