International Journal of Cardiology 286 (2019) 7–12

Contents lists available at ScienceDirect

International Journal of Cardiology

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

Optical coherence tomography and C-reactive protein in risk stratification of acute coronary syndromes☆

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ARTICLE INFO

Article history:
Received 27 November 2018
Received in revised form 6 January 2019
Accepted 16 January 2019
Available online 18 January 2019

Keywords:
Acute coronary syndrome
Optical coherence tomography
Macrophage infiltration
Inflammation
Secondary prevention

ABSTRACT

Background: Patients with acute coronary syndrome (ACS) associated to high C-reactive protein (CRP) levels exhibit a higher risk of future acute ischemic events. Yet, the positive predictive value of CRP is too low to guide a specific treatment. Our study aims to identify a high-risk patient subset who might mostly benefit from anti-inflammatory treatment on the basis of the combination of optical coherence tomography (OCT) assessment of the culprit vessel and CRP serum levels.

Methods: Patients admitted for ACS and undergoing pre-interventional OCT assessment of the culprit vessel were selected from "Agostino Gemelli" Hospital OCT Registry. The primary end-point was recurrent ACS (re-ACS). CRP levels ≥2 mg/L were considered abnormal.

Results: The overall study population consisted of 178 patients. Among these, 156 patients were included in the primary end-point analysis. The re-ACS rate was 23% at 3-year follow-up. High CRP (2.587, 95% CI:1.345–10.325, $p = 0.031$), plaque rupture (3.985, 95% CI:1.698–8.754, $p = 0.009$), macrophage infiltration (3.145, 95% CI:1.458–9.587, $p = 0.012$) and multifocal atherosclerosis (2.734, 95% CI:1.748–11.875, $p = 0.042$) were independent predictors of re-ACS. All patients (14/14) with high CRP and with all OCT high-risk features had re-ACS. At the other extreme, only 4 of the 82 patients with low CRP levels and lack of high-risk features at OCT examination exhibited re-ACS at follow-up.

Conclusions: The combination of systemic evidence of inflammation and OCT findings in the culprit plaque identifies very high-risk ACS. Future studies are warranted to confirm these findings and to test an anti-inflammatory treatment in this patient subset.

1. Introduction

Despite lifestyle and risk factors modification, annual rate of recurrent acute coronary syndrome (ACS) (unstable angina or myocardial infarction with or without ST-segment elevation) is still high at population level [1]. Indeed, in spite of current pharmacologic and reperfusion therapies, 20–25% of patients present recurrent acute ischemic events at 3-year follow-up [2,3]. Several studies have previously shown that patients with an ACS and raised levels of C-reactive protein (CRP), a prototypic marker of inflammation, have a worse outcome as compared to that of patients with low CRP levels [4–7].

Optical coherence tomography (OCT) is an intracoronary imaging modality, introduced in clinical practice in the last decade, that allows to obtain in vivo images of coronary plaque morphology and to study the pathologic substrate of ACS [8–10] with higher definition than intravascular ultrasound [11] and an excellent correlation with histology in validation studies [12]. Recent OCT studies reported a higher incidence of major adverse cardiovascular events (MACE) at follow-up for patients presenting a plaque rupture at baseline as compared with those with intact fibrous cap plaque [13,14]. Moreover, an OCT study from our group described local macrophage infiltration in two-thirds of ACS patients with plaque rupture; but not all cases were associated to high CRP serum levels [15]. Of note, CRP is the main down-stream marker of inflammation associated with an increased risk of cardiovascular events [4–7,16].

The Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS) trial has recently shown that anti-inflammatory therapy with canakinumab, an antagonist of interleukin-1β, in patients with history of acute myocardial infarction and raised baseline levels of CRP was associated to a modest reduction of the rate of major cardiovascular events as compared to placebo [17]. A retrospective analysis found that the benefit was confined to patients who achieved levels of CRP

☆ All the authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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https://doi.org/10.1016/j.ijcard.2019.01.058
0167-5273/

on treatment of <2 mg/L [18]. In view of the high cost of canakinumab and of the potential serious side effects of this form of treatment it would be highly desirable to prospectively identify the potential responders to an anti-inflammatory treatment.

In this study we sought to assess risk prediction based on the combined assessment of OCT features of the unstable plaque and of CRP levels in peripheral blood. Indeed, a better comprehension of the mechanisms underlying recurrent coronary instability could be of help to individualize the secondary prevention strategy.

