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OCT study in detection of thin cap fibroatheromas in STEMI patients

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ABSTRACT

Aim: Using an optical coherence tomography (OCT) to assess plaque characterisation of culprit lesion of infarct-related vessel and to detect possible thin cap fibroatheromas (TCFA) of noninfarcted vessels in patients with ST elevation myocardial infarction (STEMI) treated with primary PCI (pPCI).
Method: 30 consecutive patients with single vessel disease and STEMI were enrolled in the study. OCT study of the culprit lesion of infarct-related vessel was performed initially after the insertion of intracoronary wire either with or without lesion predilatation. Final OCT of culprit lesion after stenting/aspiration and also other two non-infarcted vessels was performed after pPCI.
Results: Culprit lesion was mainly located in right coronary artery (RCA) (57%) followed by left anterior descending artery (LAD) (30%). Plaque rupture of culprit lesion was found in 10 (70%) patients. In the infarct-related/culprit lesion, TCFA and thrombus was found in 100% of cases. Plaque rupture was recognized in 70% of lesions. In the OCT findings of non-infarcted vessels, the frequency of TCFAs was 47%. In the majority of cases (37%), only 1 non-infarct-related vessel was involved. However, 3 patients (10%) have TCFAs in both non-infarcted arteries. Moreover, plaque rupture and thrombus formation were found in 23% of cases of non-infarct-related vessels. Both, 30-day and 6-month follow-ups were uneventful.
Conclusions: Present study demonstrates high frequency of OCT-derived TCFA, plaque ruptures and thrombus of both, infarct- and non-infarct-related coronary vessels in patients with evolving STEMI. Our findings support the theory of multifocal destabilization in ACS.

Klíčová slova:
Infarkt myokardu s elevacemi úseku ST
Nestabilní pláty
Optická koherentní tomografie
Ruptura plátu

SOUHRN

Cíl: S použitím optické koherentní tomografie (OCT) posoudit výskyt a charakter plátu v infarktové tepně a detekovat případné nestabilní pláty neinfarktových tepen u nemocných s infarktem myokardu s elevacemi úseku ST (STEMI) léčených přímou perkutánní koronární intervencí (dPCI).
Metodika: Třicet konsekutivních nemocných se STEMI a postižením jedné tepny bylo zahrnuto do studie. Vyšetření pomocí OCT infarktové tepny bylo provedeno po zavedení tenkého intrakoronárního vodiče s balonkovou predilatací nebo bez ní. Konečné OCT vyšetření infarktové tepny i neinfarktových tepen bylo provedeno po dPCI.
Výsledky: Pláty v infarktových tepnách byly lokalizovány nejvíce v pravé věnčité tepně (57 %) a dále v ramus interventricularis anterior levé věnčité tepny (30 %). Ruptura plátu v infarktové tepně byla zjištěna u 70 % nemocných. Nestabilní plát a trombus byl nalezen ve všech infarktových tepnách. Četnost nestabilních plátů v neinfarktových tepnách byla 47 %. Ve většině případů (37 %) byl nestabilní plát nalezen pouze na jedné neinfarktové tepně. Nicméně u tří nemocných (10 %) byly nestabilní pláty zjištěny v obou neinfarktových tepnách. U 23 % nemocných byla navíc nalezena ruptura plátu a zaznamenána přítomnost trombu. Během třicetidenního i šestiměsíčního klinického sledování se nevyskytly žádné kardiovaskulární příhody.
Závěry: Studie prokázala vysoký výskyt nestabilních plátů, ruptur plátů a trombu jak v infarktových, tak i v neinfarktových tepnách u nemocných se STEMI. Práce potvrzuje teorii multifokální destabilizace plátů u akutních koronárních syndromů.

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Introduction

Cardiovascular diseases and especially acute coronary syndromes (ACS) are the main causes of mortality and morbidity in developed countries [1]. Either coronary plaque rupture or erosion of thin cap fibroatheroma (TCFA; fibrous cap thickness ≤ 65 μm) with subsequent thrombus formation are thought to be the most important mechanism leading to ST-elevation myocardial infarction (STEMI) [2,3]. It has been recently shown in numerous studies that coronary artery disease (CAD) is a diffuse disease and may involve rapid development and diffuse destabilization of atherosclerotic plaques in ACS when compared to the stable angina pectoris (SAP) [4–6]. The optical coherence tomography (OCT) is the latest imaging technique with the highest resolution for plaque assessment. Recent studies have demonstrated the potential of OCT to identify TCFA [7,8]. However, there is still lack of data on presence of TCFA in patients with evolving STEMI. The aim of this study was to assess the frequency of TCFA in the infarct-related and also in non-infarct-related vessels in the setting of STEMI.

