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Optical coherence tomography assessment and quantification of intracoronary thrombus: Status and perspectives

Italo Porto [a,*], Alessio Mattesini [b], Serafina Valente [b], Francesco Prati [c,d], Filippo Crea [e], Leonardo Bolognese [a]

[a] Interventional Cardiology Unit, San Donato Hospital, Arezzo, Italy
[b] Interventional Cardiology Unit, Careggi Hospital, Florence, Italy
[c] Interventional Cardiology San Giovanni Hospital, Rome, Italy
[d] CLI foundation, Italy
[e] Department of Cardiovascular Sciences, Catholic University of the Sacred Heart, Rome, Italy

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ABSTRACT

Coronary angiography is the "golden standard" imaging technique in interventional cardiology and it is still widely used to guide interventions. A major drawback of this technique, however, is that it is inaccurate in the evaluation and quantification of intracoronary thrombus burden, a critical prognosticator and predictor of intraprocedural complications in acute coronary syndromes. The introduction of optical coherence tomography (OCT) holds the promise of overcoming this important limitation, as near-infrared light is uniquely sensitive to hemoglobin, the pigment of red blood cells trapped in the thrombus. This narrative review will focus on the use of OCT for the assessment, evaluation and quantification of intracoronary thrombosis.

1. Introduction

Coronary angiography is accepted as the "golden standard" imaging modality in interventional cardiology, and it is commonly used to guide percutaneous coronary interventions (PCI). However, as physicians deal with increasingly complex procedures, they have come to appreciate a major drawback of this technique, namely its limitation in the evaluation and quantification of the thrombotic burden [1,2]. Intracoronary thrombi are indeed a common occurrence in acute coronary syndromes (ACS) [3], and exhibit special physical properties and profoundly abnormal behavior [4]. The response of thrombus to standard management with pharmacotherapy and mechanical displacement is variable and, at times, unpredictable. Large evidence has accumulated relating thrombus quantity and quality to intraprocedural complications and adverse prognosis [5–9]. The introduction of optical coherence tomography (OCT), first as a research tool [10] and more recently as a guide to complex interventions [11], however, holds the promise of allowing precise thrombotic burden evaluation, due to its high resolution (in the order of 10–20 μm) and to the peculiar optical properties of thrombus as compared to other components of atherosclerotic plaques [12].

This review will focus on the use of OCT for the assessment, evaluation and quantification of intracoronary thrombus.

2. How does OCT identify thrombus?

Intracoronary OCT is a high-resolution imaging modality that uses a light source with a near-infrared spectrum (wavelengths ranging from 1280 to 1350 nm) to produce cross-sectional images of coronary arteries by measuring the "echo time delay" and the intensity of backscattered light [13]. OCT is not able to image under the condition of blood flow [14]. The poor penetration of light through blood is mainly due to the RBCs (containing no nucleus or organelles, but transporting hemoglobin and delimited by a membrane), to the high concentration (40%) of these scatterers (RBCs) in blood, and to the different refractive index of plasma and RBCs [15]. Thus, it is necessary to create a blood-free environment using a transparent media flush [16]. The peculiar optical properties of RBCs, however, besides representing an obstacle for light propagation, allow the distinction of intracoronary thrombosis into white and red thrombi on OCT.

At histologic examination red thrombus appears as a dark red mass protruding into the vessel lumen, consisting of mainly RBCs and fibrin, while white thrombus can be observed as a willow-like structure composed by platelets and white blood cells (WBCs), with a small amount of RBCs [12]. At OCT analysis red thrombus can be defined as high-

Abbreviations: OCT, optical coherence tomography; (FD)-OCT, frequency domain OCT; 3D-OCT, three dimensional OCT; ACS, acute coronary syndrome(s); IVUS, intravascular ultrasound; RBC(s), red blood cell(s); WBC(s), white blood cell(s); AMI, acute myocardial infarction; STEMI, ST-elevation myocardial infarction; TCFA, thin-cap fibroatheroma; TS, thrombus score; TA, thrombus area; TV, thrombus volume; SV, stent volume; FTA, free thrombus area; ISA, incomplete strut apposition; ST, stent thrombosis; DES, drug-eluting stent; BMS, bare metal stent; TIMI, thrombolysis in myocardial infarction; IRA, index related artery.

* Corresponding author at: Interventional Cardiology Unit, Ospedale San Donato, Via Pietro Nenni 22, 52100 Arezzo, Italy.
E-mail address: italo.porto@gmail.com (I. Porto).

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backscattering, with signal-free shadowing protrusion (Fig. 1A), while white thrombus is depicted as signal-rich, low-backscattering mass projecting into the lumen (Fig. 1B). However, a mixed thrombus with intermediate features is often observed (Fig. 1C) [10].

Due to its high content in RBCs, red thrombus is characterized by elevated values of total light attenuation coefficient, μ_t[17]. In a study by Kume et al. [12], OCT was able to differentiate between the two types of thrombi with high sensitivity (90%) and specificity (88%). In particular, the ½ width of signal intensity attenuation was greater in white than in red thrombus (324 ± 50 μm vs 183 ± 42 μm, p = 0.0001) and the cut-off value of 250 μm differentiated white from red with high sensitivity and specificity. Interestingly, no significant differences in peak intensity measured at the surface of the thrombus were found (145 ± 34 μm vs 130 ± 18 μm, p = 0.12) [12]. In practical terms, this means that the penetration of light is more rapidly attenuated by red than by white thrombus, and that it is the presence of optical shadowing (and not the bright appearance at the trailing edge) which has to be used to identify red thrombi.