2. Methods

2.1. Study population

Patients with a diagnosis of ACS undergoing OCT imaging of the culprit vessel were retrospectively selected from the "Agostino Gemelli" Hospital OCT Registry, a prospectively-enrolling registry of patients undergoing OCT imaging during coronary angiography and/or percutaneous coronary intervention at Catholic University of the Sacred Heart Teaching Hospital, Rome. Exclusion criteria were: stent-related acute coronary events, coronary bypass graft disease, severe hepatic or renal dysfunction, malignant disease or acute or chronic inflammatory disease, extreme age (<18 or >80 years), electric or hemodynamic instability. On the basis of these criteria, 19 patients were not enrolled in the study. During OCT images analysis, 8 patients were excluded for poor visualization of plaque characteristics due to large thrombus amount or residual luminal blood. Cardiovascular risk factors were collected and routine blood test, including high sensitivity CRP serum levels measurement, were performed in all patients. High CRP was defined for serum levels ≥2 mg/L [17]. All patients underwent coronary angiography followed by OCT imaging of the culprit vessel and angioplasty. Detailed information on risk factors definition, blood tests, clinical diagnosis and treatment, as well as procedural data are reported in the Online Appendix.

2.2. Primary and secondary study end-point

A clinical follow-up was performed after 3 years from discharge by direct interview, phone call and/or clinical check (time to follow-up: 37.5 ± 5.3 months). The primary end-point was recurrent ACS (re-ACS) (STEMI, NSTEMI or unstable/progressive angina according to Braunwald Unstable Angina Classification [19]). Patients who experienced a different MACE ($n = 22$) were not included in the primary end-point analysis (final population $n = 156$). Recurrent myocardial infarction was diagnosed by the detection of raise and fall of cardiac biomarkers above the 99th centile of the upper reference limit, along with evidence of myocardial ischemia with at least one of the following criteria: ischemic symptoms; electrocardiographic changes indicative of new ischemia (new ST-T changes or new left bundle branch block); development of pathological Q waves in the electrocardiogram; imaging evidence of new loss of viable myocardium or new regional wall motion abnormalities [20].

The secondary end-point was the incidence of MACE, defined as the composite of cardiovascular death, re-ACS and myocardial revascularization (final population $n = 178$). Cardiac death included sudden death and death preceded by typical chest pain; myocardial revascularization was defined as either repeat percutaneous or surgical revascularization for either stable angina or positive ischemia non-invasive test and did not include staged procedures for multivessel coronary disease planned during index admission.

2.3. OCT image analysis

OCT image analysis was performed using an offline review work station (Ilumien Optis, St Jude Medical) by two expert investigators (F.F. and G.N.) who were blinded to patients' data.

Analysis was conducted at the culprit site to characterize the culprit plaque and along the entire OCT pullback for the presence of multifocal atherosclerosis. Mechanisms of ACS were sought: plaque rupture was defined as the presence of fibrous cap discontinuity leading to a communication between the inner (necrotic) core of the plaque and the lumen [12,21]; lesions other than plaque rupture were defined as intact fibrous cap lesions. Minimal lumen area was evaluated along the length of the target lesion. Tissue characteristics of underlying plaque were defined with previously established criteria [12,21]. The presence of fibrous (homogeneous, signal-rich region) and lipid (signal-poor region with diffuse borders) plaques was recorded. Calcifications within plaques were identified by the presence of well delineated, low back-scattering heterogeneous regions [21]. In order to identifying the presence of local inflammation at the level of culprit plaques, the presence of macrophages accumulation at the culprit site was assessed with both qualitative and quantitative method as previously described [15]. According to International Working Group for Intravascular Optical Coherence Tomography (IWG-IVOCT) Consensus standards [12], macrophages have been visualized by OCT imaging as signal-rich, distinct, or confluent punctate regions that exceed the intensity of background speckle noise and generate a backward shadowing. A quantitative analysis was performed with a dedicated software provided by St Jude Medical by measuring the normalized standard deviation, known to have a high degree of positive correlation with histological measurements of macrophage content [22]. Thrombus was defined as an irregular mass protruding into the lumen or adjacent to the luminal surface. The thinnest part of the fibrous cap was measured three times, and the average value was calculated. In plaque rupture, residual fibrous cap was identified as a flap between the lumen of coronary artery and the cavity of plaque, and its thickness was measured at the thinnest part. Thin-cap fibroatheroma (TCFA) was defined as a plaque with lipid content in at least 2 quadrants and the thinnest part of a fibrous cap measuring ≤65 μm [21]. The maximum arc of lipids was measured. Microvessels were defined as signal-poor circular structures with a diameter <250 μm in a plaque recognized on more than three consecutive cross-sectional OCT images [12]. A multifocal distribution of atherosclerosis was defined as the presence of at least one remote mild or moderate lesion (>30% stenosis) in each analyzed vessel. Inter-observer and intra-observer analysis variability was assessed by the evaluation of random samples of 40 patients by two independent observers and by the same observer at two separate time points with a 2-week interval. The inter-observer Kappa coefficients were 0.90 for diagnosis of rupture or erosion and 0.87 for macrophage infiltration. The intra-observer Kappa coefficients were 0.96 for diagnosis of rupture or erosion and 0.94 for macrophage infiltration. In case of discordance, a consensus was obtained with a third investigator (R.M. or R.V.). Details on OCT acquisition are reported in the Online Appendix.