Methods

Between January and December 2010, 30 patients with STEMI and angiographically detected one-vessel disease, were enrolled in this study. All patients were scheduled for primary percutaneous intervention (pPCI). The exclusion criteria were as follows: 1) reference diameter > 4 mm; 2) left main disease; 3) cardiogenic shock; and 4) ostial lesions. The radial approach was used in all patients. STEMI was defined as a chest pain > 20 minutes and < 12 hours, ST-segment elevation > 0.1 mV in ≥ 2 contiguous leads on 12-lead electrocardiogram followed by the rise of cardiac enzymes (creatine kinase-MB and troponin I) three times upper the normal limit. As mentioned above, only patients with single-vessel disease (assessed based on angiography) were enrolled in the trial. The study was approved by a local ethical committee and all patients signed the informed consent before the procedure. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [9]. All patients were pretreated with acetylsalicylic acid 500 mg intravenously, heparin 5000 IU intravenously and clopidogrel 600 mg orally. If the duration of the entire procedure exceeded 30 min, the activated clotting time (ACT) was measured and additional heparin was given to keep it within 250–300 seconds. Glycoprotein IIb/IIIa receptor antagonists were administered at the discretion of the operator. Furthermore, the use of aspiration catheter before procedure was also left at the discretion of interventionalist. However, its use was strongly recommended too. Both, pre- and post-procedural angiography were performed at least at two orthogonal projections with quantitative coronary analysis employing Quantcore software (Pie Medical, The Netherlands). The OCT studies were performed initially in the infarct-related vessel before intervention and at the end of the procedure and after that also in 5 cm long segment of proximal part of non-infarct-related vessels. In case of complete occlusion or Thrombolysis in Myocardial Infarction flow grade 1, either thrombectomy or balloon angioplasty employing a small balloon (≤ 1.5 mm) were allowed according to the physician discretion. Before introducing an OCT catheter, 0.1 mg of isosorbide dinitrate was given intracoronary. The OCT images were obtained with C7-XRTM intravascular imaging system (LightLab Imaging, St. Jude Medical Company, St. Paul, Minnesota, USA) using a C7 Dragonfly intravascular imaging catheter. Non-occlusive technique was used in all patients with continuous-flushing of the artery with contrast material (total amount of 15 cc through the guiding catheter using an injector with the speed of 4 cc/s). Motorized pull-back was performed at the rate of 20 mm/s for the length of 50 mm. The images were recorded in the OCT system console for off-line analysis. OCT images were analysed by 2 investigators. The presence of plaque rupture, intracoronary thrombus, or TCFA was noted. In case of fibrous cap, the thinnest part was measured 3 times, and the average value was calculated. TCFA was diagnosed when the fibrous cap was measured ≤ 65 μm and large necrotic core was present. PCI was performed according to standard practice with stent implantation at low pressure (≤ 10 atms) with high-pressure post dilatation employing (≥ 15 atms) a non-compliant balloon shorter then implanted stent. Either biolimus A9 (BioMatrix, Biosensors International, Biosensors Europe, Morges, Switzerland) or everolimus (Promus, Boston Scientific, Natick, MA, USA) drug eluting stents were used in this cohort of patients. Dual antiplatelet treatment was recommended for 12 months. All patients were scheduled for 30-day and 6-month clinical follow-ups.

Statistical analysis was performed employing NCSS97 program (NCSS, Kaysville, Utah, USA). Discrete data are presented as frequencies and percentage, whereas continuous variables are presented as means and SDs. The Student *t* test was used for a comparison between fibrous cap thickness in infarct- and non-infarct-related arteries. Categorical variables were compared by means of the chi-square test. A two-tailed value of $p < 0.05$ was considered statistically significant.

