Medical sciences 1 (2017) 1–9

Index Medicine International

Medical Sciences
Official website :
www.medicsciences.com

CORONARY ARTERIAL REMODELING IS ASSOCIATED WITH CORONARY PLAQUE COMPONENTS: VIRTUAL HISTOLOGY-INTRAVASCULAR ULTRASOUND ANALYSIS.

Norvydas Zapustas[1], Robertas Pranevičius[2], Kasparas Briedis[2], Ąžuolas Sirtautas[1], Kamilija Tvaronavičiūtė[1]
[1]Lithuanian University of Health Sciences, Kaunas, Lithuania
[2]Hospital of Lithuanian University of Health Sciences Kauno klinikos. Department of interventional Cardiology, Kaunas, Lithuania

Abstract

Objective: We used virtual histology-intravascular ultrasound (VH-IVUS) to evaluate the relation between coronary artery remodeling pattern and plaque components in 47 patients.
Methods: We divided the patients into two groups according to the remodeling pattern as positive remodeling (PR, remodeling index>1.05) (n=19) and intermediate remodeling (IR, remodeling index≤1.05 and ≥0.95)/negative remodeling (NR, remodeling indexb0.95) (n=28). VH-IVUS analysis classified the color-coded tissue into four major components: green (fibrotic, FT); yellow–green (fibro-fatty); white (dense calcium); and red (necrotic core, NC). Thin-cap fibro-atheroma (TCFA) was defined as focal, NC-rich (≥10% of the cross-sectional area) plaques being in contact with the lumen in a plaque burden≥40%.
Results: At the minimum lumen site, PR group had greater plaque plus media area (12.3±4.1vs. 10.8±4.1mm^2, p<0.001) and greater %NC area (30.1±12.3 vs. 26.2±11.6%, p<0.001) and smaller %FT area (59.0±14.5 vs. 51.4±14.6%, p=0.037) compared with IR/NR group. PR group had greater greater %NC volume (18.3±9.6 vs. 15.4±9.2%, p=0.001) and smaller %FT volume (59.6±11.7 vs. 52.9±11.0%, p=0.009) compared with IR/NR group.
Conclusions: VH-IVUS analysis demonstrates that PR was associated with more vulnerable plaque components compared with IR/NR regardless of their clinical presentation.
Keywords: coronary plaque, plaque components, intravascular ultrasound, positive remodeling.

Introduction

Coronary arterial remodeling is the geometric alteration of the arterial wall in response to the progression or regression of atherosclerosis. Patterns of arterial remodeling have been shown to play an important role in both the progression of de novo atherosclerosis [1–3] and in the restenotic process following percutaneous coronary interventions (PCI) [4,5]. Positive remodeling (PR) can be defined as increase of vessel area, in contrast negative or intermediate remodeling (NR/IR) can be defined as decrease or no change of vessel area [6,7]. PR is associated with unstable plaque morphology and morphometry, poor post-PCI outcome and poor long-term clinical outcome compared with IR/NR [8–19]. However, so far plaque characteristics according to the remodeling pattern were not fully assessed and the results are controversial. Therefore, the purpose of the present study was to attempt to evaluate virtual histology-intravascular ultrasound (VH-IVUS) images and to compare the VH-IVUS findings between lesions with PR and those with IR/NR in large population of patients with coronary artery disease.

Methods

Patient population

We reviewed 47 patients with coronary artery disease who underwent VH-IVUS between January 2016 and September, 2016, and we analyzed all lesions for which grey-scale and VH-IVUS examinations were performed regardless of the percutaneous coronary intervention.We excluded patientswith stent thrombosis, restenotic lesion, coronary artery bypass graft failure, severe heart failure or cardiogenic shock, important systemic disease, serum creatinine≥2.5 mg/dl, and patients in whom adequate IVUS images could not be obtained. The protocol was approved by the institutional review board and informed, written consent was obtained from patients before IVUS examinations. Hospital records of all patients were reviewed to obtain clinical demographics and medical history.

Laboratory analysis

Peripheral blood samples were obtained before coronary angiography using direct venipuncture. The blood samples were centrifuged, and serum was removed and stored at −70 °C until the assay could be performed. Absolute creatine kinase-MB levels were determined by radioimmunoassay (Dade Behring Inc., Miami,

Florida). Cardiac-specific troponin I levels were measured by a paramagnetic particle, chemiluminescent immunoenzymatic assay (Beckman, Coulter Inc., Fullerton, California). The serum levels of total cholesterol, triglyceride, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol were measured by standard enzymatic methods. High-sensitivity C-reactive protein was analyzed turbidimetrically with sheep antibodies against human C-reactive protein; this has been validated against the Dade-Behring method [20].