2.4. Statistical analysis

Data distribution was assessed according to Kolmogorov–Smirnov test. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, if they followed a normal or non-normal distribution, respectively. Study population was divided into two groups according to the occurrence of primary and secondary end-point, respectively. Comparison of continuous variables between two groups was performed by unpaired Student *t*-test or Mann-Withney *U* test, as appropriate. Comparison of categorical variables was performed by the χ^2 test or Fisher's exact test, as appropriate. Binomial logistic regression analysis was performed to identify the independent predictors of re-ACS; variables having a *p*-value <0.05 at univariable model entered in the multivariable model. Plaque type variable was not included in the model because of its collinearity with plaque rupture. Plaque rupture, macrophage infiltration and multifocal atherosclerosis were, consequently, defined OCT high-risk features for re-ACS. In order to better characterize and compare the CRP's and OCT high-risk features' predictive values, receiver operating characteristic (ROC) curves were displayed and areas under curves calculated; DeLong's method [23] was used to compare the ROC curves. All tests were two-sided, and a *p*-value of <0.05 represented statistical significance. All analyses were performed by using the SPSS version 23.0 (SPSS, Inc., Chicago, IL, USA). The study was approved by Catholic University Ethics Committee and all participants gave their written informed consent to be included in the study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

3. Results

3.1. Primary end-point and baseline clinical and angiographic data

Data are reported in Table 1. Among 156 ACS patients (age 65.0 ± 11.6 years, male gender 65%, 41% STEMI and 59% NSTE-ACS), 36 (23%) patients had a re-ACS at follow-up. The events at follow-up were due equally to the stented lesion and to lesion localized in other segments or vessels. No differences concerning cardiovascular risk factors, clinical presentation or medical treatment at discharge were found between the two cohorts of patients. High CRP levels and type B2/C lesions rates were significantly higher within re-ACS patients (75% vs 29%, $p < 0.001$ and 50% vs 30%, $p = 0.044$, respectively).

3.2. Primary end-point and baseline plaque morphology

Plaque rupture and lipid plaque type were more frequent in patients with re-ACS as compared with patients without events at follow-up (83% vs 42%, $p < 0.001$ and 83% vs 63%, $p = 0.026$, respectively). Similarly, the rate of multifocal atherosclerosis was higher in re-ACS group (69% vs 25%, $p < 0.001$). Macrophages infiltration was more frequent and macrophages density higher in patients with re-ACS as compared with patients without events at follow-up (86% vs 24%, $p < 0.001$ and 7.11 ± 0.67 vs 6.33 ± 0.45, $p = 0.019$, respectively). Consistently, the combination of plaque rupture, macrophage infiltration (inflammatory plaque rupture) and multifocal atherosclerosis was more frequent in patients with re-ACS (52.8% vs 5.8%, $p < 0.001$).

3.3. Independent predictors of the primary end-point

At multivariable analysis (Table 2), high CRP levels (OR 2.587, 95% CI 1.345–10.325, $p = 0.031$), plaque rupture (OR 3.985, 95% CI 1.698–8.754, $p = 0.009$), macrophage infiltration (OR 3.145, 95% CI 1.458–

Table 1
Baseline clinical, laboratory, angiographic, procedural and optical coherence tomography data of the overall study population and according primary end-point occurrence.

