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Effects of statins on plaque rupture assessed by optical coherence tomography in patients presenting with acute coronary syndromes: insights from the optical coherence tomography (OCT)-FORMIDABLE registry

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Aims Chronic pre-treatment with statins may reduce mortality and morbidity in patients experiencing acute coronary syndromes (ACS), but mechanisms accounting for these findings are not completely understood.

Methods and results The optical coherence tomography (OCT)-Formidable registry retrospectively enrolled 285 consecutive patients with ACS undergoing OCT in 9 European centres. Mean age was 60.4 ± 12.8 years, 148 (51.9%) patients had hyperlipemia, 45 (15.8%) diabetes mellitus and 142 (49.8%) presented with ST Segment Elevation Myocardial Infarction (STEMI). Patients were stratified according to statin prescription: 150 (52.6%) were on chronic pre-treatment with statins before ACS and were more likely to present with non-ST segment elevation acute coronary syndromes (NSTE-ACS) at admission (111, 74%) rather than STEMI, while the opposite was observed for patients not on statins. The primary end-point of ruptured plaque at OCT occurred significantly less frequently in the patients on chronic pre-treatment with statins [odds ratio (OR) 0.375, 95% confidence interval (CI) 0.185–0.759, $P = 0.006$]. The secondary end-point of thin-cap fibro-atheroma (TCFA) at any site was significantly less frequent in the statin group (OR 0.423, 95%CI 0.213–0.840, $P = 0.014$). No differences were observed for the secondary end-point of not-ruptured TCFA as the culprit lesion. Pre-specified sensitivity analysis was conducted according to the pattern of ACS: the reported differences were confirmed for NSTE-ACS patients, with a trend towards less plaque rupture and a significant reduction of TCFA at any site with statins, but not for STEMI.

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Conclusions Chronic pre-treatment with statins is associated with a reduced prevalence of ruptured plaques in patients presenting with ACS, particularly in those with NSTE-ACS. Statins bear hence the potential to reduce morbidity during the acute phase of ACS.

Keywords acute coronary syndromes • statin therapy • optical coherence tomography

Introduction

Statins have been shown to positively reduce cardiovascular (CV) morbidity and mortality in many settings by lowering the rate of CV events in both primary and secondary prevention.[1–3] Moreover, patients chronically treated with statins may experience more favourable outcomes when experiencing acute coronary syndromes (ACS) compared with patients starting the treatment after the event.[4–6] The mechanisms contributing to the prognostic improvement related to statins in this latter situation are not completely understood.

Optical coherence tomography (OCT) is an intracoronary imaging technique, which can qualitatively describe and precisely define features of different atherosclerotic plaques. OCT and intravascular ultrasound studies have demonstrated that chronic treatment with statins reduce the atherosclerotic burden and the prevalence of plaques with a higher risk of destabilization.[7,8] In the ACS setting OCT may identify the culprit lesions and define their features, particularly the presence of thrombus, ruptured plaques or eroded thin-cap fibro-atheromas (TCFA), which may differently impact the long-term prognosis.[9]

To date, there has been little data detailing the effects of statins on atherosclerotic plaques during the acute phase of ACS. Therefore, the present study was conducted with the aim to assess if chronic treatment with statins prior to an ACS may reduce the incidence of ruptured plaques.

Methods

The OCT-FORMIDABLE is a multicentre retrospective registry including consecutive patients presenting with ACS and undergoing OCT evaluation of the culprit and non-culprit plaques between January 2014 and October 2015 in nine centres ('AOU Città della Scienza e della Salute', Turin, Italy; 'SG Bosco Hospital', Turin, Italy; 'Policlinico Gemelli', Rome, Italy; 'Policlinico Umberto I', Rome, Italy; 'Ferrarotto Hospital', Catania, Italy; 'Ospedale Maggiore della Carità', Novara, Italy; 'Centre Hospitalier Universitaire de Clermont-Ferrand', Clermont-Ferrand, France; 'Hôpitaux de Marseille', Marseille, France; 'Hippokration Hospital', Athens, Greece). Patients with poor image quality, incomplete pullback or missing data were excluded. Of note, the choice to perform OCT was left to the operator's decision.

