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Original article

Distribution of tissue characteristics of coronary plaques evaluated by integrated backscatter intravascular ultrasound: Differences between the inner and outer vessel curvature

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ABSTRACT

Background: The purpose of the present study was to evaluate the tissue characteristics of plaques with moderate or mild stenosis in the inner and outer curvature of the left anterior descending artery (LAD) using integrated backscatter intravascular ultrasound.

Methods: We evaluated 66 plaques with moderate stenosis (plaque burden >50% but ≤75%) and 49 plaques with mild stenosis (plaque burden >30% but ≤50%) in 66 patients undergoing percutaneous intervention to the LAD. All plaques were >10 mm away from any side branch or previously implanted stents. We divided vessel cross-sections into four quadrants (inner curvature, outer curvature, clockwise lateral side, and counterclockwise lateral side) using the septal branch as a landmark for the inner curvature. We averaged relative lipid area, relative fibrous area, and relative calcified area in minimal lumen area (MLA), three cross-sections proximal to the site of MLA, and three cross-sections distal to the site of MLA.

Results: In plaques with moderate stenosis, the relative lipid area in the inner curvature was significantly greater than in the outer curvature and lateral sides, whereas there was no significant difference in plaques with mild stenosis.

Conclusion: The present study provides new findings that lipid pool is clustered in the inner curvature and fibrous tissue is clustered in the outer curvature of plaques with moderate stenosis in non-branching LAD lesions.

Introduction

The stability of atherosclerotic plaques is related to histological composition and the thickness of fibrous caps. Therefore, recognition of the tissue characteristics of coronary plaques is important to understand and prevent acute coronary syndrome [1,2]. Atherosclerotic plaques in coronary arteries are unevenly distributed within the coronary tree in the same patient exposed to the same risk factors [3]. Several reports have shown that these uneven distributions are due to the difference of wall shear stress [4,5] and blood flow turbulence [6]. Low shear stress accelerates atherosclerosis at midcap regions downstream from the stenosis in the inner curvature of the vessel compared with the outer curvature [7]. However, differences in tissue components between the inner and outer curvature have not been adequately investigated *in vivo*.

Intravascular ultrasound (IVUS) allows cross-sectional imaging of coronary arteries and provides a comprehensive assessment of atherosclerotic plaques *in vivo* [8,9]. We previously reported that integrated backscatter (IB)-IVUS had high sensitivity and specificity (90–95%) for the tissue characterization of coronary plaques using histology as a gold standard [10–13]. In those studies, we constructed two-dimensional (2D) or three-dimensional (3D) color-coded maps of plaque components based on the IB values [10–14]. The reliability and the usefulness of IB-IVUS have been established in many previous reports [10–16].

The purpose of the present study was to evaluate the tissue characteristics of coronary plaques with moderate or mild stenosis in the inner and outer curvature of the left anterior descending coronary artery (LAD) using IB-IVUS.

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Methods

Patients and coronary plaques

We enrolled 293 consecutive patients with stable angina pectoris who were undergoing percutaneous coronary intervention (PCI) to the LAD (Fig. 1). We selected the LAD because the septal branch was able to indicate the inner curvature and showed similar morphology in almost all patients. Right coronary and left circumflex arteries were excluded because they often have ectasia that results from medial replacement of smooth muscle cells with hyalinized collagen and this is not typical of coronary atherosclerotic lesions [17]. Non-targeted plaques with moderate stenosis (plaque burden at the minimal lumen area >50% but ≤75%) that were apart from any side branch or previously implanted stents more than 10 mm were evaluated in order to potentially minimize the effects of blood flow turbulence due to vessel branching [6]. After enrolling eligible patients, plaques with mild stenosis (plaque burden at the minimal lumen area >30% but ≤50%) that were >10 mm away from any side branch or previously implanted stents were also included in the analysis, when eligible plaques with mild stenosis were present. Patients were excluded if they had unstable angina or myocardial infarction within the previous three months, an ejection fraction ≤30%, or chronic atrial fibrillation that resulted in different pattern of blood flow in coronary arteries. Plaques with an arc of calcification >30° were excluded in order to perform rigorous analysis because acoustic shadow due to calcification hinders the rigorous measurement of plaque components. Plaques with an imaging quality that was not adequate for analysis were also excluded. Risk factors for coronary artery disease were evaluated in enrolled patients, including hypertension (medication-dependent or systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg), type 2 diabetes mellitus [medication-dependent or hemoglobin (Hb) A1c ≥ 6.5%], dyslipidemia (medication-dependent, low-density lipoprotein cholesterol ≥140 mg/dl and/or high-density lipoprotein cholesterol <40 mg/dl), and current smoking. The protocol was approved by the institutional ethics committees and informed consent was obtained from each patient.

