International Journal of Cardiology 253 (2018) 55–60

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Correlation between frequency-domain optical coherence tomography and fractional flow reserve in angiographically-intermediate coronary lesions

Francesco Burzotta [a,*], Roberto Nerla [a], Jonathan Hill [b], Lazzaro Paraggio [a], Antonio Maria Leone [a], Jonathan Byrne [b], Italo Porto [a], Giampaolo Niccoli [a], Cristina Aurigemma [a], Carlo Trani [a], Philip MacCarthy [b], Filippo Crea [a]

[a] Institute of Cardiology, Catholic University of the Sacred Heart, Policlinico A. Gemelli, 8, 00168 Rome, Italy
[b] Cardiac Department, King's College Hospital, Denmark Hill, London, United Kingdom

ARTICLE INFO

Article history:
Received 8 January 2017
Received in revised form 15 September 2017
Accepted 2 October 2017

Keywords:
Optical coherence tomography
Fractional flow reserve
Intermediate coronary lesions

ABSTRACT

Background: The decision-making process of patients with angiographically-intermediate coronary lesions (ICL) is clinically challenging and may benefit from adjunctive invasive techniques. Fractional-flow-reserve (FFR) represents the gold standard to evaluate ICL but frequency-domain optical-coherence-tomography (OCT) is a novel, promising, high resolution coronary imaging technique, which allows physiopathologic assessment of coronary plaque. We investigated the possible relation between OCT and FFR in selected ICL patients.

Methods: Stable or unstable patients with ICL who underwent both FFR and OCT assessment at two large tertiary centers were retrospectively enrolled. FFR was performed according to standard methodology. OCT images were (on blind to clinical and FFR results) analyzed to assess minimal lumen area (MLA), percentage area stenosis (AS), thrombus and plaque ulceration.

Results: Forty patients were identified (62 ± 10 years, 93% symptomatic, 35% acute presentation, 93% left-anterior-descending artery ICL). Percentage diameter stenosis at quantitative coronary angiography was 40 ± 12% and FFR was 0.85 ± 0.07. MLA ($p = 0.009$), AS ($p < 0.001$) and plaque ulceration ($p = 0.02$) were significantly associated with FFR values. An integrated assessment of AS (≥ or <70%), MLA (≥ or <2.5 mm^2) and presence or absence of thrombus and plaque ulceration was found to have the potential to accurately (sensitivity 91%, specificity 93%) predict FFR results.

Conclusion: In patients with ICL, a combination of different OCT parameters may help predict FFR results. These findings suggest that only a comprehensive assessment of lesion features by OCT can allow an accurate prediction of lesion severity assessed by FFR.

1. Introduction

Among patients undergoing coronary angiography, those with angiographically-intermediate coronary lesions (ICL) constitute a clinically challenging subset. In this setting, coronary angiography fails to allow detailed assessment of coronary atherosclerotic plaque morphology and severity. As a consequence, new techniques have been developed in order to identify lesions which may hinder coronary blood flow and cause clinical complications. To date, measurement of fractional flow reserve (FFR) by pressure wire represents a valuable "functional" evaluation of ICL proven to safely guide myocardial revascularization decision and its role has been demonstrated by previous randomized clinical trials [1,2]. Yet, a detailed assessment of vessel wall anatomy by intracoronary imaging may offer additional information. Among the different imaging modalities, frequency-domain optical coherence tomography (OCT) represents a cutting-edge technology able to provide fast, high-resolution, coronary lumen contour assessment [3], which is increasingly adopted. Notwithstanding, the prediction of functional severity of coronary stenoses on the basis of their morphology as assessed by OCT is poorly known.

In the present study, we investigated the possible correlations between OCT features and fractional-flow-reserve (FFR) in a series of patients with ICL who underwent both forms of assessments.

Abbreviations: OCT, optical coherence tomography; FFR, fractional flow reserve; IVUS, intravascular ultrasound; QCA, quantitative coronary analysis; ICL, intermediate coronary lesions; PCI, percutaneous coronary intervention; MLA, mean lumen area; AS, percentage of area stenosis; ROC, receiver operating characteristic.