	Overall (n = 156)	re-ACS (*n* = 36, 23%)	No recurrent events (*n* = 120, 77%)	p
Clinical characteristics				
Age, years	65.0 ± 11.6	65.6 ± 11.9	64.4 ± 11.3	0.33
Male gender	101 (65)	24 (67)	77 (64)	0.84
Cardiovascular risk factors				
Smoking	73 (47)	18 (50)	55 (46)	0.71
Diabetes mellitus	41 (26)	8 (28)	33 (27)	0.67
Hypertension	101 (65)	21 (58)	80 (66)	0.43
Hyperlipidemia	90 (58)	20 (55)	70 (58)	0.84
Family history of CAD	89 (57)	19 (53)	70 (58)	0.57
Presentazione at index event				0.22
STEMI	64 (41)	16 (44)	48 (40)	
NSTEACS	92 (59)	20 (56)	72 (60)	
Medications at discharge				
Beta-blockers	126 (81)	30 (84)	96 (80)	0.81
ACE-inhibitors or ARB	131 (84)	31 (86)	100 (83)	0.80
Statins	133 (85)	32 (89)	101 (84)	0.59
Insulin	16 (10)	3 (8)	13 (11)	1.0
Oral hypoglycemic agents	25 (16)	5 (14)	20 (17)	0.80
Laboratory data				
GFR, mL/min	81 ± 40	75 ± 33	84 ± 39	0.75
hs-CRP, mg/dL	5.57 (1.56–8.99)	7.84 (5.13–10.19)	2.25 (1.55–5.33)	0.004
High hs-CRP	62 (40)	27 (75)	35 (29)	<0.001
TC, mg/dL	195 (125–255)	190 (120–270)	205 (135–260)	0.43
TG, mg/dL	114 (103–195)	111 (101−201)	117 (98–198)	0.61
LDL-C, mg/dL	92 (52–155)	95 (65–140)	84 (58–151)	0.73
HDL-C, mg/dL	35 (30–78)	36 (28–65)	41 (33–74)	0.42
CK-MB, ng/mL	3.05 (1.25–8.99)	3.15 (1.74–6.24)	4.32 (1.34–10.9)	0.73
TnI, ng/mL	0.125 (0.098–1.003)	0.199 (0.110–1.216)	0.137 (0.012–0.647)	0.49
Angiographic data				
Multivessel disease	75 (48)	17 (46)	58 (47)	0.99
Culprit vessel				0.49
LAD	93 (60)	22 (61)	71 (59)	
LCx	37 (24)	12 (33)	25 (21)	
RCA	33 (21)	7 (19)	26 (22)	
B2/C lesion	54 (35)	18 (50)	36 (30)	0.044
OCT qualitative analysis				
Mechanism of ACS				<0.001
Plaque rupture	80 (52)	30 (83)	50 (42)	
Intact fibrous cap	76 (48)	6 (17)	70 (58)	
Plaque type				0.026
Lipidic	106 (68)	30 (83)	76 (63)	
Fibrous	50 (32)	6 (17)	44 (37)	
TCFA	47 (30)	10 (28)	37 (31)	0.84
Macrophages infiltration	60 (38)	31 (86)	29 (24)	<0.001
Calcifications	28 (18)	4 (10)	24 (20)	0.32
Microchannels	27 (17)	7 (20)	20 (16)	0.80
Multifocal atherosclerosis	55 (35)	25 (69)	30 (25)	<0.001
Inflammatory plaque rupture and multifocal atherosclerosis	26 (16.7)	19 (52.8)	7 (5.8)	<0.001
OCT quantitative analysis				
Macrophages density (NSD)	6.67 ± 0.75	7.11 ± 0.67	6.33 ± 0.45	0.019
MLA, mm2	1.66 (1.17–2.89)	1.69 (1.15–3.32)	1.70 (1.27–2.49)	0.52
Fibrous cap thickness, μm	74.7 ± 29.6	74.5 ± 27.2	75.4 ± 32.9	0.41
Lipidic arc, °	198.3 ± 105.3	210.2 ± 104.3	176.4 ± 107.1	0.14
Analyzed length vessel, frames	176.4 ± 61.3	174.4 ± 62.9	181.8 ± 59.0	0.51

