Time Course of Coronary Artery Aneurysms in Kawasaki Disease

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Objectives To determine the timeframe in which coronary artery aneurysms (CAAs) caused by Kawasaki disease reach their maximum diameter, the timeframe in which they regress to normal size, and the cutoff point of the diameter for CAA regression.

Study design We reviewed 195 CAAs of the right coronary artery, left anterior descending artery, and left coronary artery measured by 2-dimensional echocardiography ≥5 times for 1 year after Kawasaki disease in 84 patients using medical records from 1995. The maximum diameters of CAAs were investigated retrospectively. The time to CAA regression using both absolute diameter and Z score were investigated. The cutoff points of the diameter of CAA regression in the 2 classifications were identified using receiver operator characteristic curve analysis. One year after Kawasaki disease, a CAA of <3.0 mm in absolute diameter and a Z score of <2.5 were defined as CAA regression.

Results The time when CAAs reached their maximum diameter ranged from 11 days to 87 days, with a median of 35 days (n = 195). The time to CAA regression ranged from 41 to 386 days, with a median of 136 days in the absolute diameter classification (n = 92); 78% of CAA regression regressed by 200 days. The cutoff point for CAA regression at one year was 5.7 mm for the absolute diameter (area under the curve, 0.887; $P < .0001$; n = 190) and 9.5 for the Z score (area under the curve, 0.815; $P < .0001$; n = 195).

Conclusions CAAs with a smaller diameter regressed earlier, and most CAAs of <6 mm regressed by 6 months after Kawasaki disease. *(J Pediatr 2021;230:133-9)*.

Acute vasculitis owing to Kawasaki disease can often lead to coronary artery aneurysms (CAAs). High-dose intravenous immunoglobulin (IVIG) therapy has markedly decreased the incidence of CAAs since the mid-1980s.[1] Nevertheless, IVIG therapy for acute Kawasaki disease and additional therapies have been performed, and CAAs were found to have occurred in about 5% of patients in a national survey in Japan in the 2010s.[2] The morphologic changes of CAAs are marked within 1 year, especially after the onset of acute Kawasaki disease. Most small CAAs regress, whereas large CAAs often persist.[3-5] Friedman et al reported that CAA regression occurred in 75% of cases in the US population.[4] CAA regression is one of the characteristics of CAA owing to Kawasaki disease vasculitis. CAA regression can be caused by the alleviation of acute inflammation and coronary artery wall thickening.[6] Some cases of CAAs regression may revert to "apparently normal coronary arteries." However, in some cases, CAA regression can be the beginning of the progression of coronary artery disease in the late period after acute Kawasaki disease vasculitis. In the follow-up of this population, it is important to know when CAA reaches its maximum diameter, and when it normalizes in size, as well as the cutoff point of the maximum internal diameter of CAA regression. The changes in the maximum internal diameters of CAAs over 1 year after the onset of Kawasaki disease were investigated retrospectively by 2-dimensional echocardiography (2DE).

Methods

Patients with coronary artery lesions were evaluated by 2DE ≥5 times over 1 year after Kawasaki disease in our institution. The timing of 2DE from the onset of Kawasaki disease was as follows: 1, in week 2 ; 2, at 1 month; 3, at 2-3 months; 4, at 4-6 months; and 5, at 12 months. Furthermore, they were closely followed depending on the degree of their disease. The patients who had ≥1 CAA caused by Kawasaki disease within 100 days after Kawasaki disease and who had a record of having undergone ≥5 measurements of the maximum internal diameters using 2DE in the medical records from 1995 were reviewed. The maximum internal diameters of the left main coronary artery (LCA, segment 5), proximal portion of the right coronary artery (RCA,

AUC	Area under the curve	LAD	Left anterior descending artery
BSA	Body surface area	LCA	Left main coronary artery
CAA	Coronary artery aneurysm	M	Medium
CAG	Coronary angiography	RCA	Right coronary artery
2DE	2-Dimensional echocardiography	S	Small
IVIG	Intravenous immunoglobulin	VS	Very small
L	Large		

