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In-vivo iMap IVUS comparison of in-stent neointima and native coronary atherosclerosis ☆

Karlis Trusinskis [a,b,*], Karlis Strenge [a,1], Dace Juhnevica [a,2], Andrejs Erglis [a]

[a] Latvian Centre of Cardiology, Pauls Stradins Clinical University Hospital, Riga, Latvia
[b] Faculty of Medicine, Riga Stradins University, Riga, Latvia

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ABSTRACT

Purpose: The purpose of this study was to compare plaque characteristics of native coronary atherosclerosis and in-stent neointima ten months after ST elevation myocardial infarction (STEMI) using iMap intravascular ultrasound (IVUS).
Methods: In 49 patients in-stent neointima and the coronary segment proximal to the stent were analyzed with iMap intravascular ultrasound (IVUS) ten months after primary PCI for STEMI.
Results: A higher percentage of necrotic tissue was observed in the proximal coronary segment compared to the in-stent neointima by iMap IVUS (25.5% ± 12.8% vs 12.3% ± 3.3%, $p < 0.0001$) ten months after STEMI. The proportion of fibrotic tissue in the proximal segment was lower (63.6% ± 14.8% vs 72.0% ± 5.7%, $p = 0.002$) and the proportion of the lipidic tissue was higher (8.8% ± 3.0% vs 5.9% ± 2.0%, $p < 0.0001$) than in-stent neointima.
Conclusions: In patients ten months after STEMI, in-stent neointima contained a higher proportion of fibrotic tissue and lower proportion of necrotic and lipidic tissue compared the native atherosclerotic lesion.

1. Introduction

In-stent neointimal thickening is thought to arise from proliferation of smooth muscle cells and accumulation of extracellular matrix to form fibrotic tissue within the stent [1]. However, recent studies using both IVUS and OCT have shown that in-stent restenosis is not necessarily a stable process and has characteristics of de novo atherosclerosis [2]. iMap™ intravascular ultrasound (iMap; Boston Scientific Corp, Fremont, CA, USA) is a new software package for assessing plaque composition (fibrotic, lipidic, necrotic, calcific) according to backscattered ultrasound frequency spectrum [3,4].

The purpose of the study was to study the composition of in-stent neointima formation in patients 10 months after primary PCI for acute STEMI and to compare the results to immediately adjacent coronary segments proximal and distal to the stent using iMap intravascular ultrasound (IVUS).

2. Methods

2.1. Study population and design

For current study data source we used 63 consecutive STEMI patient data, who underwent primary percutaneous coronary intervention (PPCI) at Latvian Centre of Cardiology. Detailed inclusion criteria and study methods are described elsewhere [5]. The present analyses focused on 49 patients with stable coronary artery disease who underwent IVUS with iMap tissue characterization for infarct related artery at least 8 months after acute myocardial infarction. All patients signed informed consent and were more than 18 years of age. Exclusion criteria included acute coronary syndrome and/or target lesion revascularization within 8 months, non-cardiac illness associated with life-expectancy less than one year and patients with history of coronary artery bypass surgery. All study patients underwent coronary angiography and IVUS with iMap tissue characterization of the stented artery.

2.2. Procedures and iMap IVUS analyses

All coronary angiography and IVUS procedures were performed through a femoral or radial approach using a 6F guiding catheter. After wiring of the stented artery the ultrasound Imaging Catheter Atlantis™ SR Pro (40 MHz, mechanical-type transducer, 3.2 F, Boston Scientific Corporation, Natick, MA, USA) was advanced >10mm beyond the

Abbreviations: ACE-inhibitors, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; BMS, bare metal stent; DES, drug eluting stent; HDL-C, high-density lipoprotein cholesterol; IVUS, intravascular ultrasound; MLA, minimal lumen area; MLD, minimal lumen diameter; % NIV, percent neointimal tissue volume obstruction; LDL-C, low-density lipoprotein cholesterol; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; PPCI, primary percutaneous coronary intervention; STEMI, ST elevation myocardial infarction; TLR, target lesion revascularization; VH, virtual histology; VH-IVUS, virtual histology intravascular ultrasound.

☆ Disclosure: We certify that all authors have nothing to disclose.

* Corresponding author at: Pilsonu 13, Riga, LV-1002, Latvia. Tel.: +371 29411747.
E-mail addresses: cardio@inbox.lv (K. Trusinskis), karlis.strenge@gmail.com (K. Strenge).
[1] Postal address: Pilsonu 13, Riga, LV-1002, Latvia. Tel.: +371 29580037.
[2] Deceased.

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Table 1
Baseline characteristics.

Characteristic	Value
Age, yrs	59.3 ± 12.1
Male, n (%)	40 (70.2)
Diabetes, n (%)	6 (10.5)
Current smoker, n (%)	17 (29.8)
Ejection fraction, %	53.8 ± 7.6
Creatinine, mμmol/l	86.6 ± 18.9
Glucose, mmol/l	6.3 ± 1.5
Total cholesterol, mmol/l	4.5 ± 1.2
LDL-C, mmol/l	2.9 ± 1.1
HDL-C, mmol/l	1.1 ± 0.3
Triglyceride, mmol/l	1.3 ± 0.8
Body mass index, kg/m^2	28.0 ± 5.4
Medications:	
Statins, n (%)	53 (93.0)
Aspirin, n (%)	51 (89.5)
ACE-inhibitors, n (%)	41 (71.9)
Beta-blockers, n (%)	46 (80.7)
ARB, n (%)	3 (5.3)
Analyzed coronary artery	
Left main	0
Left anterior descending artery	18 (37.5)
Left circumflex artery	6 (12.5)
Right coronary artery	24 (50.0)