Values shown are n (%), mean ± standard deviation.
ACS, acute coronary syndrome; CAD, coronary artery disease; STEMI, ST-elevation myocardial infarction; NSTEACS, non-ST-elevation myocardial infarction; ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blockers; GFR, glomerular filtration rate; hs-CRP, high-sensitive C-reactive protein; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; CK-MB, creatine kinase myocardial band; TnI, troponin I; LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery; BMS, bare metal stent; DES, drug-eluting stent; TCFA, thin cap fibroatheroma; high-sensitive C-reactive protein; MLA, minimal lumen area; NSD, normalized standard deviation.

9.587, $p = 0.012$) and multifocal atherosclerosis (OR 2.734, 95% CI 1.748–11.875, $p = 0.042$) were independent predictors of re-ACS at follow-up (see Fig. 1).

3.4. Systemic inflammation and OCT assessment in risk prediction

Supplementary Table 1 and Fig. 2 show primary end-point occurrence according to OCT high-risk features and CRP serum levels. *Re*-ACS were observed in: 14/14 (100%) patients with OCT high-risk features and high CRP, 5/12 (41.6%) patients with OCT high-risk features and low CRP, 13/48 (27.1%) patients without OCT high-risk features and high CRP and 4/82 (4.9%) patients without OCT high-risk features and low CRP. The difference among the four groups was statistically significant (overall $p < 0.001$). Of note, 48/130 (36.9%) patients without events at follow-up had high CRP in absence of OCT high-risk features.

Table 2
Predictors of recurrence of acute coronary syndrome at follow-up at multivariable analysis.

	OR	95% CI	p
B2/C lesion	1.201	0.354–4.254	0.452
High CRP	2.587	1.345–10.325	0.031
Plaque rupture	3.985	1.698–8.754	0.009
Macrophage infiltration	3.145	1.458–9.587	0.012
Multifocal atherosclerosis	2.734	1.748–11.875	0.042

OR, odds ratio; CI, confidence interval; CRP, C-reactive protein.

3.5. ROC curve analysis and predictive value of OCT high-risk features and CRP levels

ROC curve analysis showed a significant predictive value for CRP and each OCT high-risk features, as reported in Supplementary table 2. Moreover, area under curve for the combination of OCT high-risk features (inflammatory plaque rupture and multifocal atherosclerosis) was significantly greater than area under curve for CRP (0.831 vs 0.659, $p = 0.010$) (Supplementary Fig. 1). Positive predictive values were 43.5% and 73.1% for CRP and OCT high-risk features, respectively.

3.6. Secondary end-point analysis

58 out of 178 (32.6%) patients experienced a MACE. In particular, 3 (1.7%) patients died, 36 (20.2%) patients presenting a re-ACS (primary end-point analysis) and 19 (10.7%) patients underwent myocardial revascularization. Type B2/C lesions, high CRP levels, plaque rupture and macrophage infiltration were more frequent in patients who experienced a MACE at follow-up than in patients who did not (46.6% vs 30.0%, $p = 0.044$; 55.2% vs 29.2%, $p = 0.001$; 63.8% vs 41.7%, $p = 0.007$; 58.6% vs 24.2%, $p = 0.001$, respectively). At multivariable analysis only high CRP (OR 2.347, 95% CI 1.169–4.713, $p = 0.016$) and plaque