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segment 1), and left anterior descending artery (LAD, segment 6) were retrospectively investigated.[7]

Diagnosis of CAA and Measurement of the Maximal Internal Diameter of Each Branch on 2DE

The diagnosis and measurements of CAAs were determined by a pediatric cardiologist and echocardiographers. The measurements of the CAAs were made with a SONOS 5500 (Hewlett Packard Company) and iE 33 (intelligent Echocardiography System 33, Philips). In this study, CAAs were evaluated using 2 classifications, the absolute diameter classification and the Z score classification. A CAA was defined as having a maximum internal diameter of ≥3 mm in the absolute diameter classification and a Z score of ≥2.5 in the Z score classification.[8,9] A CAA regression was defined as one having a maximum internal diameter of <3 mm and a Z score of <2.5.[4,5] A nonregressed CAA at 1 year after Kawasaki disease was defined as having a maximum internal diameter of ≥3 mm and a Z score of ≥2.5. First, the time when CAAs reach their maximum diameter within 100 days after Kawasaki disease were analyzed. Second, the time to CAA regression was investigated, including in the 4 groups. In the absolute diameter classification, the CAAs were divided into 4 groups based on the maximum diameter within 100 days after the onset of Kawasaki disease in each branch: very small (VS), ≥3.0 mm but <4.0 mm; small (S), ≥4.0 mm but <6.0 mm; medium (M), ≥6.0 mm but <8.0 mm; and large (L), ≥8.0 mm.[9,10] Using the Z score classification, the CAAs were also divided into 4 groups based on the Z score of the maximum diameter within 100 days after Kawasaki disease: ZS ($Z \geq 2.5$ but $Z < 5.0$); ZM_1 ($Z \geq 5.0$ but $Z < 7.5$); ZM_2 ($Z \geq 7.5$ but $Z < 10.0$); and ZL ($Z \geq 10.0$). In the present study, the Z score in the Japanese population was used.[7,8] Third, the cutoff value of the maximum CAA diameter within 100 days after Kawasaki disease for CAA regression was analyzed. Last, the relationship between the maximum diameter of the largest CAA within 100 days after Kawasaki disease and its diameter at 1 year after Kawasaki disease was investigated. Furthermore, the prospective maximum CAA diameter at 1 year after Kawasaki disease was calculated. The ethics committee of our institution approved this retrospective study (R19003-2). For this study, the final diagnoses of Kawasaki disease and CAA after Kawasaki disease were based on the diagnostic guidelines prepared by the Japanese Circulation Society.[8]

Statistical Analyses

Statistical analyses were performed using JMP 10 software (SAS Institute Inc). The measurements are expressed as medians with range. When significant differences were found with the Tukey test, a post hoc analysis was then performed. The cutoff point of the diameter for regressed CAAs was determined using receiver operator characteristic curve analysis. A P value of <.05 was considered significant.