Informed consent was obtained from all patients. The study was approved by the local Ethics Committees and registered on ClincalTrials.gov (NCT02486861). Clinical and OCT data were recorded, as well as medications taken on admission and at hospital discharge. For the index admission, diagnosis of ACS was adjudicated according to ESC guidelines (STEMI, ST segment elevation myocardial infarction and NSTE-ACS, non-ST segment elevation ACS, including non-ST segment elevation MI and unstable angina).[10,11]

Diabetes mellitus was defined according to the American Diabetes Association criteria[12] [fasting blood glucose >126 mg/dL or treated diabetes mellitus (intake of a diabetic diet or oral hypoglycaemic agents); hyperlipemia according to the current ESC guidelines (i.e., low-density lipoprotein cholesterol above the reference values based on the estimated CV risk) or treated hyperlipemia; hypertension as systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg or treated hypertension].

For the purpose of this sub-analysis, patients were stratified according to the prescription of statins prior to the index event. A 6-month follow-up was planned for each patient. Follow-up was performed by clinical outpatient visit or telephone contact.

Invasive treatment and clinical data collection

All patients were treated according to current ESC guidelines. Particularly, aspirin and clopidogrel or prasugrel or ticagrelor were administered upon admission to the Emergency Department. Coronary angiographies and percutaneous coronary interventions were performed through a radial or femoral access according to operator's preference; heparin or bivalirudine was used according to local protocols. NSTE-ACS patients received fondaparinux or enoxaparin as well. Manual thrombus aspiration was performed according to operator's decision.[10,11]

OCT procedure

A 0.014-inch guidewire was placed distally in the target vessel and an intracoronary injection of nitroglycerin was performed. Frequency domain OCT (FD-OCT) images were acquired by a commercially available system (C7 System, LightLab Imaging Inc/St Jude Medical, Westford, MA) connected to an OCT catheter (C7 Dragonfly; LightLab Imaging Inc/St Jude Medical, Westford, MA), which was advanced to the culprit lesion. The FD-OCT run was performed using the integrated automated pullback device. In case of STEMI, OCT was performed after vessel reopening and thrombus aspiration. During image acquisition, coronary blood flow was replaced by continuous flushing of contrast media directly from the guiding catheter with a power injector in order to create a virtually blood-free environment.

OCT image analysis

OCT image analysis was performed at each treating center unblinded to the clinical features of the patients. Centralized, offline review of the images was performed by a single operator (MI) who was blinded to patients' clinical features and particularly to statin therapy. Culprit lesion was identified by means of angiography, electrocardiographic ST-segment alterations, and/or regional wall motion abnormalities on echocardiographic assessment.

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. Plaque rupture also included fibrous cap disruption detected over a calcified plaque characterized by protruding calcification, superficial calcium, and the presence of substantive calcium proximal or distal to the lesion. TCFA was defined as cap thickness < 65 nm. Fibrocalcific, fibrotic plaque, lipid component or macrophage infiltration were recorded. OCT lesions were defined according to International

Working Group for Intravascular Optical Coherence Tomography (IWG-IVOCT) consensus standards.[13]

Study end-points

The primary endpoint was the presence of ruptured plaque at OCT. Secondary end-points were the presence of TCFA without signs of rupture as the culprit lesion, TCFA at any site and MACE (death, myocardial infarction, target vessel revascularization) at the 6-month follow-up. A pre-specified sensitivity analysis was conducted according to the clinical presentation of ACS (STEMI vs. NSTE-ACS).