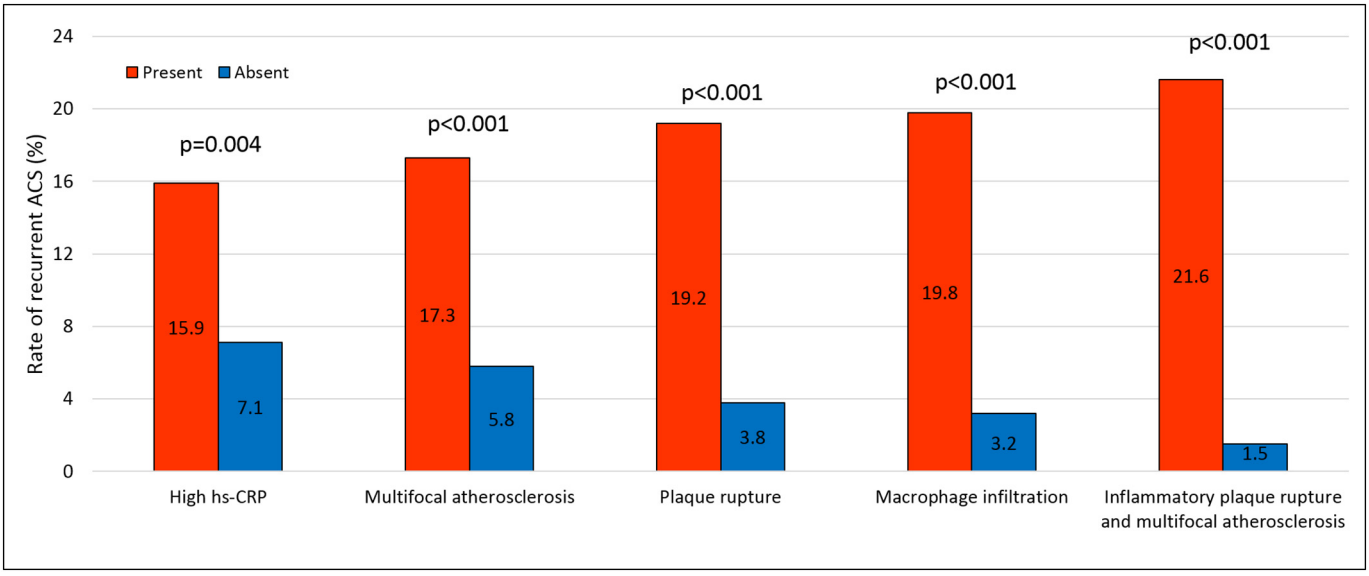

Fig. 1. Rate of recurrent ACS at follow-up according to the presence or absence of high C-reactive protein and each OCT high-risk feature for recurrent ACS (plaque rupture, macrophage infiltration, multifocal atherosclerosis) and their combination (inflammatory plaque rupture and multifocal atherosclerosis).

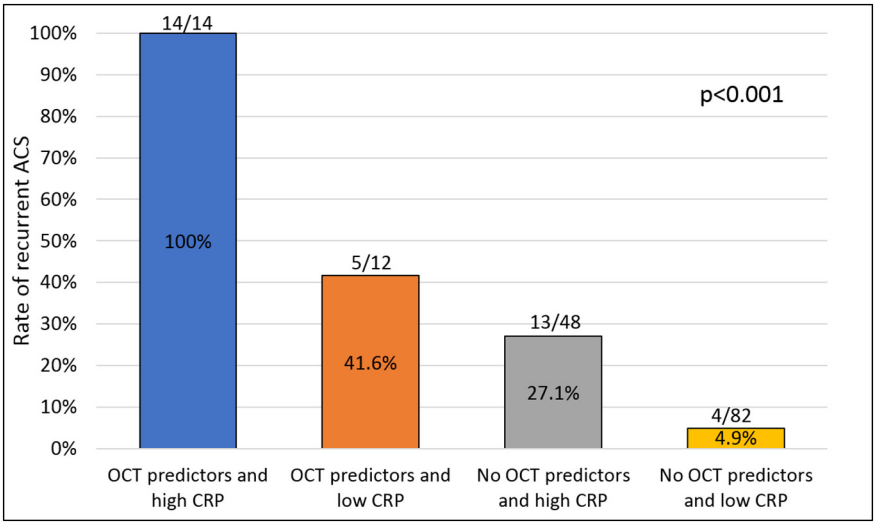

Fig. 2. Rate of recurrent ACS according to C-reactive protein serum levels and detection of OCT high-risk features for recurrent ACS (plaque rupture, macrophage infiltration, multifocal atherosclerosis).

rupture (OR 3.295, 95% CI 1.585–6.850, $p = 0.001$) were independent predictors of MACE at follow-up.

4. Discussion

In the present study, systemic inflammation and OCT findings, i.e. plaque rupture, macrophage infiltration and multifocal atherosclerosis are all independent predictors of future non-fatal acute cardiac events in patients presenting with ACS. In addition, the combination of the aforementioned OCT high-risk features detains a higher predictive value for ACS recurrence than CRP alone. Finally, and most importantly, all patients with high-risk OCT features and CRP levels ≥2 mg/L had a recurrent ACS during 3-year follow-up in this study.