Results

Patients

A total of 84 of the 103 patients (60 males and 24 females) with CAA who visited our institution from 1995 were included (**Table I**; available at www.jpeds.com). Nineteen patients were excluded because they lacked the 5 measurements. The number of patients per decade was as follows: 1995-1999, n = 16; 2000-09, n = 47; and 2010-2018, n = 21. The age at onset of the acute Kawasaki disease episode ranged from 2 months to 13 years, with a median of 26 months. During the initial 2DE, the number of patients with a body surface area (BSA) of <0.50 m^2 and with a BSA of ≥0.50 m^2 was 39 (46%) and 45 (54%), respectively. There were 79 patients (94%) who were treated with aspirin and IVIG therapy as the first-line treatment for acute Kawasaki disease. The initial day of IVIG treatment ranged from 2 to 20 days with a median of 5 days after the onset of Kawasaki disease. Sixty-nine patients (82%) had the initial IVIG treatment within 7 days after the onset of Kawasaki disease. However, 2 patients were treated with the initial IVIG treatment beyond 10 days after the onset of Kawasaki disease. Seven patients with a high risk score for IVIG therapy resistance had initial aggressive therapy with IVIG and steroids. No acute treatment was performed in 5 patients (6%). In 60 of the 79 patients (76%), the first IVIG therapy of 2 g/kg was ineffective; 52 patients received an IVIG dose of ≥2 g/kg in total. Furthermore, 38 patients had adjunctive therapy. The treatment added to IVIG is shown in **Table I**. The duration of fever ranged from 3 to 25 days, with a median of 10 days. The time of CAA appearance by 2DE ranged from 4 to 34 days, with a median of 12 days. As an antithrombotic therapy after Kawasaki disease during the late period, antiplatelets were administered in 55 patients, and antiplatelets and coumadin were administered in 29 patients. If all CAAs in each patient regressed, the medication was stopped. The medication was stopped in 48 of 84 patients (57%) within 1 year, and coumadin was stopped in 5 of 29 patients. There were no cardiac events within 1 year in any of the 84 patients, although 5 patients had cardiac events later. The number of 2DE examinations ranged from 5 to 15, with a median of 7 (**Figure 1**; available at www.jpeds.com).

Classifications Based on the Maximum Diameter and the Z-Score of the Largest CAA

The total number of branches in which the maximum diameter was measured ≥5 times over 1 year after the onset of Kawasaki disease was 190 in the absolute diameter classification and 195 in the Z score classification, respectively (**Tables I** and **II**). The time when CAAs reached their maximum diameter ranged from 11 to 87 days, with a median of 35 days (**Figure 2**; available at www.jpeds.com). At the site of CAAs, the number of RCAs, LADs, and LCAs analyzed using the absolute diameter classification was 69, 72, and

Table II. Prevalence of CAA regression based on the maximum diameter and the Z score of the largest CAA within 100 days after Kawasaki disease

	VS	S	M	L
The absolute diameter classification (total = 190)				
No. of CAAs	21	80	55	34
Maximum diameter of the largest CAA* (mm)	3.5 (3.1 to 3.9)	4.5 (4.0 to 5.9)	6.6 (6.0 to 7.9)	9.1 (8.1 to 16.8)
No. of CAA regression	20 (95%)	59 (74%)	13 (24%)	0
Maximum diameter of regressed CAA† (mm)	2.0 (1.9 to 2.8)	2.2 (1.3 to 2.9)	2.4 (1.4 to 2.9)	–
Time to CAA regression (days)	90 (41 to 187)	155 (56 to 386)	156 (117 to 360)	–
No. of nonregressed CAAs	1 (5%)	21 (26%)	42 (76%)	34 (100%)
Maximum diameter of nonregressed CAA‡ (mm)	3.1	3.4 (3.0 to 5.6)	4.4 (3.0 to 8.7)	8.8 (3.2 to 8.7)
	ZS	ZM1	ZM2	ZL
The Z score classification (total = 195)				
No. of CAAs	19	54	62	60
Z score of the largest CAA	3.5 (2.7 to 4.9)	6.3 (5.0 to 7.4)	7.5 (6.0 to 9.9)	10.0 (11.6 to 16.0)
No. of CAA regression	19 (100%)	37 (69%)	32 (52%)	7 (12%)
Z score of regressed CAA	0.9 (−1.4 to 2.1)	1.1 (−0.8 to 2.4)	1.4 (−0.6 to 2.4)	1.4 (−1.2 to 2.4)
Time to CAA regression (days)	85 (45 to 187)	151 (41 to 379)	210 (60 to 386)	244 (137 to 377)
No. of nonregressed CAAs	0	17 (31%)	30 (48%)	53 (88%)
Z score of nonregressed CAA	–	3.2 (2.5 to 5.1)	5.6 (2.9 to 11.5)	8.8 (2.9 to 15.9)

The values are median (range).
*The CAA which is the largest within 100 days after Kawasaki disease.
†The maximum diameter of regressed CAA in the late period.
‡The maximum diameter of nonregressed CAA in the late period.