Values are mean ± SD or n (%).
HDL-C — high-density lipoprotein cholesterol.
LDL-C — low-density lipoprotein cholesterol.
ACE-inhibitors — angiotensin-converting enzyme inhibitors.

stent distal edge and was pulled back to a point >20mm proximal to the lesion using motorized transducer pullback at 0.5mm/s. The IVUS data were stored on a hard disk for offline analysis, which was performed independently by two analysts. Quantitative analysis of grayscale IVUS images was performed according to the criteria of the American College of Cardiology Clinical Expert Consensus Document on IVUS [6]. We defined the segment of interest 20 mm proximal to the proximal stent edge during IVUS analysis. The proximal segment was <20 mm in length, when the proximal edge of the stent to the ostium of the vessel was <20 mm. Virtual plaque assessment was performed with iMap software (QIvus 2.0; Medis Medical Imaging Systems, Leiden, The Netherlands). The percentage of each tissue component was determined. Plaques unsuitable for analysis because of acoustic shadowing behind calcification or wire artifact were removed automatically by iMap software.

2.3. Statistical analyses

Demographic, clinical, angiography and IVUS data were collected and entered into a prospective database. Data analysis was performed with the Statistical Package for Social Sciences (SPSS) software for Windows version 17.0.1 (Chicago, Illinois, USA). Categorical data were presented as frequencies and percentages; continuous variables were expressed as the mean ± standard deviation (SD). Continuous variables were compared with analysis of variance (ANOVA) test. A p value < 0.05 was considered statistically significant. Fibrotic and necrotic tissue was analyzed as categorical values.

Table 3
Neointimal tissue characteristics depending on NIV%.

Characteristic	NIV% ≤25 (n = 39)	NIV% >50 (n = 18)	p-value
Fibrotic tissue, %	70.4 ± 6.9	73.5 ± 4.2	0.089
Lipidic tissue, %	5.8 ± 2.2	6.2 ± 2.2	0.502
Necrotic tissue, %	13.4 ± 4.2	11.8 ± 3.8	0.179
Calcific tissue, %	10.4 ± 5.1	8.4 ± 3.2	0.143

3. Results

Baseline characteristics are summarized in Table 1. In-stent neointimal tissue evaluation was done 290.00 ± 45.03 days after stent implantation during PPCI. Tissue characteristics of stent neointima and atherosclerotic lesions proximal and distal to the stent are shown in Table 2. Stent neointima had a higher percentage of calcific tissue, but a lower percentage of lipidic and necrotic tissue compared with the proximal and distal coronary segments. The proportion of fibrotic tissue was higher in the proximal segment but did not differ between the distal segment and the stent neointima. In-stent neointima contained lower plaque volume compared with atherosclerotic lesion proximal to the stent (Table 2). Binary restenosis and neointimal tissue characteristics by iMap IVUS are presented in Table 3. Neointimal tissue characteristics in percent did not differ among patients with and without TLR (Table 4). Patients with TLR had higher % NIV and neointimal tissue volume.

We did not find any difference in-stent neointimal tissue composition among DES and BMS subgroups (Table 5).

4. Discussion

In the present study in-stent neointima contained a high percentage of fibrotic tissue by iMap IVUS and a relatively lower proportion of necrotic and lipidic tissue. This finding is consistent with the previous understanding about neointimal tissue as an expansive proliferation of smooth muscle cells, which later become dominated by the accumulation of extracellular matrix [7–9], consequently being recognized as fibrotic tissue by radiofrequency analyses. Previously it has been suggested that the differences between restenosis and nonrestenosis are quantitative rather than qualitative. It was also advocated that the main histological features are basically the same whether restenosis had developed or not [10]. However, recent studies have suggested that neointima can have characteristics of neoatherosclerosis with necrotic core and neovascularization [11]. OCT analysis have demonstrated that heterogeneous or layered tissues, low backscatter, and visible microvessels were associated with an increased burden of neointimal tissue [12]. We compared in-stent neointimal tissue composition

Table 2
Comparison of neointimal tissue and atherosclerosis in proximal segment.

Characteristic	Neointima	Proximal segment	Distal segment	p-value (proximal vs neointima)	p-value (distal vs neointima)	p-value (proximal vs distal)
Fibrotic tissue, %	71.5 ± 6.1	62.1 ± 14.8	72.4 ± 11.0	<0.0001	0.513	<0.0001
Fibrotic tissue, mm^3	37.6 ± 26.7	66.7 ± 38.1	36.8 ± 17.3	<0.0001	0.631	<0.0001
Lipidic tissue, %	6.0 ± 2.1	9.1 ± 2.9	7.5 ± 2.8	<0.0001	<0.0001	0.021
Lipidic tissue, mm^3	3.2 ± 2.9	9.9 ± 6.9	3.9 ± 2.8	<0.0001	0.136	<0.0001
Necrotic tissue, %	12.8 ± 3.8	26.7 ± 12.7	17.3 ± 8.6	<0.0001	<0.0001	<0.0001
Necrotic tissue, mm^3	6.3 ± 5.0	29.5 ± 24.7	10.1 ± 11.9	<0.0001	0.054	<0.0001
Calcific tissue, %	9.8 ± 4.8	2.1 ± 1.5	2.0 ± 1.5	<0.0001	<0.0001	0.179
Calcific tissue, mm^3	4.2 ± 2.3	6.3 ± 5.0	1.0 ± 0.7	<0.0001	<0.0001	0.002
Volume obstruction, %	23.8 ± 14.7	52.8 ± 9.4	46.1 ± 11.9	<0.0001	<0.0001	0.005
Plaque volume, mm^3	53.2 ± 38.7	112.3 ± 60.4	54.1 ± 26.3	<0.0001	0.885	<0.0001