Coronary angiographic findings

Coronary angiogram was analyzed with validated quantitative coronary angiography (QCA) system (Phillips H5000 or Allura DCI program, Philips Medical Systems, the Netherlands). With the outer diameter of the contrast-filled catheter as the calibration standard, the reference diameter and minimal lumen diameter were measured in diastolic frames from orthogonal projections. Perfusion was evaluated according to TIMI criteria [21].

Grey-scale and VH-IVUS imaging and analysis

All grey-scale and VH-IVUS examinations were performed after intracoronary administration of 300 μg nitroglycerin. A 20-MHz, 2.9F IVUS imaging catheter (Eagle Eye, Volcano Corp, Rancho Cordova, CA) was advanced >10 mm beyond the lesion; and automated pullback was performed to a point >10 mm proximal to the lesion at a speed of 0.5 mm/s. One lesion per patient has been analyzed in the present study. If patient had multivessel disease and it was difficult to know which lesion is culprit one, we chose the lesions with maximum stenosis for the IVUS examinations.

Quantitative volumetric grey-scale and VH-IVUS analyses were performed across the entire lesion segment, and cross-sectional analyses were performed at the minimum lumen sites and at the largest NC sites. Conventional quantitative volumetric grey-scale IVUS analysis was performed according to the American College of Cardiology Clinical Expert Consensus Document on Standards for Acquisition, Measurement and Reporting of Intravascular Ultrasound Studies [22]. Measurements were made by every 1-mm interval for the region of interest, which was defined as the segment between distal to proximal reference sites that were the most normal looking within 5 mm proximal and distal to the lesion. References were the single slices with the largest lumen and smallest plaque CSAs within 10 mm proximally and distally. Remodeling index was the ratio of lesion site EEM CSA divided by the average of the proximal and distal reference EEM CSA. PR was defined as a remodeling index>1.05, IR as a remodeling index between 0.95 and 1.05, and NR as a remodeling indexb0.95 [8]. Hypoechoic plaque was less bright

than the adventitia, hyperechoic noncalcified plaque was as bright as or brighter than the adventitia without acoustic shadowing, and hyperechoic calcified plaque was brighter than the adventitia with acoustic shadowing.

VH-IVUS analysis classified the color-coded tissue into four major components: green (FT); yellow–green (FF); white (DC); and red (NC) [23–26]. The VH-IVUS analyses were reported in absolute amounts and as a percentage (relative amounts) of plaque volume. Thin-cap fibroatheroma (TCFA) was defined as focal, NC-rich (≥10% of the CSA) plaques being in contact with the lumen in a plaque burden≥40% [24].

Statistical analysis

The statistical Package for Social Sciences (SPSS) for Windows, version 15.0 (Chicago, Illinois) was used for all analyses. Continuous variables were presented as the mean value±1SD; comparisons were conducted by Student's t-test or nonparametric Wilcoxon test if normality assumption was violated. Discrete variables were presented as percentages and relative frequencies; comparisons were conducted by chi-square statistics or Fisher's exact test as appropriate. A p value <0.05 was considered statistically significant.

Results

Baseline characteristics and laboratory findings

The baseline characteristics are summarized in Table 1. Patients with PR tended to be younger. Low-density lipoprotein cholesterol and cardiac specific troponin-I levels were tended to be higher in PR group compared IR/NR group.