49, respectively. The numbers of the respective groups based on the maximum diameter of the largest CAA within 100 days after Kawasaki disease were: VS 21; S 80; M 54; and L 34 (Table II). At the site of CAAs, the number of RCAs, LADs, and LCAs analyzed using the Z diameter classification was 72, 73, and 50, respectively. The numbers of the respective groups based on the maximum diameter of the largest CAA within 100 days after Kawasaki disease were: ZS 19; ZM_1 54; ZM_2 62; and ZL 60. The median and range of the maximum diameter in each group are shown in Table II.

The Relationship between the Maximum Diameter of the Largest CAA within 100 Days after the Onset of Kawasaki Disease and the Time to CAA Regression

The number of CAA regression using the real diameter and the Z score classification was 92 of 190 patients (48%) and 95 of 195 patients (49%), respectively (Table II). The time to CAA regression ranged from 41 to 386 days. The median number of days in the absolute diameter classification and Z classification were 136 and 155, respectively. Seventy-two CAAs (78%) of CAA regression in the absolute diameter classification had regressed by 200 days. The maximum diameter of CAA regression ranged from 3.2 to 7.9 mm, with a median of 4.6 mm in the absolute diameter classification. Sixty-six CAAs (69%) of CAA regression also regressed by 200 days in the Z classification. The maximum Z score of CAA regression ranged from 2.7 to 11.1, with a median Z score of 6.7. The number of CAA regression by the interval from the onset of Kawasaki disease is shown in the 4 groups based on the maximum diameter of the largest CAA within 100 days after the onset of Kawasaki disease in Figure 3.

The Number and Time to CAA Regression Based on Its Maximum Diameter within 100 Days after the Onset of Kawasaki Disease

In the absolute diameter classification, the number of CAA regression in each group was as follows (Table II): VS 20 (95%); S 59 (74%); and M 13 (24%). There was no CAA regression in the L group. The time to CAA regression in each group (days) is shown in Table II. The mean time to CAA regression was earlier in the VS group than in the S and M groups ($P < .05$). Using the Z score classification, the number of CAA regression in each group was: ZS 19 (100%); ZM_1 37 (69%); ZM_2 32 (52%); and ZL 7 (12%). The maximum diameter in 7 regressed CAAs in the ZL group was <8 mm. The mean time to CAA regression was earlier in the ZS group than in the ZM_2 group ($P < .05$).

Cutoff Points of CAA Regression at 1 Year

The cutoff point of the maximum diameter within 100 days after Kawasaki disease for an internal diameter of <3 mm at 1 year was 5.7 mm (area under the curve [AUC], 0.887; $P < .0001$; n = 190) for all branches (Table III), 5.2 (AUC, 0.910; $P < .0001$; n = 69) for the RCA, 5.3 mm (AUC, 0.925; $P < .0001$; n = 72) for the LAD, and 5.7 mm (AUC, 0.743; $P = .0009$; n = 49) for the LCA. The cutoff point for a BSA of <0.50 m^2 was 5.5 mm (AUC, 0.874; $P < .0001$; n = 91), and that for a BSA of ≥0.50 was 5.7 mm (AUC, 0.920; $P < .0001$; n = 99); those for respective branches in the 2 groups are shown in Table III. The cutoff point of the Z score within 100 days after Kawasaki disease for a Z score of <2.5 at 1 year was 9.5 (AUC, 0.815; $P < .0001$, n = 195) for all branches, 7.4 (AUC, 0.846; $P < .0001$, n = 72) for the RCA, 9.2 (AUC, 0.818; $P < .0001$, n = 73) for the LAD, and 9.5 (AUC, 0.735; $P = .0008$, n = 50)