Results

All OCT studies but one were carried out successfully without serious procedural complications. One ventricular fibrillation was observed during flushing of the artery with contrast agent. This complication was managed by electric defibrillation without any further complications. Baseline, angiographic, and procedural characteristics are presented in Tables 1 and 2. The mean age was 57 ± 9 years; the majority of patients were males (90%). The most treated vessel was the right coronary artery (RCA) (57%) followed by the left anterior descending artery (LAD) (30%). The initial TIMI flow 0 was found in 66% of patients. GPIIb/IIIa inhibitors and thromboaspiration were used in 63% and 69% respectively. TIMI flow III was observed at the end of the procedure in all patients. Complete OCT analysis is presented in Table 3. In the infarct-related/culprit lesion, TCFA was found in 100% of cases. The mean thickness of fibrous cap was 50 ± 9 μm. Furthermore, thrombus was also apparent in all cas-

Table 1 – Baseline characteristics.

N	30
Age (years)	57
Male	27 (90%)
SM	29 (98%)
DM	11 (38%)
HY	15 (51%)
HC	21 (71%)
Family history of CAD	14 (48%)
hsCRP	13 (42%)
Treated vessels	
LAD	9 (30%)
RCA	17 (57%)
LCx	4 (13%)

CAD – coronary artery disease; DM – diabetes mellitus; HC – hypercholesterolemia; hsCRP – high sensitive C-reactive protein; HY – hypertension; LAD – left anterior descending artery; LCx – left circumflex artery; RCA – right coronary artery; SM – smoking.

Table 2 – Angiographic and procedural characteristics.

	N = 30	
TIMI flow (%)	Pre-procedure	Post-procedure
0	66	0
I–II	34	0
III	0	30 (100%)
MLD (mm)	Pre-procedure	Post-procedure
	0.42	3.62
DS (%)	Pre-procedure	Post-procedure
	87	10
RD (mm)	3.4	
GPIIb/IIIa inhibitors	20 (63%)	
Manual thromboaspiration	21 (69%)	
OCT complication	1 (3%)	

DS – diameter stenosis; GP – glycoprotein; MLD – minimal lumen diameter; OCT – optical coherence tomography; RD – reference diameter; TIMI – Thrombolysis in Myocardial Infarction.

es. Plaque rupture was recognized in 70% of lesions. In the OCT findings of non-infarcted vessels, the frequency of TCFA was 47%. In the majority of cases (37%), only 1 non-infarct-related vessel was involved. However, 3 patients (10%) had unstable plaques in both non-infarcted arteries. Moreover, plaque rupture and thrombus formation were found in 23% of cases of non-infarct-related vessels (representative OCT image is shown in Fig. 1). The mean thickness of fibrous cap in non-infarct-related vessels was 57 ± 3.5 μm. This was comparable with the thickness of fibrous cap in the infarct-related/culprit lesion (p = 0.16). Both, 30-day and 6-month follow-ups were uneventful, including those with TCFA/plaque rupture and thrombus in non-infarcted vessels.

Discussion

To the best of our knowledge, this is the largest study in patients with evolving STEMI and 3 coronary vessels OCT analysis in patients with single vessel disease. Present study revealed that TCFA with plaque rupture is the main cause of AMI in the infarct-related vessel. However, almost 50% of patients with STEMI had also TCFAs in non-infarct-related arteries. Furthermore, among these patients, plaque rupture and thrombus formation were found in 23%. In agreement with others, our findings support the theory of multifocal process in ACS [5,6].

It has been shown in postmortem studies that atherosclerotic plaque rupture/erosion might be a trigger for coronary thrombotic events [2,3]. Virmani et al. [2] presented that in cases of sudden cardiac death, 70% of the cases had non-ruptured TCFA. Furthermore, most of both, ruptured and non-ruptured plaques are localized in the proximal one third of the major coronary vessels. Because coronary angiography has only limited possibility to detect plaque rupture [9,5], other modalities have been tested in patients with ACS with the aim to identify TCFA/plaque rupture in the coronary tree. Rioufol et al. [5] demonstrated the possibility of IVUS for a detection of plaque ruptures in both, infarct- and non-infarct-related vessels. In his study, plaque rupture of the culprit lesion