Table 1. Baseline characteristics

	Intermediate/negative remodeling (n=28)	**Positive remodeling (n=19)**	**p**
Age (years)	62.1±10.4	60.9±10.1	**0,048**
Male gender	12 (35,3)	22 (64,7)	0,512
Diabetes mellitus, n (%)	1(4,5)	2 (8)	0,055
Hypertension, n (%)	21 (95,5)	22 (88,0)	0,611
Family history of coronary artery disease,n (%)	11 (50,0)	16 (64,0)	0,342
Prior myocardial infarction n, (%)	1 (4,5)	2 (8,0)	0,6
Dyslipidemia,n (%)	19 (86,4)	23 (92,0)	0,061
Low physical activity, n (%)	13 (59,1)	17 (68,0)	0,141
Smoking, n (%)	4 (18,2)	9 (36,0)	0,621
Total cholesterol, mmol/l	4,85±1,3	5,02±1,7	0,51
Low-density lipoprotein cholesterol, mmol/l	2,84±1,0	3,08±1,2	**0,044**
High-density lipoprotein cholesterol, mmol/l	0,98±1,0	0,75±1,2	0,352
Cardiac specific troponin - I, µg/l	0,007	0,19±0,1	**0,001**
Glukose, mmol/l	5,64±0,9	5,58±0,5	0,624
Creatinin, µmol/l	83,05±13,8	88,32±16,8	0,430
NT-pro-BNP ng/mL)	192±428	248±502	0,07
Triglyceride	1,82±0,4	2,42±0,07	0,441

Grey-scale IVUS results

Grey-scale IVUS results are summarized in Table 2. EEM CSA, lumen CSA, and P&M CSA at the proximal and distal reference segments were significantly smaller in PR group compared IR/NR group. At the minimum lumen sites lumen CSA was significantly smaller in PR group compared IR/NR group and P&M CSA and plaque burden were significantly greater in PR group compared IR/NR group. IVUS lesion length was significantly longer in PR group compared with IR/NR group. EEM and plaque volumes were significantly greater in PR group compared IR/NR group.

Table 2. Grey-scale intravascular ultrasound findings

Variable	Intermediate/negative remodeling (n=28)	Positive remodeling (n=19)	p
Proximal reference			
EEM CSA area (mm^2)	22.4±3.9	18.4±4.8	**0.04**
Lumen CSA area (mm^2)	12.8±1.8	11.1±3.9	**0.02**
P&M CSA area (mm^2)	10.8±4.1	8.2±4.1	**0.001**
Plaque burden (%)	38 ±8	38±8	0.251
Minimum lumen site			
EEM CSA area (mm^2)	15.2±4.9	18.4±5.8	**0.02**
Lumen CSA area (mm^2)	7.9±4.8	6.1±3.9	**0.02**
P&M CSA area (mm^2)	10.8±4.1	12.3±4.1	**0.001**
Plaque burden (%)	54 ±12	65±11	0.251
Distal reference			
EEM CSA area (mm^2)	15,9±3.9	14.4±6.8	**0.04**
Lumen CSA area (mm^2)	10.9±0.8	7.8±3.6	**0.02**
P&M CSA area (mm^2)	7.8±4.1	6.1±3.1	**0.001**
Plaque burden (%)	39 ±8	38±8	0.251
Remodeling index	0.92±0.1	1.17±0.18	**0.001**
IVUS lesion lenght (mm)	22.8±9.5	17.4±11.4	**0.036**
Volumetric analysis			
EEM volume (mm^3)	270±315	330±215	**0.025**
Lumen volume (mm^3)	130±110	139±100	**0.001**
Plaque volume (mm^3)	135±125	190±150	**0.001**

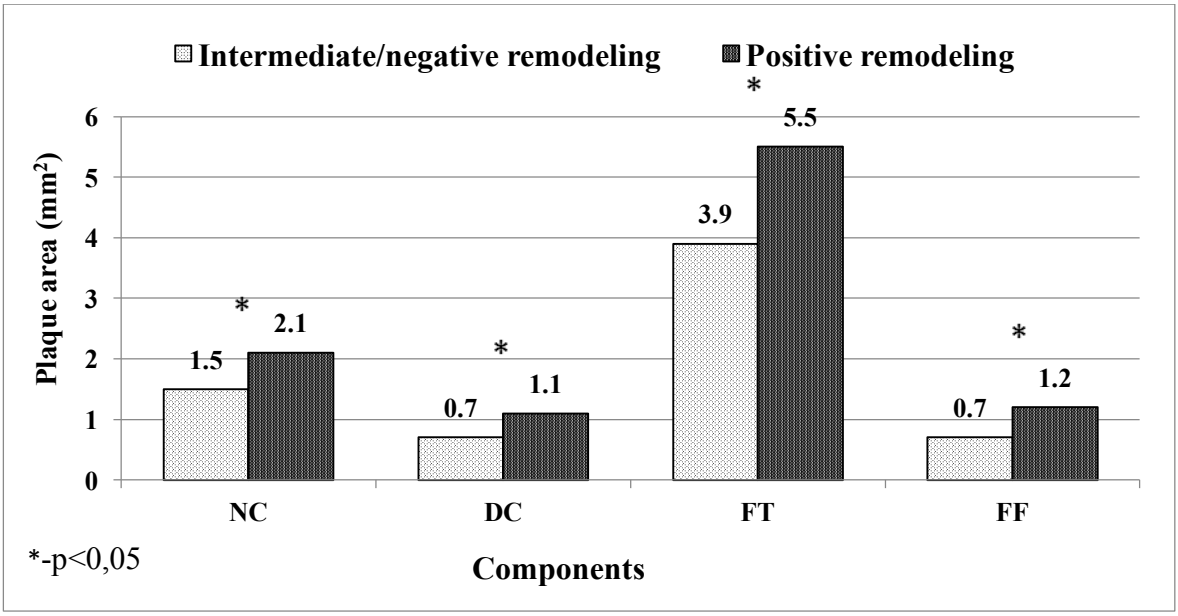
EEM: external elastic membrane, CSA: cross-sectional area; P&M: plaque plus media, IVUS: intravascular ultrasound.