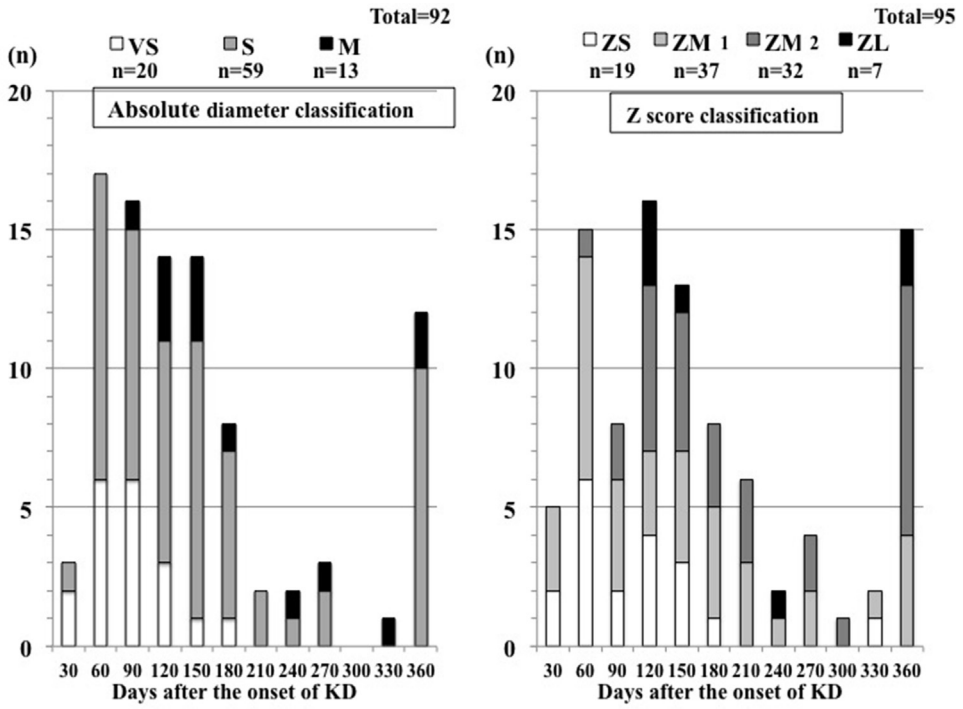

Figure 3. The time to CAA regression based on the maximum diameter and the Z score of the largest CAA within 100 days after Kawasaki disease. The number by the interval from the onset of Kawasaki disease to CAA regression is shown. **Left,** The detection of CAA regression based on the maximum diameter. A CAA of <3 mm was defined as regression of the CAA. **Right,** The detection of CAA regression based on the Z score of the maximum diameter. A Z score of <2.5 was defined as regression of the CAA.

Table III. Cutoff points of the maximum diameters for CAA regression at 1 year after Kawasaki disease

Branches	Diameter (mm)	AUC	*P* Value	n	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	PA (%)
The absolute diameter classification (total = 190) diameter of <3 mm at 1 year									
Total									
Total	5.7	0.887	<.0001	190	82	82	81	84	82
RCA	5.2	0.910	<.0001	69	70	95	90	83	86
LAD	5.3	0.925	<.0001	72	81	94	94	83	88
LCA	5.7	0.743	.0009	49	89	59	90	83	86
BSA < 0.50 m^2									
Total	5.5	0.874	<.0001	91	78	81	86	71	79
RCA	5.3	0.969	<.0001	31	76	93	93	76	84
LAD	5.3	0.907	<.0001	35	79	100	100	69	86
LCA	6.1	0.703	.0566	25	100	45	70	100	76
BSA ≥ 0.50 m^2									
Total	5.7	0.920	<.0001	99	86	86	78	92	86
RCA	6.6	0.909	<.0001	38	100	71	56	100	79
LAD	5.6	0.984	<.0001	37	100	88	81	100	92
LCA	5.7	0.843	.0019	24	92	64	75	88	79
	Z score								
The Z score classification (total = 195) Z score of < 2.5 at 1 year									
Total	9.5	0.815	<.0001	195	89	58	67	85	73
RCA	7.4	0.846	<.0001	72	62	89	76	80	79
LAD	9.2	0.818	<.0001	73	85	74	79	81	79
LCA	9.5	0.735	.0008	50	100	40	71	100	76

