Cardiac Events and the Maximum Diameter of Coronary Artery Aneurysms in Kawasaki Disease

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Objectives To clarify the occurrence of cardiac events based on the maximal diameter of the maximal coronary artery aneurysm (CAA) in Kawasaki disease (KD).

Study design Two hundred fourteen patients (160 male and 54 female) who had had at least 1 CAA in the selective coronary angiogram less than 100 days after the onset of KD were studied. We measured the maximal CAA diameters in the major branches of the initial coronary angiograms. Death, myocardial infarction and coronary artery revascularization were included as cardiac events in this study. We divided the patients into three groups based on the maximal CAA diameter (large ≥8.0 mm; medium ≥6.0 mm and <8.0 mm; small <6.0 mm). Further, we also analyzed the cardiac events based on laterality of maximal CAA (bilateral, unilateral) and body surface area (BSA).

Results Cardiac events occurred in 44 patients (21%). For BSA < 0.50 m^2, the 30-year cardiac event-free survival in the large and medium groups was 66% (n = 38, 95% CI, 49-80) and 62% (n = 27, 95% CI, 38-81), respectively. For BSA ≥ 0.50 m^2, that in large group was 54% (n = 58, 95% CI, 40-67). There were no cardiac events in the medium group for BSA ≥0.50 m^2 (n = 36) and the small group (n = 56). In the large analyzed group, the 30-year cardiac event-free survival in the bilateral and unilateral groups was 40% (n = 48, 95% CI, 27-55) and 78% (n = 48, 95% CI, 63-89), respectively ($P < .0001$).

Conclusions The group with the highest risk of cardiac events was the patient group with the maximal CAA diameter ≥6.0 mm with BSA < 0.50 m^2 and the maximal CAA diameter ≥8.0 mm with BSA ≥ 0.50 m^2. At 30 years after the onset of KD, cardiac event-free survival was about 60%. Given the high rate of cardiac events in this patient population, life-long cardiovascular surveillance is advised. *(J Pediatr 2017;188:70-4).*

Kawasaki disease (KD) is an acute febrile disease that can lead to coronary artery lesions (CALs) in about 15% of affected children treated without intravenous immunoglobulin before the 1990s and about 5% of patients with intravenous immunoglobulin IVIG since 2000.[1,2] CALs caused by KD lead to cardiac events such as acute myocardial infarction (MI), and they are a cause of acquired ischemic heart disease in children. Children with KD between the 1970s and 1990s who developed CAL are now young adults. However, there are few long-term reports about the occurrence of cardiac events after the onset of KD.[3,4] We investigated the occurrence of cardiac events based on the maximal diameters of coronary artery aneurysms (CAAs) in the initial coronary angiograms (CAGs) obtained immediately after the onset of KD.

Methods

There were 579 patients with CAL who had previously undergone CAGs between 1978 and 2011 in our institution. Selective CAG by cardiac catheterization was the only method for the precise diagnosis of CAL until 1990. In the early 1980s, most of the patients with KD had undergone CAG for the diagnosis of CAL in our institution. Between 1990 and 2011, the patients who were diagnosed with CAA by 2-dimensional echocardiography had undergone CAG. The diagnosis of CAA has recently been improved by the application of noninvasive methods such as 2-dimensional echocardiography, computed tomography angiography, and magnetic resonance angiography. Therefore, CAG for the diagnosis of CAA within 2-3 months after the onset of acute KD was not done after 2011 in our hospital. Among the 579 patients, there were 214 patients who had had at least 1 coronary artery aneurysm in the initial CAGs less than 100 days after the onset of KD. For this study, the final diagnosis of KD and CAA was based on diagnostic guidelines by the Japanese Circulation Society.[5,6] The age at onset of acute KD ranged from

BSA	Body surface area
CAAs	Coronary artery aneurysms
CABG	Coronary artery bypass grafting
CAGs	Coronary angiogram
CALs	Coronary artery lesions
KD	Kawasaki disease
MI	Myocardial infarction
PCI	Percutaneous coronary intervention