Statistical analysis

Categorical variables are reported as count and percentages. Continuous variables are reported as mean and standard deviation or interquartile range (IQR). Gaussian or non-Gaussian distribution was evaluated by Kolmogorov-Smirnoff test. *T*-test was used to assess differences between parametric and continuous variables. Mann–Whitney U test was used to assess non-parametric variables. Chi-square test and Fisher exact test were used to assess categorical variables. Multivariate assessment of study outcomes was performed by logistic regression or Cox regression analysis to account for potential confounding. A model including all covariates associated with chronic statin prescription with a *P*-value < 0.10 was built for each study outcome. Results were reported as odds-ratios (OR) or hazard ratios (HR), as appropriate.[14] Sensitivity analysis was performed for clinical presentation (STEMI vs. NSTE-ACS). A two-sided *P*-value <0.05 was considered statistically significant. All analyses were performed with SPSS 21.0 (IBM, Armonk, NY, USA).

Results

A total of 285 patients were included in this study. The mean age was 60.4 ± 12.8 years and 58 (20.4%) were female. From the total patient population, 164 (57.5%) had hypertension, 148 (51.9%) had hyperlipemia and 45 (15.8%) had diabetes mellitus (*Table 1*). Clinically, 142 (49.8%) patients presented with STEMI while 143 (50.2%) patients presented with NSTE-ACS. Patients presenting with NSTE-ACS were older and had a greater burden of CV risk factors compared to those presenting with STEMI (*Tables 2* and *3*).

Left anterior descending coronary artery was the target vessel in 178 (62.5%) patients. As expected, a low number of patients with LM lesions were included (13, 4.6%). A stent was implanted in the majority of patients (247, 86.3%; 125, 43.9%, second generation drug-eluting stents).

At OCT analysis (*Figure 1*, *Table 2*), a ruptured plaque was recognized as the culprit lesion in 186 (65.3%) cases and TCFA without signs of rupture in 22 (7.7%). Plaque rupture was associated with a higher prevalence of TCFA at any site, a thinner minimum fibrous-cap thickness and other features of higher risk plaques (see Supplementary data online, *Table S1*).

One hundred and fifty patients (52.6%) were on statin treatment prior to hospital admission. As shown in *Table 1*, patients on statin treatment were older, more frequently female and presented a higher prevalence of CV risk factors (except smoking). Beta-blockers, angiotensin converting enzyme inhibitors (ACE-I) or angiotensin receptor blockers (ARB) and aspirin were prescribed more frequently to patients on statins. At admission, patients treated with statins were more likely to present with NSTE-ACS rather than STEMI, while the opposite pattern was encountered for patients not on statins. Chronic treatment with statins was associated at univariate analysis with a lower incidence of ruptured plaques, TCFA rupture, TCFA at any site and residual thrombus (*Figure 1*, *Table 2*). Patients previously treated with statins presented, moreover, a thicker fibrous cap (*Table 2*).

A multivariate assessment by logistic regression was conducted to take into account potential confounding factors. Based on this analysis, statins were independently associated with a lower rate of the primary end-point of plaque rupture [OR 0.375, 95% confidence interval (CI) 0.185–0.759, *P* = 0.006; *Figure 2*] and the secondary end-point of TCFA at any site (OR 0.423, 95%CI 0.213–0.840, *P* = 0.014, see Supplementary data online, *Figure S1*). No differences were detected pertaining not-ruptured TCFA at the culprit site (see Supplementary data online, *Figure S2*).

NSTE-ACS vs. STEMI patients

Among patients presenting with NSTE-ACS (*Table 3*), those already on statin treatment presented with a higher prevalence of hyperlipemia and previous prescription of aspirin and beta-blockers. Plaque rupture, TCFA and TCFA rupture were less frequent in patients on treatment with statins, even if these differences failed to reach statistical significance (*Figure 3*). Patients from the statin group presented a thicker fibrous cap, even if difference did not reach statistical significance (see Supplementary data online, *Table S2*).