NPV, negative predictive value; *PA*, predictive accuracy; *PPV*, positive predictive value.

for the LCA. There was no significant difference in the cutoff point among the 3 branches.

Relationship between the Largest CAA Diameter within 100 Days after the Onset of Kawasaki Disease and the Maximum Internal Diameter of the CAA at 1 Year

The relationship between the largest diameter within 100 days after the onset of Kawasaki disease and the maximum internal diameter of the CAA at 1 year was: $y = -1.943 + 0.973x + 0.132\ (x - 5.363)^2$ ($P < .001$; n = 195) (Figure 4). One year after Kawasaki disease, the maximum diameters of most CAAs of <6 mm within 100 days after the onset of Kawasaki disease decreased. In 4 CAAs (2 RCAs and 2 LADs) of the 195 branches, the maximum internal diameter after 1 year was larger than that of the largest diameter within 100 days after the onset of Kawasaki disease. The age at the onset of Kawasaki disease in patients with larger CAA ranged from 6 to 11 years, and the median age was 8 years. The mean ± SD maximum diameter changed from 9.3 ± 1.5 to 11 ± 2.3 mm.

Discussion

This study showed that the changes in the coronary arterial diameters for 1 year after Kawasaki disease depended on the degree of the maximum diameter of the peak CAA within 100 days after Kawasaki disease. It has been reported that the timing of the appearance of a CAA was 11 days in 1981.[11] In our study, the median day of CAA appearance was 12 days. However, there have been no reports of when the diameter of the CAA is the largest. The present study showed that the detection time of the peak CAA was around 30 days. The CAAs usually occur in the second week after the onset of Kawasaki disease, and the diameters of the CAAs can still increase after the alleviation of the fever. Pathologically, the acute vasculitis is reported to end in the seventh week after the onset of Kawasaki disease.[12,13] Therefore, it has been recognized that the formation and peak time of CAAs occur between the second and seventh weeks. Furthermore, it has been thought that CAA formation and diameter depend on the degree of destruction of the coronary arterial wall structure during the acute phase.

In contrast, the timing of CAA regression was clarified using 2DE in the present study. The regression of CAAs depended on the largest diameter of each CAA within 100 days after Kawasaki disease. The smaller CAAs regressed earlier. The time to CAA regression was around 140 days, and most CAAs regressed around 6 months. The cutoff point of the absolute diameter was 5.7 mm, and that of the Z score was 9.5. There was a difference between the 2 classifications. In the absolute diameter classification, the physical growth for 1 year is not considered in the cutoff point of CAA regression at 1 year after Kawasaki disease. In contrast, the Z values of regressed CAAs are modified by the factor of physical growth. Even if the value of the absolute diameter at 2 months after Kawasaki disease was the same as that at 1 year after Kawasaki disease, the Z score would decrease because of the increased BSA of the children. There was a discrepancy