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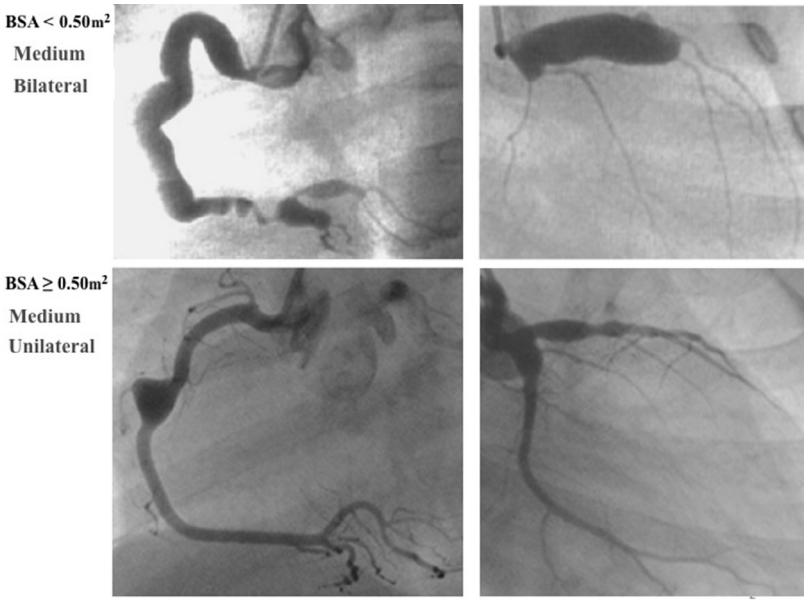

Figure 2. Coronary artery angiograms. A 4-month-old boy with acute KD (*upper*). In the initial CAG done 71 days after the onset of KD, the maximum diameter at the segment 1 of the right coronary artery was 6.5 mm (*left*). The maximum diameter at the segment 6 of the left coronary artery was 7.5 mm (*right*). The patient was included in the bilateral medium group of BSA < 0.50 m^2. A 2-year-old girl with acute KD (*lower*). In the initial CAG done 60 days after the onset of KD, the maximum diameter of the right coronary artery was 6.8 mm (*left*). The maximum diameter at the segment of the left anterior descending artery and the segment 11 of the left circumflex were 3.2 mm and 3.6 mm (*right*). The patient was included in the unilateral medium group of BSA ≥ 0.50 m^2.

2 months to 13 years with the median of 23 months. Initial CAG was performed from 20 to 99 days with the median of 59 days, and body surface area (BSA) at the initial CAG ranged from 0.31 to 1.63 with a median of 0.52 m^2. The follow-up period ranged from 2.5 months to 37.8 years with the median of 16.8 years.

The ethics committee of our institution approved this retrospective study. No extramural funding was used to support this work.

The diagnosis of CAA was determined by 2 pediatric cardiologists. Two pediatric cardiologists had measured the maximal CAA diameters in the major branches from the initial CAGs. The major branches included the right coronary artery, the left anterior descending artery, and the left circumflex. If an aneurysm was present at the bifurcation of the left coronary artery, the diameter of the aneurysm at the left coronary artery was also measured. We previously described how to measure coronary arteries and the intra- and interobserver accuracy.[7,8] We divided the patients into 3 groups determined by the maximal CAA diameter in each patient (large ≥8.0 mm; medium ≥6.0 mm and <8.0 mm; and small <6.0 mm) (**Figure 1**; available at www.jpeds.com).

Cardiac events included cardiac death, MI, and coronary artery revascularization (coronary artery bypass grafting [CABG] and percutaneous coronary intervention [PCI]). PCI included percutaneous transluminal coronary balloon angioplasty and percutaneous transluminal coronary rotational ablation. We determined cardiac events for the respective groups from medical records.

First, we analyzed the survival, MI-free survival, coronary artery revascularization-free survival, and survival for total cardiac events in the 3 groups based on the maximal CAA diameter. Second, we determined total cardiac event-free survival in the groups based on the maximal CAA diameter and BSA in the initial CAGs. BSA was calculated using the Heycock formula. One group had BSA less than 0.50 m^2, and the other group had BSA greater than or equal to 0.50 m^2. Third, we determined cardiac event-survival in the groups based on the maximal CAA diameter and the laterality of maximal CAA in the initial CAGs. They were divided into groups depending on the laterality of the maximal CAA, which determined each group (**Figures 1** and **2**). Finally, we also determined the cardiac event-free survival in the groups based on the maximal CAA diameter, BSA, and the laterality of maximal CAA in the initial CAGs.

Statistical Analyses

Statistical analysis was performed using JMP v 10 (SAS Institute Inc, Cary, North Carolina). Measurements are expressed as mean ± SD. The Turkey-Kramer test was used to test for differences of variables among the groups. Survival, MI-free survival, coronary artery revascularization-free survival, and total cardiac event-free survival were analyzed by the Kaplan-Meier method with 95% CIs. Differences were assessed by the log-rank test. A *P* value of less than .05 was considered statistically significant.