Coronary Artery Dilatation Exceeding 4.0 mm During Acute Kawasaki Disease Predicts a High Probability of Subsequent Late Intima–Medial Thickening

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Abstract. We used intravascular ultrasound (IVUS) to compare the degree of coronary artery dilatation during the acute phase of Kawasaki disease with the extent of intima–medial thickening more than 10 years later. We wanted to determine if there was a threshold degree of dilatation that was highly predictive of later thickening. Twenty-eight patients with a mean age of 17.3 ± 1.7 years were studied; the mean interval from the initial selective coronary angiography to the IVUS study was 15.0 ± 1.6 years. We measured the maximum intima–medial thickness of selected coronary arterial segments in IVUS images and measured the largest diameters of the corresponding coronary arterial segments in the initial coronary angiograms. A significant correlation was found between the initial diameters of the coronary arteries and the intima–medial thickness more than 10 years later in the right coronary, the left anterior descending coronary, and the left circumflex arteries. The coefficient of correlation was 0.77 (n = 120, p < 0.0001), and for the bifurcation of the left coronary artery it was 0.50 (n = 26, p < 0.01). For this study, abnormal intima–medial thickness was defined as more than 0.40 mm. When the initial coronary arterial dilatation exceeded 4.0 mm, the sensitivity was 28/31 (90%) and the specificity was 87/89 (98%) in the right coronary, the left anterior descending coronary, and the left circumflex arteries. For the bifurcation of the left coronary artery, the sensitivity was 14/21 (67%) and the specificity was 5/5 (100%).

Key words: Kawasaki disease — Coronary aneurysm — Localized stenosis — Intravascular ultrasound — Intimal thickening

Kawasaki disease (KD) is an acute febrile disease complicated by coronary arterial lesions in 10% to 15% of the patients [14, 16]. In the acute phase of KD, coronary arterial dilatations may develop that, in some patients, may persist for years. In others, they either regress or evolve into stenotic lesions. Stenotic lesions can lead to myocardial ischemia and even myocardial infarction [10, 11]. These events influence the prognosis of the patient.

Regression and stenotic lesions are mainly caused by thickening of the vessel walls. It is unknown whether thickening of the vascular wall can develop more than 10 years after the acute illness, but such information is essential to determine patient prognosis. Recently, assessment and quantitative measurements of the vascular wall by intravascular ultrasound (IVUS) in coronary atherosclerosis have become useful in its diagnosis and elucidation of morbidity [2, 4, 5, 9, 12].

We examined the coronary arteries of a group of patients more than 10 years after an episode of acute KD using IVUS with special attention to the relationship between dilatation of coronary arteries in the acute phase and late thickening of the vessel walls.

With respect to aneurysms at the bifurcation of the left coronary artery (LCA), we analyzed the impact of their peripheral extension as well as their diameter on late thickening of the vascular walls. We compared the intima–medial thickness of extended aneurysms which were dilated to segment 7 and/or segment 13 with that of localized aneurysms.

Patient Population

Twenty-eight patients were studied—20 males and 8 females. All participants gave informed consent for the IVUS study. The mean age at IVUS study was 17.3 ± 1.7 years (± SD) (range 14.5–21.1 years) and the mean age at the onset of KD was 2.4 ± 1.8 years.
(range 4 months to 6.4 years). All 28 patients underwent an initial coronary angiogram (CAG) less than 100 days after the onset of KD. The mean interval from the onset of KD to the initial CAG was 61 ± 19 days (range 30–98 days). All 28 had coronary arterial lesions due to KD. The mean interval from the initial coronary angiographic study to the IVUS study was 15.0 ± 1.6 years (range 10.8–18.3 years). The treatments of the acute phase of KD were as follows: aspirin (13), aspirin and steroid (7), steroid (1), or none (7). All patients had been treated with antiplatelet agents since the initial CAG. The mean total cholesterol was 162 ± 30 (range 119–225).

**Methods**

*Intravascular Ultrasound Imaging and the Initial Selective Coronary Angiograms*

The IVUS study was performed as follows. After anticoagulation with heparin and a dose of nitroglycerin, diagnostic coronary angiography was performed. After a 0.014-mm guidewire was advanced through a 6F guiding catheter, a 3.5-F and 30-MHz intravascular ultrasound catheter (Boston Scientific, Inc., USA) was inserted. The intravascular ultrasound equipment used was SONOS (Model 2400A, Hewlett-Packard, Inc., Palo Alto, CA, USA) and we recorded the ultrasonic images continuously on s-VHS videotape.

Coronary arterial lesions after KD by IVUS were characterized by intima–medial thickening. Because IVUS cannot identify the borderline of intima and media, we measured intima–medial thickness as a marker of intimal thickening of the coronary artery (Figs. 1 and 2). In all 28 cases at IVUS study, there was no thrombus. The maximum intima–medial thickness of respective coronary arterial segments in the ultrasonic images was measured by two independent observers. Frames showing the thickest vascular wall in respective segments were chosen by both observers. Each observer then made two measurements of the maximum intima–medial thickness at the frame using a software program (Hewlett-Packard). Measurements by each observer and between observers were reproducible with high correlation coefficients \( r = 0.99 \).

The diameters of coronary arteries at the corresponding coronary arterial segments in the initial selective CAGs were also measured by two observers. In the branches, the greatest diameter of the segment is taken as the point of maximal dilatation. At the bifurcation of LCA, the diameter shown in Fig. 3 was measured. Measurements between observers were reproducible with a high correlation coefficient \( r = 0.98 \).

The number of branches examined by IVUS were as follows: right coronary artery (RCA), 24; left anterior descending coronary artery (LAD), 23; and the left circumflex artery (LCX), 22. The number of segments evaluated in respective branches were as follows: RCA, 52; LAD, 36; and LCX, 32. The bifurcation of the LCA was examined in 26 patients.