Among STEMI patients (*Table 4*), those previously treated with statins were older, and had a higher prevalence of hyperlipemia and diabetes. Statin treatment was significantly associated with prescription of aspirin, beta-blockers, ACE-I/ARB. No significant differences were reported pertaining to study end-points (*Figure 3*). Supplementary data online, *Tables S2 and S3* report the complete results of the OCT analysis stratified by clinical presentation.

Effect of statins on plaque rupture was assessed in both NSTE-ACS and STEMI patients by logistic regression analysis. In NSTE-ACS, previous treatment with statins showed a trend towards an independent association with the absence of ruptured plaque at OCT (OR 0.410, 95%CI 0.162–1.038, *P* = 0.060) in a model including CV risk factors and drugs (*Figure 4*). In the same patients, statins showed a protective effect towards detection of TCFA in any vessel (OR 0.372, 95%CI 0.147–0.939, *P* = 0.036), while no significant relationship was reported for TCFA without signs of plaque rupture (see Supplementary data online, *Figures S3 and S4*). Interestingly, in these patients, plaque rupture was independently associated with an increased rate of MACE after 6-months follow-up (HR 3.755, 95%CI 1.253–11.250, *P* = 0.018).

In contrast, STEMI patients with previous statin treatment did not show a significant relationship with the presence of plaque rupture nor TCFA at OCT (see Supplementary data online, *Figure S5–S7*) after controlling for possible confounding factors.

Discussion

The main findings of our study are:

(1) Chronic pre-treatment with statins may reduce the incidence of plaque rupture in patients presenting with ACS
(2) The protective effect of chronic pre-treatment with statins is probably more accentuated in patients presenting with NSTE-ACS, as

Table 1 Baseline features of the study population, stratified according to previous treatment with statins

	Overall ($n = 285$)	Previously not treated with statins ($n = 135$)	Previously treated with statins ($n = 150$)	*P*
Age (years)	60.4 ± 12.8	56.5 ± 12.6	64.0 ± 12.0	<0.001
Female	58 (20.4)	20 (14.8)	38 (25.3)	0.028
Hypertension	164 (57.5)	60 (44.4)	104 (69.3)	<0.001
Hyperlipemia	148 (51.9)	48 (35.6)	100 (66.7)	<0.001
Diabetes mellitus	45 (15.8)	8 (5.9)	37 (24.7)	<0.001
Smoker	175 (61.4)	90 (66.7)	85 (56.7)	0.083
STEMI	142 (49.8)	103 (72.5)	39 (27.5)	<0.001
NSTE-ACS	143 (50.2)	32 (22.4)	111 (77.6)	<0.001
ACE-I/ARB	116 (40.7)	26 (19.3)	90 (60.0)	<0.001
Beta-blockers	122 (42.8)	19 (14.1)	103 (68.7)	<0.001
Aspirin	143 (50.2)	25 (18.5)	118 (78.7)	<0.001
Left main coronary	13 (4.6)	7 (5.2)	6 (4.0)	0.632
Left anterior descending coronary	178 (62.5)	75 (55.6)	103 (68.7)	0.022
Circumflex coronary	81 (28.4)	29 (21.5)	52 (34.7)	0.014
Right coronary	129 (45.3)	67 (49.6)	62 (41.3)	0.145

ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; STEMI, ST-segment elevation myocardial infarction; NSTE-ACS, non-ST segment elevation acute coronary syndromes.
Values reported as counts and percentage, unless differently stated.

Table 2 OCT findings in the overall study population, stratified by previous chronic therapy with statins