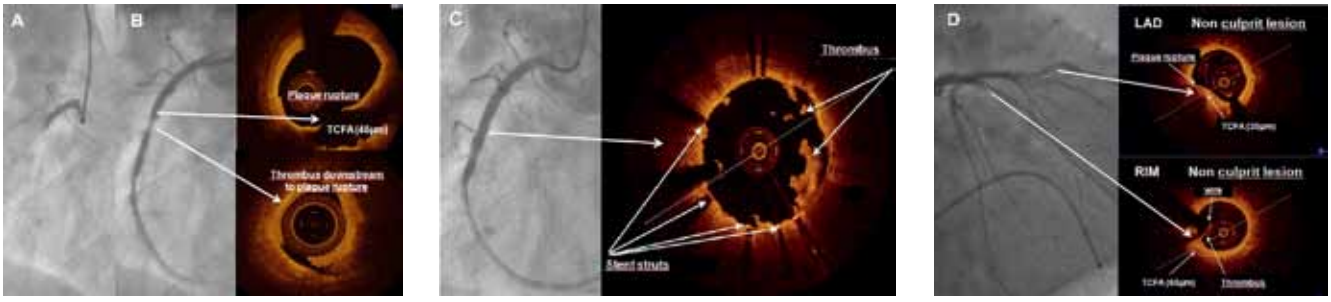

Fig. 1 – Representative angiographic and OCT image in STEMI. (A) Right coronary occlusion. (B) Recanalization with the wire insertion and OCT image of culprit lesion with TCFA and thrombus downstream. (C) Final angiographic result with OCT study of implanted stent. (D) Angiography and OCT study of non-infarct-related vessels.
LAD – left anterior descending artery; RIM – ramus intermedius; TCFA – thin cap fibroatheroma.

Table 3 – OCT analysis.

N	Age (years)/ gender	Risk factors	Culprit vessel	Infarct-related lesions				Non-infarct-related lesions				Vessels with plaques		
				Plaque rupture	Thrombus	Fibrous cap thickness (μm)	TCFA	Plaque rupture	Thrombus	Fibrous cap thickness (μm)	TCFA	1 vessel	2 vessels	3 vessels
1	54/female	HY, DM, SM	RCA	Yes	Yes	57	Yes	No	No	30	Yes		1	
2	45/male	SM	LAD	No	Yes	45	Yes	No	No	NA	No	1		
3	48/male	SM, HY, HC	LAD	No	Yes	53	Yes	No	No	50	Yes		1	
4	48/male	SM, HY, HC, DM	LAD	Yes	Yes	50	Yes	Yes	Yes	50	Yes		1	
5	44/male	SM, HY, HC	RCA	Yes	Yes	42	Yes	No	No	42	Yes		1	
6	41/male	SM, HY, HC	RCA	No	Yes	62	Yes	Yes	No	65	Yes		1	
7	58/female	SM, HY, HC, DM	LAD	Yes	Yes	36	Yes	No	No	NA	No	1		
8	58/male	SM, HY, DM	RCA	Yes	Yes	65	Yes	No	No	NA	No	1		
9	48/male	SM, HC	RCA	No	Yes	49	Yes	No	No	NA	No	1		
10	58/male	HY, DM, HC	RCx	Yes	Yes	31	Yes	Yes	Yes	31	Yes		1	
11	51/female	SM, HC	RCA	Yes	Yes	63	Yes	No	No	NA	No	1		
12	45/male	SM, HY	RD	No	Yes	47	Yes	No	No	NA	No	1		
13	50/male	SM, HY, HC, DM	RCA	No	Yes	37	Yes	No	No	NA	No	1		
14	58/male	SM	RCx	Yes	Yes	65	Yes	Yes	No	65	Yes			1
15	67/male	HY, HC, DM	RCx	Yes	Yes	43	Yes	Yes	Yes	33	Yes			1
16	42/male		RCA	Yes	Yes	39	Yes	No	No	NA	No	1		
17	52/male	SM, HY, DM	RCA	No	Yes	59	Yes	No	No	NA	No	1		
18	50/male	SM, HC	RCA	No	Yes	63	Yes	Yes	No	41	Yes		1	
19	51/male	SM, HY	RCA	Yes	Yes	51	Yes	No	No	NA	No	1		
20	52/male	SM	LAD	Yes	Yes	36	Yes	No	Yes	36	Yes		1	
21	53/male	SM, HY, HC	LAD	Yes	Yes	40	Yes	No	Yes	40	Yes		1	
22	57/male	HC	LAD	Yes	Yes	56	Yes	No	No	No	No	1		
23	42/male	SM, HY, HC	LAD	Yes	Yes	32	Yes	No	No	NA	No	1		
24	60/male	HY, HC	RCA	Yes	Yes	65	Yes	Yes	Yes	39	Yes		1	
25	53/male	SM, HY	RCA	Yes	Yes	41	Yes	No	No	40	Yes			1
26	52/male	SM, HC, DM	RCA	Yes	Yes	64	Yes	No	Yes	64	Yes		1	
27	40/male	SM, HC	RCA	No	Yes	51	Yes	No	No	NA	No	1		
28	62/male	SM, HC	RCA	Yes	Yes	61	Yes	No	No	NA	No	1		
29	55/male	SM, HY, HC	RCx	Yes	Yes	49	Yes	No	No	NA	No	1		
30	47/male	HY, HC	RCA	Yes	Yes	48	Yes	No	No	NA	No	1		