* Corresponding author at: L.go Gemelli 8, 00168 Rome, Italy.
E-mail address: f.burzotta@rm.unicatt.it (F. Burzotta).

https://doi.org/10.1016/j.ijcard.2017.10.011
0167-5273/

2. Methods

2.1. Patients' selection

The catheterization laboratory databases of two large tertiary centers were retrospectively reviewed in order to identify all consecutive patients who underwent both FFR and OCT, performed according to operator discretion, to assess an ICL during a 4 year period (2011–2014). ICL was defined as a coronary lesion determining a visually estimated percentage diameter stenosis ranging from between 30% and 80% [4]. Demographical, clinical, angiographic and procedural data were collected in the institutional databases approved by the local Institutional Review Board. Patients with ST-elevation acute myocardial infarction were excluded from the present study. Left main disease was also considered as an exclusion criterion because its different MLA cut-off and the higher (even if more predictable) amount of myocardial perfusion territory could improve heterogeneity of our results. The study was conducted in accordance with the Declaration of Helsinki on ethical principles for medical research involving human subjects. All patients have read and signed informed consent for the procedure.

2.2. Quantitative coronary angiography

Quantitative coronary angiography (QCA) was performed offline by a skilled analyzer using a standard commercial software (CASS QCA 5.9, Pie Medical Imaging BV, Maastricht, The Netherlands), on a single, selected 2D end-diastolic image frame.

Care was taken to select projections and frames with minimal foreshortening and vessel overlap, to obtain the best lesion assessment. Vessel diameters were calculated in absolute values (mm). For contour detection, the user indicated the vessel by choosing two centre positions proximal and distal to the stenosis. The vessel contours were automatically determined and, in case of incorrect automated analysis, manual correction was applied. The reference vessel diameter was based on the computer estimation of the original arterial dimensions at the stenosis site. The following angiographic parameters were obtained: minimal lumen diameter (MLD, mm), proximal and distal reference diameter (RD, mm), percentage diameter stenosis (% DS) and lesion length (LL, mm).

2.3. FFR assessment

After guiding catheter positioning (shape and size chosen by the operator), a 0.014″ pressure monitoring guidewire (Pressure Wire, St. Jude Medical, St. Paul, New Mexico, United States or Verrata pressure guide wire, Volcano, San Diego, California, United States) was calibrated, advanced into the guiding catheter and the transducer equalized to catheter pressure just outside the catheter tip. The guidewire was then advanced beyond the lesion under examination and position angiographically checked. The absence of drift (i.e. abnormal equalization with a variability of >0.02 in Pd/Pa value just outside the catheter tip) was checked at procedure end. In case of documented drift, all steps were repeated until FFR measure in the absence of drift was obtained. FFR was calculated as the lowest ratio of distal coronary pressure (Pd) divided by aortic pressure (Pa) after achievement of maximal hyperemia, obtained using intravenous or intracoronary adenosine [5]. A cut-off value ≤0.80 was considered as indicative of significant ICL-associated ischemic burden [1,2,6].

2.4. OCT assessment

OCT is an imaging modality analogous to ultrasound imaging, but uses light instead of sound. Cross-sectional images are generated by measuring the echo time delay and intensity of light that is reflected or back-scattered from internal tissue structures [7]. OCT images were acquired with a commercially available system (C7 System; St. Jude Medical, Westford, Massachusetts, United States) after the OCT catheter (C7 Dragonfly; St. Jude Medical, Westford, Massachusetts, United States) was advanced to the distal end of the target lesion. The entire length of the region of interest was scanned using the integrated automated 54 mm length pull-back device at 20 mm/s, with complete segment coverage in all documented cases. During image acquisition, coronary blood flow was replaced by the continuous flushing of contrast media in order to create a virtually blood-free environment. All images were digitally recorded and stored using a proprietary software (LightLab Imaging).