	Overall ($n = 285$)	Previously not treated with statins ($n = 135$)	Previously treated with statins ($n = 150$)	*P*
Residual thrombus	83 (46.4)	58 (48.7)	25 (41.7)	0.37
Plaque rupture	186 (65.3)	103 (76.3)	83 (55.3)	<0.001
Not ruptured TCFA	22 (7.7)	7 (5.2)	15 (10.0)	0.128
TCFA at rupture site	144 (50.5)	89 (65.9)	55 (36.6)	<0.001
TCFA other site	54 (26.2)	31 (24.8)	23 (28.4)	0.567
TCFA at any site	174 (61.1)	97 (71.9)	77 (51.3)	<0.001
Minimum fibrous cap thickness (μm)	75.5 ± 49.9	67.1 ± 47.5	83.1 ± 50.9	0.007
Fibrocalcifique plaques	89 (31.2)	33 (24.4)	56 (37.3)	0.019
Fibrous plaques	145 (50.9)	44 (32.6)	101 (67.3)	<0.001
Lipid component	238 (83.5)	124 (91.9)	114 (76.0)	<0.001
Necrotic core with macrophage infiltration	96 (33.8)	32 (23.7)	64 (43.0)	0.001

TCFA, thin-cap fibro-atheroma.
Values reported as counts and percentage, unless differently stated.

these patients trended towards significantly lower prevalence of plaque rupture and significantly less TCFA at any site.

Prognostic benefits relating to statin therapy are usually mediated by a reduction in the incidence of CV events, both in the primary and secondary prevention settings.[3] Even when they 'fail' to prevent CV events, as in the case of ACS, statins have been shown to exert protective effects as patients chronically treated with statins before experiencing ACS have reported more favourable outcomes at both short and long-term follow-up.[4–6] Our finding that statins are associated with a lower incidence of plaque rupture could partially explain the mechanisms of this protective effect. As highlighted by previous anatomo-pathological and OCT studies, culprit lesions during ACS may present various features, which are associated with different clinical presentations (i.e., STEMI vs. NSTE-ACS) and outcomes.[15–17] Plaque rupture is often encountered in more severe clinical presentations of ACS and relates to higher morbidity and mortality as compared with milder lesions like erosion of TCFA.[18] Thrombi are more often found in association with plaque rupture and are also associated with poorer prognostic outcome.[19] Statins have been reported to reduce atherosclerotic burden and to stabilize atherosclerotic plaques in patients with stable, chronic, ischaemic heart disease. Previous OCT studies have shown a reduction in the total plaque volume and a relative increase of fibrotic and fibrocalcifique plaques as compared with lipidic macrophage rich and necrotic-core plaques,

Table 3 Baseline features of patients presenting with non-ST segment elevation acute coronary syndromes, stratified according to the previous chronic prescription of statins

	Overall ($n = 143$)	Previously not treated with statins ($n = 32$)	Previously treated with statins ($n = 111$)	P
Age (years)	64.70 ± 11.9	62.4 ± 11.3	65.4 ± 12.1	0.208
Female	37 (25.9)	8 (25.0)	29 (26.1)	0.898
Hypertension	109 (76.2)	21 (65.6)	88 (79.3)	0.110
Hyperlipemia	89 (62.2)	11 (34.4)	72 (64.9)	<0.001
DM	31 (21.7)	3 (9.4)	28 (25.2)	0.086
Smokeer	78 (54.5)	18 (56.3)	60 (54.1)	0.826
LVEF	52.3 ± 9.9	54.2 ± 10.8	51.8 ± 9.6	0.242
ACE-I/ARB	87 (60.8)	15 (46.9)	72 (64.9)	0.066
Beta-blockers	89 (62.2)	4 (43.8)	75 (67.6)	0.014
Aspirin	107 (74.8)	17 (53.1)	90 (81.1)	0.001
Left main coronary	8 (5.6)	2 (6.3)	6 (5.4)	0.855
Left anterior descending coronary	103 (72.0)	25 (78.1)	78 (70.3)	0.383
Circumflex coronary	51 (35.7)	13 (40.6)	38 (34.2)	0.506
Right coronary	56 (39.2)	11 (34.4)	45 (40.5)	0.529

ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; LVEF, left ventricle ejection fraction.
Values reported as counts and percentage, unless differently stated.