VH-IVUS results

At the minimum lumen site, absolute FT, FF, DC, and NC areas were significantly greater in PR group compared with IR/NR group, and %NC area was significantly greater and %FT area was significantly smaller in PR group compared with IR/NR group (Fig. 1). Absolute FT, FF, DC, and NC volumes were significantly greater in PR group compared with IR/NR group. %NC volume was significantly greater, %DC volume was tended to be greater, and %FT volume was significantly smaller, and %FF volume was tended to be smaller in PR group compared with IR/NR group (Fig. 2).

Figure 1. The absolute (A) and relative (B) plaque components at the minimum lumen sites. FT: fibrotic, FF: fibro-fatty, DC: dense calcium, NC: necrotic core.

A.



B.

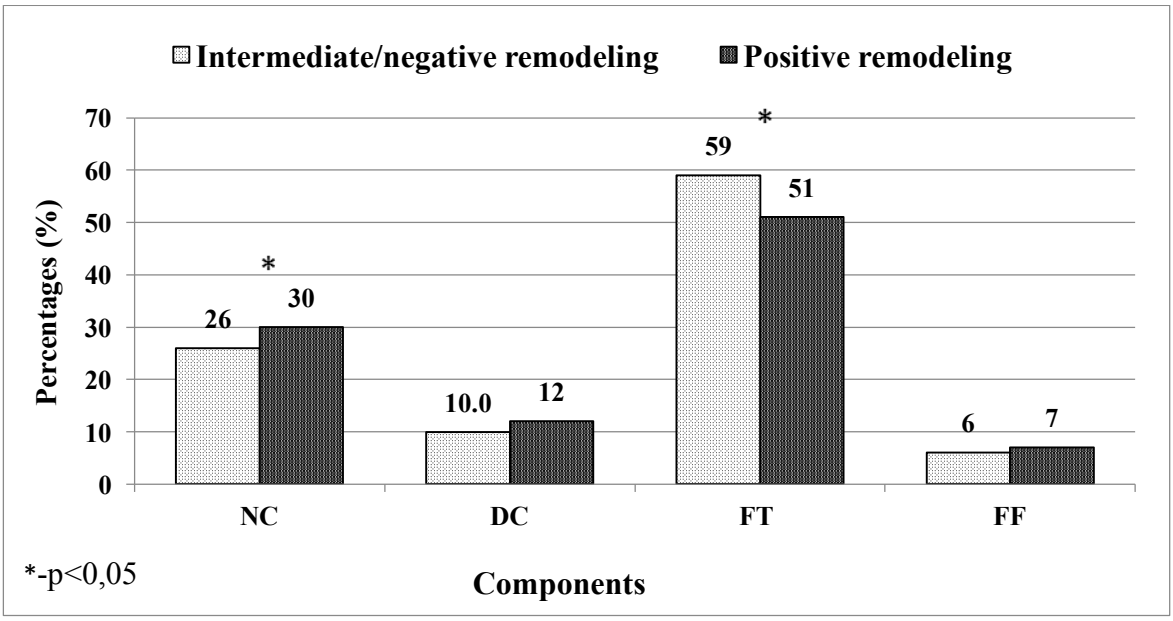
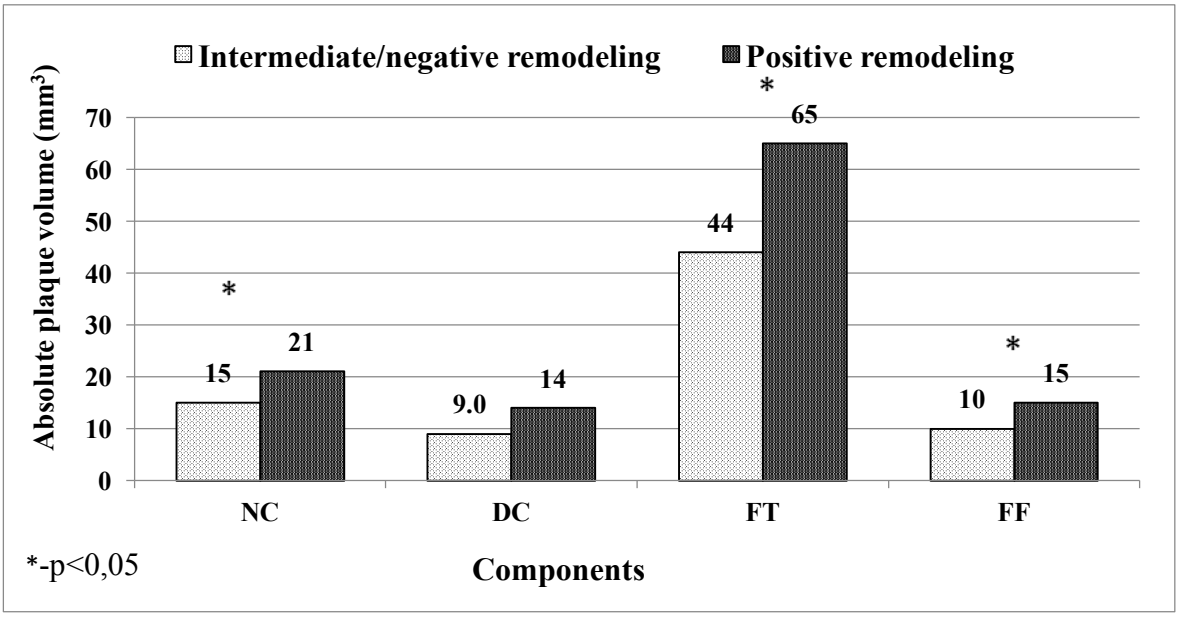
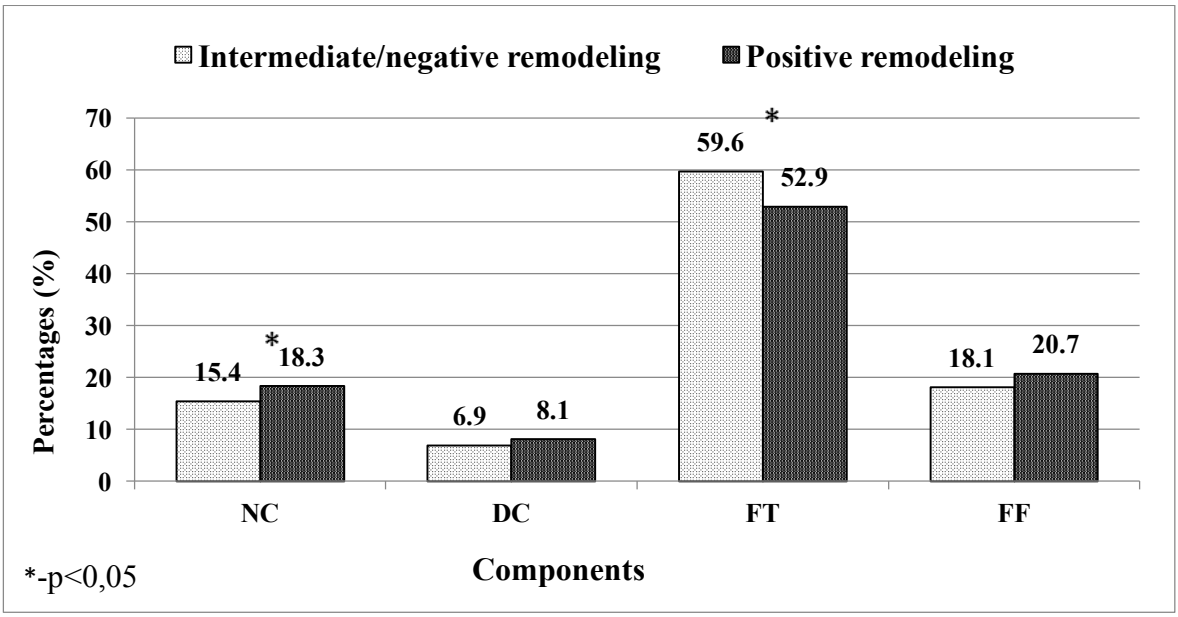