In comparison with other intracoronary imaging modalities such as angioscopy and IVUS, OCT is capable to detect and characterize coronary thrombosis with greater accuracy. In a study, OCT showed a sensitivity of 100% for the detection of intracoronary thrombus, similar to that of angioscopy but much higher than that of IVUS (33%), and, in addition, a higher sensitivity for the detection of plaque rupture as compared to both angioscopy and IVUS (respectively, 73% vs. 47% vs. 40%); moreover, plaque erosion was almost exclusively detected by OCT (23%) [18].

Ex-vivo measurements of optical properties of human blood during coagulation with OCT might also provide unique information in experimental models of thrombosis and have been used for the study of anticoagulation factors and for implementation of antithrombotic drugs. A strong linear correlation ($R^2 = 0.998$) was observed between thrombus volume measured by OCT and thrombus weight [19]. Another group developed an OCT-derived parameter, the clotting time derived from the 1/e light penetration depth ($d_{1/e}$) vs. time, applying it to the study of the effects of coagulation activators and anticoagulants at various concentrations [20].

3. Angiographic thrombus scoring systems

Angiographic thrombus grading scales are commonly used for quantification of the thrombus burden. The widely employed TIMI scale, originally created by the Thrombolysis In Myocardial Infarction study group investigators [21], was conceived in the fibrinolysis era, and reflected the view that the size and burden of intracoronary thrombi affected the efficacy of this therapy. The TIMI classification relies on the relative estimated size of the thrombotic mass and of the affected vessel, using a simple score ranging from grade 0 (no thrombus), to grade 5 (very large thrombus content that completely occludes flow).

Whereas this classification is user-friendly and universally accepted, it has two obvious limitations. At one end of the scale, angiography may easily miss small or moderate-sized thrombi, whose appearance is often of an indefinite intracoronary "haziness", difficult to differentiate from calcium, plaque rupture or dissection. The accuracy of the highest level (grade 5), on the other hand, is clearly subjective, as the ischemic vessel containing grade 5 thrombus is totally occluded. Thus, an important modification was introduced by the Thoraxcenter (Rotterdam, The Netherlands) investigators [6]. Their method utilizes either a guide wire or a 1.5 mm balloon for crossing and recanalization of the occluding thrombus. This intervention re-establishes a certain degree of antegrade coronary flow to the extent that the exposed underlying thrombotic mass can be reclassified as either a small (grade 1–3) or a large thrombus burden (grade 4).

In the early 2000s, Yip and colleagues employed six angiographic predictors of large thrombus burden, namely (1) a cutoff pattern of occlusion, (2) accumulated thrombus proximal to the occlusion, (3) a reference lumen diameter of the IRA of > 4.0 mm, (4) an incomplete obstruction with an angiographic thrombus with the greatest linear dimension more than 3 times the reference lumen diameter, (5) the presence of floating thrombus proximal to the lesion, and (6) a persistent dye stasis distal to the occlusion, showing that the first three were independent predictors of slow flow/no reflow in STEMI patients [22].

In another recent development, Aleong et al. innovatively combined edge detection and video densitometry-based quantitative coronary

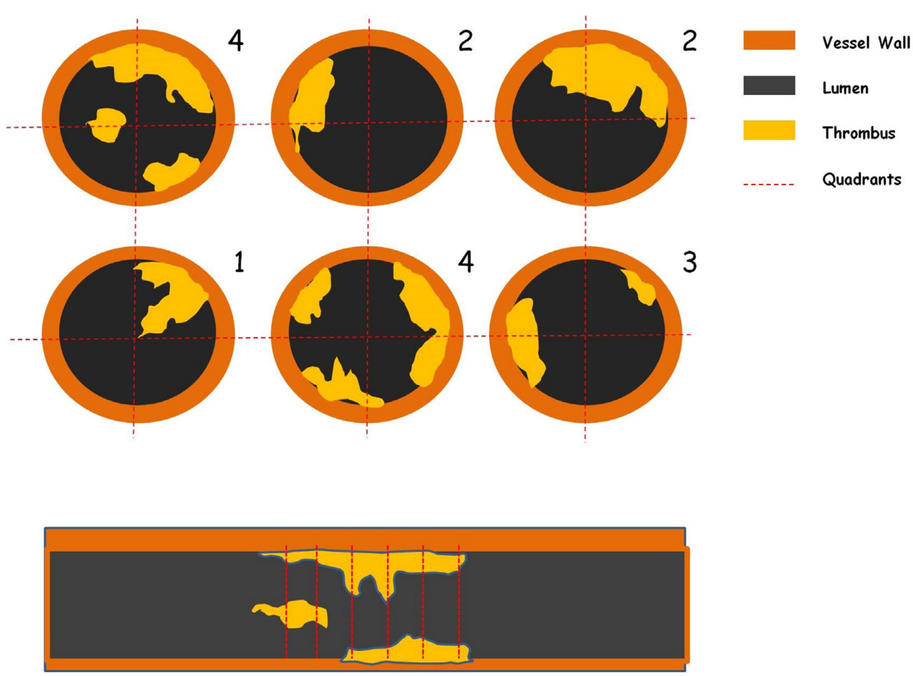

Fig. 1. Schematic representation of Prati's Thrombus Score. This schematic representation shows an example of OCT quantitative thrombus evaluation, as proposed by Prati et al. in the COCTAIL trial (Prati, Capodanno et al. *JACC Cardiovasc Interv* 2010). The Thrombus Score is obtained by calculating the absolute number of quadrants encroached by thrombus during a pullback. By applying this method, in each cross-section, the thrombus identified by OCT in the culprit lesion site is classified as absent or subtending 1, 2, 3 or 4 quadrants. In this schematic example, the total score, which is calculated as the sum of each cross-section score, equals 16.

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