DM – diabetes mellitus; HC – hypercholesterolemia; HY – hypertension; LAD – left anterior descending artery; NA – not applicable; RCA – right coronary artery; RCx – ramus circumflexus; RD – ramus diagonalis; SM – smoking; TCFA – thin cap fibroatheroma.

was found in 37.5% and at least one plaque rupture was found somewhere else than in the culprit lesion in 79% of patients. Asakura et al. [4] underwent 3-coronary arteries angioscopic study and demonstrated that yellow plaques were equally prevalent in the infarct-related and non-infarct-related coronary vessels. Belle et al. [10] found that the culprit lesions in AMI patients contain the yellow plaque more often than the white plaque. Many studies have recently shown that OCT modality might be the best imaging technique for the identification of TCFA/plaque rupture. Kume et al. [11] demonstrated an accurate ($r = 0.90$; $p < 0.001$) representation of the thickness of the fibrous cap measuring by OCT study. Sawada et al. [12] demonstrated a better capability of OCT to identify definite TCFA when compared with virtual histology. Kubo et al. [8] reported the best possibility of OCT to detect fibrous cap disruption when compared with both, coronary angioscopy and IVUS. Our data compare favourably with those published very recently by Kubo et al. [6], although it is important to point out that only patients with angiographically single-vessel disease were included in our study. Briefly, a total of 42 patients with AMI (N = 26) and stable angina (SAP) (N = 16) who underwent multivessel coronary intervention were prospectively enrolled in Kubo's et al. study. Their findings in the culprit lesions of AMI patients were as follows: plaque ruptures 77%, thrombus 100%, TCFA 85%, mean thickness of fibrous cap 57 ± 12 μm and multivessel TCFA 38%. The frequency of TCFA, plaque rupture, and thrombus were found significantly less in SAP patients. Furthermore, the fibrous cap thickness of culprit lesions was significantly higher in SAP patients.

Interestingly, both 30-day and 6-month follow-ups, including those with TCFA/plaque rupture and thrombus in non-infarcted vessels, were uneventful, in our study. These data are comparable with those presented by Rioufol et al. [5]. In his study, although 59% of the patients had untreated plaque ruptures, no events were reported during a 10-month follow-up. The explanation is only speculative. First of all, one has to take into account small cohort of patients. Our study was underpowered for individual clinical end-points. Furthermore, patients with multivessel disease were excluded from the study and all significant lesions in the infarct-related vessels were treated with stent implantation. It might also be that intensive pharmacological medication after the procedure stabilized initially unstable plaques in the non-infarct-related arteries. This remains to be assessed in prospective trials with serial OCT study.

There are limitations of our study. First of all, thrombectomy/balloon predilatation could modify the morphology of the culprit lesion in some patients. Furthermore, because of the limitation of OCT technique, it was not possible to explore the entire coronary tree. It might be that we missed more TCFA in both, infarct- and non-infarct-related arteries. Moreover, the presence of thrombus formation could also affect OCT image of the lesions.

In conclusion, our study demonstrates high frequency of OCT-derived TCFA, plaque ruptures and thrombus of both, infarct- and non-infarct-related coronary vessels in patients with evolving STEMI. Our findings support the theory of multifocal destabilization in ACS.

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