Figure 2. The volumetric absolute (A) and relative (B) plaque components. FT: fibrotic, FF: fibro-fatty, DC: dense calcium, NC: necrotic core.

A.



B.



Discussion

The present VH-IVUS study demonstrated that 1) PR group had greater P&M CSA and greater NC area at the minimum lumen site compared with IR/NR group, 2) PR group had greater plaque volume and greater NC volume compared with IR/NR group. Several grey-scale IVUS studies have shown various characteristics of coronary artery remodeling and plaque morphology in the culprit lesion of coronary artery disease [1,9]. Nakamura et al. reported that PR was observed more frequently in patients with acute coronary syndrome compared with those with stable angina [8]. By using multislice computed tomography and IVUS, Imazeki et al. [10] reported that PR was observed in 61% in the patients with acute coronary syndrome, but in none of the patients with stable angina. And patients with acute myocardial infarction have typical IVUS features including PR, plaque rupture, thrombus, and either spotty or deep calcium in the culprit lesion [11–16]. A certain characteristics of coronary artery remodeling may be observed in the culprit lesion of acute coronary syndrome with IVUS, and, if so, it may be possible to predict the plaque instability leading to acute coronary syndrome.

Limitations

Several limitations should be noted. This is a single center study with a small number of patients, thus possibly posing a risk of patient selection bias. Our results of plaque components were not evaluated by histology or other diagnostic modalities such as optical coherence tomography and angioscopy.

Conclusions

PR lesion has more vulnerable plaque component (greater plaque with greater NC component) compared with IR/NR regardless of their clinical presentation.

All authors have no financial conflicts of interest to disclosure concerning the manuscript

References

1. Nishioka T, Luo H, Eigler NL, Berglund H, Kim CJ, Siegel RJ. Contribution of inadequate compensatory enlargement to development of human coronary artery stenosis: an in vivo intravascular ultrasound study. J Am Coll Cardiol 1996;27: 1571–6.
2. Mintz GS, Kent KM, Pichard AD, Satler LF, Popma JJ, Leon MB. Contribution of inadequate arterial remodeling to the development of focal coronary artery stenosis: an intravascular ultrasound study. Circulation 1997;95:1791–8.
3. Birnbaum Y, Fishbein MC, Luo H, Nishioka T, Siegel RJ. Regional remodeling of atherosclerotic arteries: a major determinant of clinical manifestations of disease. J Am Coll Cardiol 1997;30:1149–64.
4. Mintz GS, Popma JJ, Pichard AD, et al. Arterial remodeling after coronary angioplasty: a serial intravascular ultrasound study. Circulation 1996;94:35–43.
5. Kimura T, Kaburagi S, Tamura T, et al. Remodeling of human coronary arteries undergoing coronary