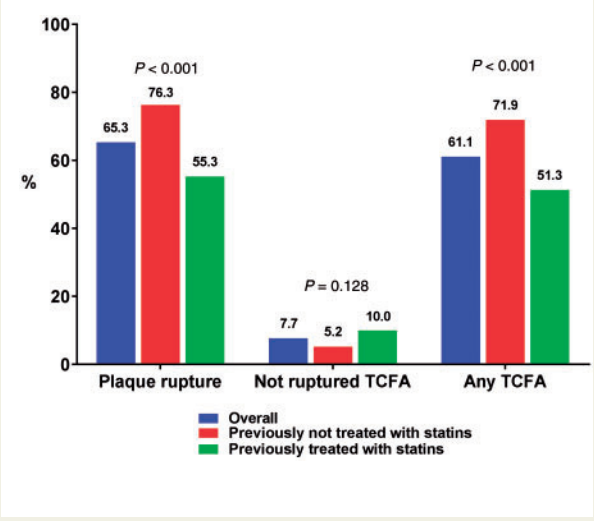

Figure 1 Prevalence at OCT analysis of plaque rupture, not-ruptured TCFAs and TCFA at any site in the overall study population, stratified according the previous treatment with statins. TCFA, thin-cap fibro-atheroma.

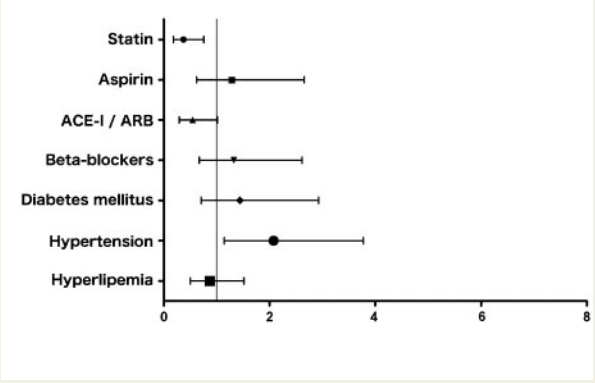

Figure 2 Independent predictors of plaque rupture by logistic regression analysis in the overall study population (ACE-I/ARB, angiotensin converting enzyme inhibitors/angiotensin receptor blockers).

which present a higher risk of destabilization.[7,17,20,21] An increase in the thickness of fibrous cap with statins has been previously reported and was also observed in our study.[22] The positive effect of statins on plaque remodelling has been shown to be a class effect observed for low, moderate, or high statin doses, even if a dose-response relationship has been demonstrated with more pronounced reductions for higher doses.[22] These effects are sustained mainly by the so-called 'pleiotropic effects' of statins, which are mediated by various mechanisms, including an anti-inflammatory effect, which may contribute to 'stabilize' atherosclerotic plaques.[23] Our results suggest that the pleiotropic effects of statins may also have a positive influence in the acute phase of ACS, by limiting the occurrence of plaque rupture.

In our study, patients on statin therapy presented with a higher CV risk profile and, thus, a higher risk of plaque rupture.[15] Additionally, these patients were more likely to be treated with ACE-I or ARB, aspirin and beta-blockers. Based on our multivariate models, statins exerted their protective effects on plaque rupture in spite of the increased CV risk of these patients and independently from the other CV drugs prescribed. Interestingly, ACE-I/ARB were also independently associated with a protective effect against plaque rupture in our global population. This is possibly due to the anti-inflammatory effect, which has been described also for this drug class.[24]