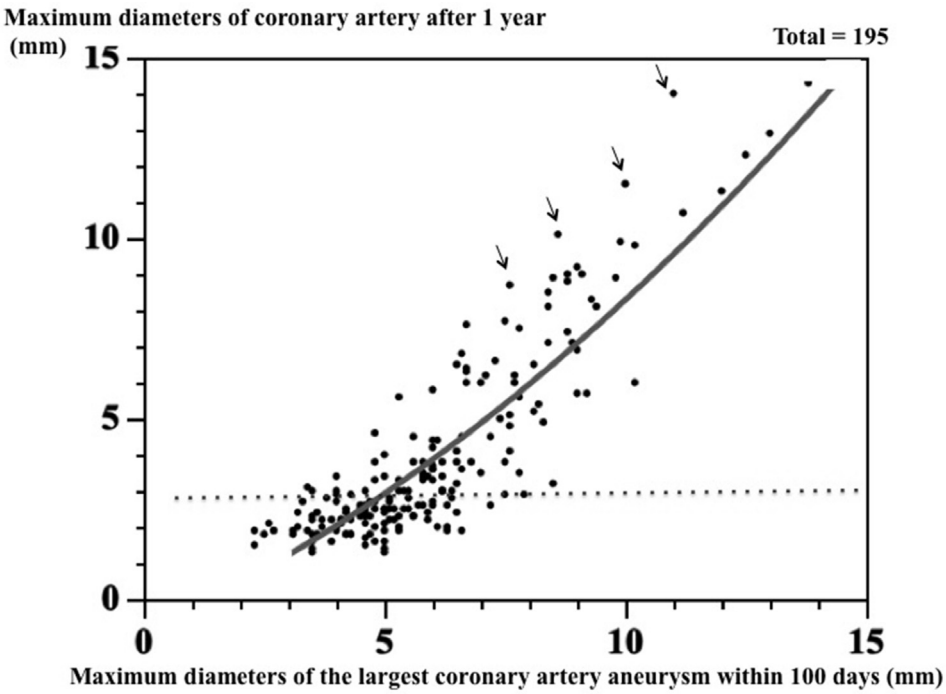

Figure 4. The relationship between the maximum diameter of the largest CAA within 100 days after Kawasaki disease and its diameter at 1 year after Kawasaki disease. →, The maximum diameters after 1 year are larger than those of the largest diameter within 100 days after the onset of Kawasaki disease.

between the 2 classifications in regression of some CAAs. When some CAAs in small children showed regression in the absolute diameter, they did not show regression at the same time in the Z score classification.

We previously reported the morphologic changes in CAAs and the incidence of stenotic lesions based on the maximal CAA diameter within 100 days after Kawasaki disease using selective coronary angiography (CAG) by cardiac catheterization.[3,14] With a larger coronary artery diameter, the incidence of stenotic lesions is much greater in the late period. Furthermore, the cutoff point of stenotic lesions by selective CAG was 7.0 mm, which was beyond the cutoff points of CAAs regression in this study. However, there may be a small difference in the cutoff points between 2DE and CAG because of the difference in the accuracies and properties of the procedures.

In the present study, the relationship between the largest diameter of a CAA within 100 days after Kawasaki disease and its diameter at 1 year after Kawasaki disease was calculated. The maximum internal diameters in most CAAs of <6 mm usually decrease 1 year after Kawasaki disease, because of the postinflammation changes and subsequent intimal thickening. However, in some large CAAs in older children, the diameters increased at 1 year after Kawasaki disease. The increasing of CAA diameter in the late period is rarely found at the proximal large CAAs in older children. We previously also reported an expanding CAA by selective CAG in the late period.[15] It has been suggested that an expanding CAA occurs because of the coronary artery pressure and the severe destruction of the coronary arterial wall. Furthermore, the somatic growth of adolescents may also be related to the increase in CAA diameter.