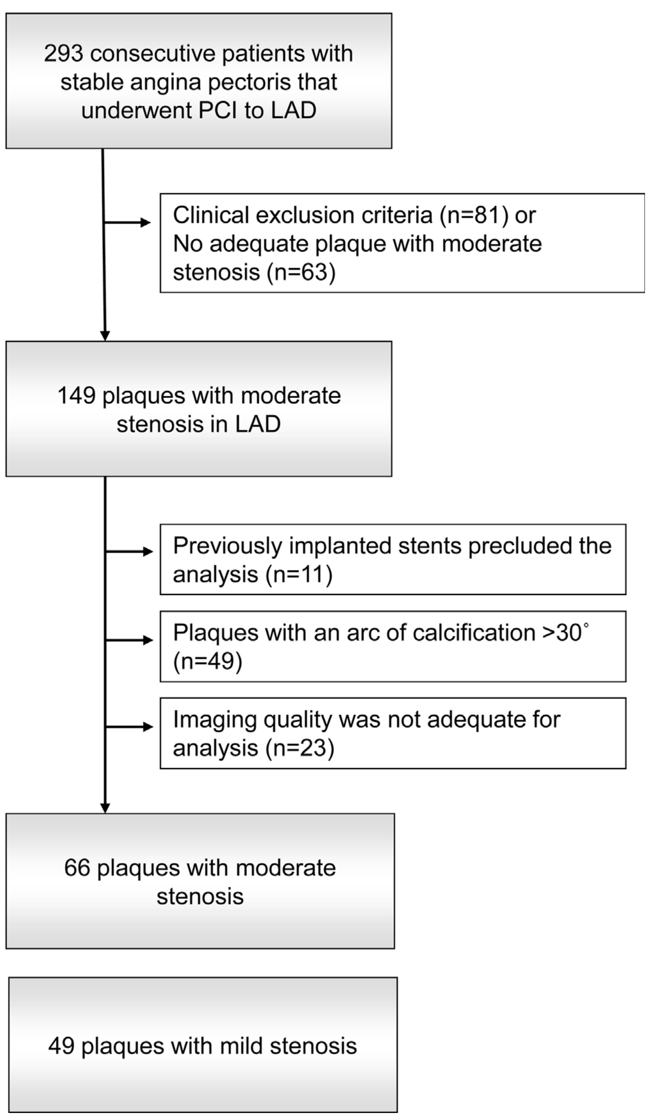

Fig. 1. Study flow chart. LAD, left anterior descending artery; PCI, percutaneous coronary intervention.

Integrated backscatter intravascular ultrasound system and data acquisition

An IVUS imaging system (VISIWAVE, Terumo, Tokyo, Japan) was used to obtain cross-sectional IB-IVUS images. Ultrasound backscattered signals were acquired using a 38 MHz mechanically rotating IVUS catheter (ViewIT, Terumo). The details of the system and its clinical usefulness have been reported previously [10–13]. We administered an optimal dose of intracoronary isosorbide dinitrate before the measurements for the prevention of coronary spasm. The IVUS catheter was advanced into the coronary artery and IB-IVUS images were acquired at the site of the plaques. We analyzed seven cross-sections in each lesion [minimal lumen area (MLA), 0.5 mm, 1.0 mm, and 1.5 mm proximal and distal to the site of MLA]. Cross-sectional images were quantified for lumen area (LA), external elastic membrane area (EEMA), and plaque area (PA = EEMA − LA) by use of software included with the IVUS system. We divided vessel cross-sections into four quadrants (inner curvature, outer curvature, clockwise lateral side that is the usual origin of diagonal branch, and counterclockwise lateral side that is not the origin of diagonal branch) using the septal branch as a landmark of the inner curvature (Fig. 2). We divided vessel cross-sections using the center of IVUS catheters as a landmark.

We averaged relative lipid area, relative fibrous area, and relative calcified area in seven cross-sections. The eccentricity rate was calculated at the lesion of MLA as: (maximum plaque plus media thickness – minimum plaque plus media thickness)/ maximum plaque plus media thickness. The remodeling index was defined as the ratio of EEM area at the lesion of MLA to average of EEM area at the proximal reference site and EEM area at the distal reference site. Radius of curvature of analyzed lesions was measured on right anterior oblique view of angiogram.

Angiographic stenosis was analyzed using an automated edge-detection algorithm (System Syngo X-workplace, Siemens, Mountain View, CA, USA). By using a contrast-filled guiding catheter as calibration, minimal luminal diameter and reference vessel diameter were measured from the projection with the least foreshortened view that was selected from multiple projections, and the least value of minimal luminal diameters was measured. The reference vessel diameter was averaged from user-defined angiographically normal segments proximal and distal to the stenosis.

Construction of 3D IB-IVUS images

We constructed 3D color-coded maps for a representative image combining 17 cross-sections (every 1 mm axial interval for 8 mm proximal, and distal to the site of minimal lumen area). The 3D construction was performed automatically by connecting consecutive 2D IB-IVUS images using computer software (T3D, Fortner Research LLC, Sterling, VA, USA).