A strong trend towards a reduction in the incidence of plaque rupture was observed for NSTE-ACS patients and not for STEMI patients even after controlling for possible confounding factors. NSTE-ACS is an entity which encompasses a wide variety of clinical presentations, ranging from unstable angina to non-ST elevation myocardial infarction which are sustained by a variety of pathophysiological substrates such as plaque rupture, white thrombus, eroded TCFA, and haemorrhagic plaques. STEMI presentation is more 'mono-dimensional' and is generally mediated by the formation of a red-thrombus over a ruptured plaque.[17,25] Plaque rupture was encountered in 78.9% of STEMI patients and in 51.7% of NSTE-ACS patients in our report. Moreover, NSTE-ACS patients presented with a higher prevalence of comorbidities and CV risk factors including hyperlipemia and diabetes mellitus. In this scenario, it is plausible that statins may exert a more incisive protective effect in NSTE-ACS rather than STEMI patients. However, the differential effect of statins between NSTE-ACS and STEMI observed in our study may also be due to sample size and statistical power issues. Only 39 patients in the STEMI group were not on statins at the time of the event. Plaque rupture was the culprit lesion in more than 80% of the STEMI patients and a lower prevalence of plaque rupture and TCFA, even if non-significant, was also observed for STEMI patients. Moreover, since duration, dosage and effectiveness of statin therapy were not assessed in the present analysis, the influence of statin therapy intensity cannot be excluded from this finding. However, if a true lower preventive efficacy of statins against plaque rupture had to be confirmed, we should suppose that a plaque-destabilization process, scarcely responsive to statin therapy, may occur in STEMI patients, as opposed to NSTE-ACS patients.

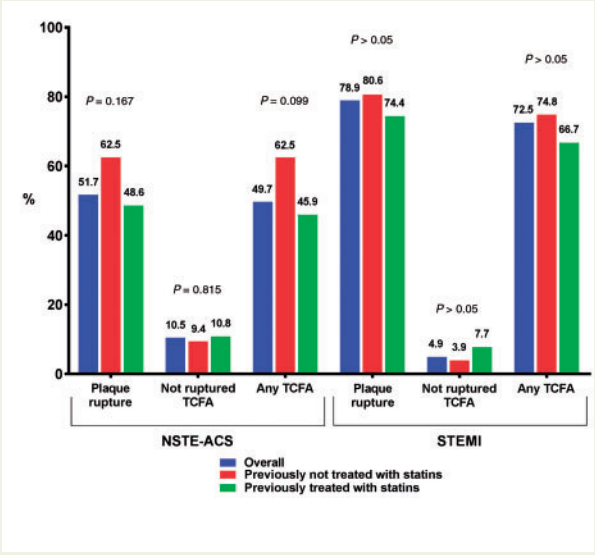

Figure 3 Prevalence at OCT analysis of plaque rupture, not-ruptured TCFAs and TCFA at any site in patients with non-ST segment elevation acute coronary syndromes (NSTE-ACS, left panel) and with ST-segment elevation myocardial infarction (STEMI, right panel), stratified according the previous treatment with statins (TCFA, thin-cap fibro-atheroma).

Beyond a reduction in plaque rupture, our results showed that, in patients with NSTE-ACS, those on statins presented a lower prevalence of TCFA at any site, with a trend towards a thicker fibrous cap. TCFA are atherosclerotic lesions with a high propensity towards destabilization. Patients with a high TCFA burden are at increased risk of progression of coronary artery disease, plaque rupture and CV events.[21,26] The protective effect of the chronic treatment with statins in the acute phase of ACS could be thus, at least partially, mediated by the reduction of these high-risk features of

Table 4 Baseline features of patients presenting with ST-segment elevation myocardial infarction, stratified according to the previous chronic prescription of statins

	Overall ($n = 142$)	Previously not treated with statins ($n = 103$)	Previously treated with statins ($n = 39$)	*P*
Age	56.10 ± 12.2	54.7 ± 12.5	60 ± 10.7	0.020
Female	21 (14.8)	12 (11.7)	9 (23.1)	0.087
Hypertension	55 (38.7)	39 (37.9)	16 (41.0)	0.730
Hyperlipemia	59 (41.5)	37 (35.9)	22 (56.4)	0.027
DM	14 (9.9)	5 (4.9)	9 (23.1)	0.001
Smoker	97 (68.3)	72 (69.9)	25 (64.1)	0.507
LVEF	54.5 ± 7.6	54.4 ± 7.7	54.8 (7.6)	0.779
ACE-I/ARB	29 (20.4)	11 (10.7)	18 (46.2)	<0.001
Beta-Blockers	33 (23.2)	5 (4.9)	28 (71.8)	<0.001
Aspirin	36 (25.4)	8 (7.8)	28 (71.8)	<0.001
Left Main coronary	5 (3.5)	5 (4.9)	0 (0.0)	0.161
Left Anterior Descending coronary	75 (52.8)	50 (48.5)	25 (64.1)	0.097
Circumflex coronary	30 (21.1)	16 (15.5)	14 (35.9)	0.008
Right coronary	73 (51.4)	56 (54.3)	17 (43.6)	0.391

ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; LVEF, left ventricle ejection fraction.

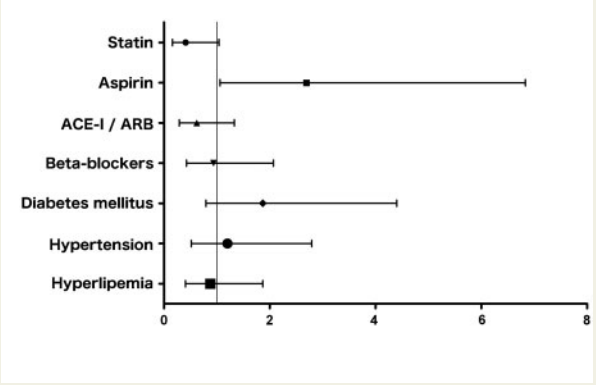

Figure 4 Independent predictors of plaque rupture by logistic regression analysis in patients with non-ST segment elevation acute coronary syndromes (ACE-I/ARB, angiotensin converting enzyme inhibitors/angiotensin receptor blockers).

atherosclerotic lesions occurring before the ACS. However, statins have been demonstrated to exert anti-inflammatory and plaque-stabilizing effects with positive prognostic repercussions also when administered in the acute phase of ACS.[27] It is plausible that our results depend on a combination of chronic and acute effects of statins, even if our data do not allow discriminating between these two actions.

The reduction of plaque rupture in NSTE-ACS associated with statin treatment may have relevant clinical repercussions. As previously reported in literature, as well in our study, plaque rupture in ACS relates to a worse long-term outcome.[18] This result may partly be explained by the higher prevalence of TCFA observed in our study in patients with plaque rupture. As TCFA relates with a higher risk of unfavourable CV events, it is plausible that the reduction of TCFA induced by statins prior to the ACS may exert protective effects also after the ACS. In any case, our data suggest that, when appropriately prescribed, statins bear the potential to exert long-term beneficial effects even in patients in where they failed to prevent a CV event, in this case, in the form of ACS.

Finally, our results confirm that OCT may be a useful tool for the assessment of the effectiveness of lipid lowering and anti-atherosclerotic treatments. Future studies and randomized controlled trials assessing the effects of such treatments in the ACS setting should include OCT, as this intracoronary imaging system could provide valuable information on parameters with potential prognostic repercussions.

Limitations

The study was not an all-comers study, as the choice to perform OCT was left to the operator's preferences and the centres' protocols, thus, potential selection bias may have been introduced. Images were analysed and interpreted in each participating center. A single operator reviewed all the images blinded to the patients' status regarding statins, but the study lacked a proper core-lab. Data on statin type, dosage, duration and LDL cholesterol values were not available for all patients and were thus not analysed. Finally, sub-group analyses (NSTE-ACS vs. STEMI) were limited by the small sample sizes of the two groups, and, for STEMI, by the low prevalence of patients not on statins in this group.

Conclusions

Chronic treatment with statins is associated with reduced incidence of plaque rupture detected by OCT in patients presenting with ACS, with a potentially more marked effect in patients with NSTE-ACS. As plaque rupture is associated with a worse prognostic outcome, our results suggest that physicians should be aware of the importance of statin therapy and prescribe this treatment whenever it is indicated, both in the primary and in the secondary prevention setting.

Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

Conflict of interest: None declared.

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