angioplasty or atherectomy. Circulation 1997;96:475–83.
6. HartmannM, von Birgelen C,Mintz GS, Verhorst PM, Erbel R. Relation between baseline plaque burden and subsequent remodelling of atherosclerotic leftmain coronary arteries: a serial intravascular ultrasound study with long-term (> or=12months) follow-up. Eur Heart J 2006;27:1778–84.
7. von Birgelen C, Hartmann M, Mintz GS, et al. Remodeling index compared to actual vascular remodeling in atherosclerotic left main coronary arteries as assessed with long-term (> or=12 months) serial intravascular ultrasound. J Am Coll Cardiol 2006;47:1363–8.
8. Nakamura M, Nishikawa H, Mukai S, et al. Impact of coronary artery remodeling on clinical presentation of coronary artery disease: an intravascular ultrasound study. J Am Coll Cardiol 2001;37:63–9.
9. Hodgson JM, Reddy KG, Suneja R, Nair RN, Lesnefsky EJ, Sheehan HM. Intracoronary ultrasound imaging: correlation of plaque morphology with angiography, clinical syndrome and procedural results in patients undergoing coronary angioplasty. J Am Coll Cardiol 1993;21:35–44.
10. Imazeki T, Sato Y, Inoue F, et al. Evaluation of coronary artery remodeling in patients with acute coronary syndrome and stable angina by multislice computed tomography. Circ J 2004;68:1045–50.
11. Fukuda D, Kawarabayashi T, Tanaka A, et al. Lesion characteristics of acute myocardial infarction: an investigation with intravascular ultrasound. Heart 2001;85:402–6.
12. Rioufol G, Finet G, Ginon I, et al. Multiple atherosclerotic plaque rupture in acute coronary syndrome: a three-vessel intravascular ultrasound study. Circulation 2002;106:804–8.
13. Hong MK, Mintz GS, Lee CW, et al. Comparison of coronary plaque rupture between stable angina and acute myocardial infarction: a three-vessel intravascular ultrasound study in 235 patients. Circulation 2004;110:928–33.
14. Tanaka A, Shimada K, Sano T, et al. Multiple plaque rupture and C-reactive protein in acute myocardial infarction. J Am Coll Cardiol 2005;45:1594–9.
15. Hasegawa T, Ehara S, Kobayashi Y, et al. Acute myocardial infarction: clinical characteristics and plaque morphology between expansive remodeling and constrictive remodeling by intravascular ultrasound. Am Heart J 2006;151:332–7.
16. Ehara S, Kobayashi Y, Yoshiyama M, et al. Spotty calcification typifies the culprit plaque in patients with acute myocardial infarction: an intravascular ultrasound study. Circulation 2004;110:3424–9.
17. Sahara M, Kirigaya H, Oikawa Y, et al. Arterial remodeling patterns before intervention predict diffuse instent restenosis: an intravascular ultrasound study. J Am Coll Cardiol 2003;42:1731–8.
18. Hong YJ, Jeong MH, Hyun DW, et al. Impact of preinterventional arterial remodeling on in-stent neointimal hyperplasia and in-stent restenosis after coronary stent implantation. Circ J 2005;69:414–9.
19. Mintz GS, Tinana A, Hong MK, et al. Impact of preinterventional arterial remodeling on neointimal hyperplasia after implantation of (non polymer-encapsulated) paclitaxel-coated stents: a serial volumetric intravascular ultrasound analysis from the ASian Paclitaxel-Eluting Stent Clinical Trial (ASPECT). Circulation 2003;108:1295–8.
20. RobertsWL,Moulton L, LawTC, FarrowG, Cooper-AndersonM, Savory J, Rifai N. Evaluation of nine automated high-sensitivity C-reactive protein methods: implications for clinical and epidemiological applications. Part 2. Clin Chem 2001;47:418–25.
21. Timi IIIB. Investigators. Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-Q-wavemyocardial infarction. Results of the TIMI IIIB Trial. Thrombolysis in Myocardial Ischemia. Circulation 1994;89:1545–56.
22. Mintz GS, Nissen SE, Anderson WD, et al. American College of Cardiology clinical expert consensus document on standards for acquisition, measurement and reporting of intravascular ultrasound studies (IVUS): a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. J Am Coll Cardiol 2001;37:1478–92.
23. Nair A, Kuban BD, Tuzcu EM, Schoenhagen P, Nissen SE, Vince DG. Coronary plaque classification with intravascular ultrasound radiofrequency data analysis. Circulation 2002;106:2200–6.
24. Rodriguez-Granillo GA, García-García HM. Mc Fadden EP, Valgimigli M, Aoki J, de Feyter P, Serruys PW. In vivo intravascular ultrasound-derived thin-cap fibroatheroma detection using ultrasound radiofrequency data analysis. J Am Coll Cardiol 2005;46:2038–42.
25. Okubo M, Kawasaki M, Ishihara Y, et al. Tissue characterization of coronary plaques: comparison of integrated backscatter intravascular ultrasound with virtual histology intravascular ultrasound. Circ J 2008;72:1631–9.
26. Yamamoto M, Takano M, Okamatsu K, et al. Relationship between thin cap fibroatheroma identified by virtual histology and angioscopic yellow plaque in quantitative analysis with colorimetry. Circ J 2009;73:497–502.