In the current practice, reperfusion, antithrombotic drugs and risk factors control are the mainstay of treatment of ACS patients. However, recurrence of fatal and non-fatal acute coronary events is still frequent during follow-up [1,2]. Although suboptimal risk factors control contributes to recurrence of instability, other potential contributors are the thrombotic response and inflammation. With regard to the former, more potent antithrombotic drugs reduce the risk of MACE as compared to current antithrombotic drugs with a similar increase in the risk of bleeding events. The CANTOS trial has proven the inflammatory hypothesis of ACS we proposed in 1994 [4] but the cost of the treatment is high and the risk of lethal complications is not negligible. Thus, a major effort is warranted in order to target the population of patients with ACS who may benefit from potent anti-inflammatory treatments.

OCT allows to visualize coronary plaques with a resolution comparable to that of histology. Consistently with pathology studies [24–26], in vivo OCT studies report plaque rupture as the most frequent cause of acute complication of coronary atherosclerotic plaques [9,14]; in comparison with intact fibrous cap unstable plaques, plaque rupture is, indeed, a ruinous event, developing mostly in presence of TCFA and causing occlusive thrombosis and a STEMI as clinical presentation [27–29]. In the present study, we report that plaque rupture, local inflammation, as defined by evidence of inflammatory cell infiltration at OCT, and multifocal atherosclerosis predict future acute coronary events in ACS patients. Of note, data from three-vessel OCT studies report that patients with ACS caused by plaque rupture exhibit pancoronary instability suggesting a more aggressive atherosclerotic disease in this subset [30,31]. Consistently, a recent investigation from our Institution found that plaque rupture was the main OCT finding predicting MACE at 3-year clinical follow-up in ACS patients [14]. In our study we propose a combined evaluation of inflammation by assessing both CRP serum levels and OCT characterization of the culprit plaque at index procedure for risk stratification. Indeed, on the one hand CRP is a sensitive but non-specific marker of inflammation, on the other hand, local plaque inflammation, not intense enough to cause systemic evidence of inflammation, might be insufficient to strongly impact on the outcome. In our study all patients, 9% of the total population, with the combination of high-risk OCT features and raised CRP levels had recurrence of an ACS at follow-up. At the other extreme, event rate in patients without high-risk OCT features and low CRP levels was about 1.5% per year.

These observations should be taken into account in the evaluation of new prevention strategies targeting inflammation in atherothrombosis. In particular, in the CANTOS study, canakinumab, an antibody neutralizing the bioactivity of interleukin-1β pro-inflammatory cytokine, significantly reduced the incidence of recurrent cardiovascular events in patients with a history of myocardial infarction and CRP serum levels ≥2 mg/L; meanwhile, the incidence of fatal infections was higher in the canakinumab than in the placebo arm [17]. The present study highlights the limitation of this approach as in our study CRP levels ≥2 mg/L were observed in 37% of patients without high-risk OCT features and without recurrent events. It is worth noting that, to the best of our knowledge, in no previous study the predictive value of OCT risk factors for ACS recurrence was so high as in the present work. In particular, in the PROSPECT study the predictive value of a combination of TCFA, plaque burden ≥70% and minimal luminal area ≤ 4 mm^2 in non-culprit plaques was no >40% [2].

5. Study limitations

We acknowledge some potential limitations in our study. First, this is a retrospective analysis of a single-center registry, thus generalization of results requires caution since the analyzed population may be not representative of all ACS patients. Second, exclusion of cases with massive thrombus or poor image quality may create selection bias. Third, in STEMI patients, the underlying plaque morphology may have been altered by thrombus aspiration, however, extreme caution was taken to avoid any damage to the vessel. Fourth, as OCT system cannot visualize endothelial cells, OCT diagnosis of erosion is primarily based on the exclusion of fibrous cap disruption and other mechanisms of plaque instability may not have been recognized.

6. Conclusions

The combination of systemic evidence of inflammation and OCT findings in the culprit plaque identifies a very high-risk ACS patients subset. If supported by further investigations, our findings may contribute to a personalized cost-effective secondary prevention therapies targeting the inflammatory mechanism of athero-thrombosis.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.01.058.

Conflicts of interest

None.

Funding

None.

Relationship with industry

None.

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