For the present study, a trained operator, blinded to all clinical and procedural variables, reviewed the images for the presence of qualitative parameters and performed quantitative measures using the LightLab Imaging software. In particular, the following series of quantitative and qualitative parameters were assessed, according to the indications of consensus document from the International Working Group for intravascular OCT standardization and validation [8]:

1. minimal lumen area (MLA) defined as cross section area at the smallest lumen area level;
2. mean reference lumen area (mRLA) defined as [proximal reference lumen area (pRLA) + distal reference lumen area (dRLA)]/2; pRLA and dRLA were defined as the cross sections at the frame with largest lumen within 10 mm proximal and distal to MLA, before any major side-branch, and with preserved three-layer vessel wall. In the case of the presence of major side-branches, like lesions located in the ostial left anterior descending artery, the dRLA was considered as the mRLA;
3. percentage area stenosis (AS) calculated using the following formula: (mRLA-MLA)/mRLA × 100;
4. major plaque ulceration: defined as a recess in the plaque beginning at the luminal-intimal border [8];
5. intracoronary *thrombi* defined as masses protruding into the vessel lumen discontinuous from the surface of the vessel wall and including both red thrombi (characterized as high-backscattering protrusions with signal-free shadowing) and white thrombi (characterized by signal-rich, low-backscattering billowing projections protruding into the lumen).

2.5. Statistical analysis

Categorical variables were presented as numbers and percentages and analyzed with Fisher's exact test. Continuous variables (such as OCT and FFR data) are normally distributed and expressed as mean ± SD and were compared by *t*-test.

Linear regression was used to establish OCT parameters predicting FFR values. Univariate and multivariate regression analyses were performed to assess clinical and OCT predictors of FFR ≤ 0.80. Variables included in analysis were age, diabetes, clinical presentation, thrombus at OCT, ulceration at OCT, MLA and AS. Those associated with abnormal FFR values at the $p < 0.10$ level in univariate analysis were included in multivariate analysis.

Receiver operating characteristic (ROC) curve analyses of MLA and AS in predicting a positive FFR (≤0.80) were realized and compared with DeLong test.

A *p*-value < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 22.0 (SPSS, Inc., Chicago, Illinois).

3. Results

3.1. Population characteristics

Clinical registry data from 40 consecutive patients (age 62.1 ± 11, 78% males) were collected. Clinical characteristics of enrolled patients are reported in Table 1. The study population constituted a highly selected cohort of patients characterized by high clinical suspicion of significant coronary lesion (93% with chest pain; the remaining patients having non-invasive documentation of inducible ischemia at non-invasive tests). In the setting of ACS, OCT and FFR assessment has been performed in other than the culprit lesion. The ICL had true borderline angiographic significance (percentage diameter stenosis at quantitative coronary angiography: 40 ± 12%) and were located in arteries without diffuse disease (correctly scanned with a single OCT run) and supplying a significant amount of myocardium (93% of LAD location, 65% proximal) (Table 1).

Fig. 1 shows an example of ICL combined assessment with FFR and OCT.

3.2. FFR and OCT findings

In keeping with such highly selected clinical and anatomical features, mean FFR was 0.85 ± 0.07 and 11 patients (27.5%) had a

Table 1
Main clinical characteristics of our study population in the two PCI sites.

	Overall
Clinical characteristics	
Age (years)	62.1 ± 10.7
Male sex (%)	31 (78)
Hypertension (%)	31 (78)
Diabetes mellitus (%)	9 (22)
Current smoking (%)	14 (35)
Hypercholesterolemia (%)	20 (50)
Acute coronary syndrome (%)	14 (35)
Previous AMI (%)	9 (22)
Angina (%)	37 (93)
Angiographic characteristics	
Number of diseased vessels (*n*)	1.35 ± 0.6
Proximal lesion location (%)	26 (65)
Left anterior descending artery (%)	37 (93)
Right coronary artery or left circumflex artery (%)	3 (7)
Disease Length (mm)	11.0 ± 3.6
QCA proximal reference (mm)	3.07 ± 0.6
QCA distal reference (mm)	2.88 ± 0.6
QCA stenosis (%)	40.4 ± 12.2

AMI = acute myocardial infarction; PCI = percutaneous coronary intervention.
QCA = quantitative coronary angiography.