"CAA regression" in this study means a CAA that normalizes in size by 2DE measurements in the late period. It is speculated that the CAA regression group can be classified into 2 apparent subgroups. One is a group in which CAA reverts to almost normal coronary artery, and the other is a group which CAA has coronary wall abnormalities.[16] CAA regression does not necessarily imply improvement of the coronary artery lesions; it indicates only that the maximum internal diameter is decreased, but the involvement of the coronary artery wall persists.[17] Therefore, regressed CAAs can cause acute coronary syndrome in adults.[18-20] It should be recognized that the outcome of patients with CAA regression is not always the same as that of patients without CAAs. However, it is often difficult to determine whether an apparently normal coronary artery on angiography in the late period after Kawasaki disease represents regression of a CAA or a normal coronary artery.[21] Most CAAs of <6 mm can regress by around 6 months after Kawasaki disease. We should evaluate this population based on this knowledge. The existence of coronary artery calcification by computed tomography angiography in the late period would be helpful to differentiate coronary artery wall abnormalities.[22] The morphologic changes of CAAs are the greatest within 1 year after Kawasaki disease. Therefore, CAAs regression within 1 year after the onset of Kawasaki disease was the specific focus of investigation in the present study. Although most CAAs regress within 1 year after the onset of Kawasaki disease, others can regress over a few years after the onset of Kawasaki disease.[4,5] Regressed CAAs must also be investigated in the long-term period, and changes in their coronary arteries with aging must continue to be observed.

This was a retrospective study. The time and number of 2DE examinations varied, but routine examinations were scheduled. To confirm the results of this study, a further prospective study is needed. However, the maximum longitudinal length of CAAs for CAAs regression was not considered in this study; it may also be related to CAAs regression. The normal value of the coronary artery lumen differs according to body size; therefore, the analyses in which the subjects were divided into 2 groups based on the BSA were added.

The cutoff point of diameter for CAAs regression was 5.7 mm. It was found that the smaller the CAA diameter was during the acute phase, the earlier the CAA regressed. Most CAAs <6 mm regressed by around 6 months after Kawasaki disease. ■

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50 Years Ago in *The Journal of Pediatrics*

Early Success of Exchange Transfusion in Treating Neonatal Disseminated Intravascular Coagulation; How Far Have We Come?

Gross S, Melhorn D. Exchange transfusion with citrated whole blood for disseminated intravascular coagulation. J Pediatr 1971;78:415-9.

In 1971, Gross and Melhorn reported successful use of whole blood exchange transfusion for neonatal disseminated intravascular coagulation (DIC). Exchange transfusion was introduced in the 1940s for the treatment of hemolytic disease of the newborn. By 1970, exchange transfusion also had been adapted to treat hyperbilirubinemia. At that time, DIC in neonates was an evolving disease entity that was challenging to both diagnose and treat. Limited information was available about normal coagulation in the neonate and about neonatal coagulation during DIC. The mortality rate was high, and treatment relied heavily on treating the underlying illness, which in contemporary reports was largely idiopathic respiratory distress syndrome or sepsis. In that context, this series of 4 neonates and one 4-year-old child who had survived DIC after receiving exchange transfusions of citrated whole blood was remarkable. However, this was a small retrospective study that would need to be validated in a randomized controlled study.

Eleven years later, a randomized controlled trial compared exchange transfusion vs plasma and platelets vs no coagulation-directed therapy. No differences were noted in survival between the 3 groups. The results were not supportive of any benefit of using exchange transfusion (or plasma and platelet transfusion) in neonatal DIC. However, there were only 11 patients in each arm, and no power calculation was reported. It remains unclear whether the study was powered to show any difference between the treatment arms.[1]

Fifty years later, whole blood has fallen out of favor as a transfusion product, to be replaced by separated blood components (packed red blood cells, plasma, platelets, cryoprecipitate). Currently, whole blood exchange transfusion does not have a role in managing neonatal DIC. In addition, exchange transfusions for approved indications are now carried out with blood components rather than with whole blood. Separated and processed blood components (plasma, cryoprecipitate, and platelets) as replacement products are used for treating neonatal DIC. In this regard, although we possess much more knowledge about neonatal coagulation, management of neonatal DIC still relies on resolving the underlying illness and replacement of blood products as needed.

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Reference

1. Gross SJ, Filston HC, Anderson JC. Controlled study of treatment for disseminated intravascular coagulation in the neonate. J Pediatr 1982;100:445-8.

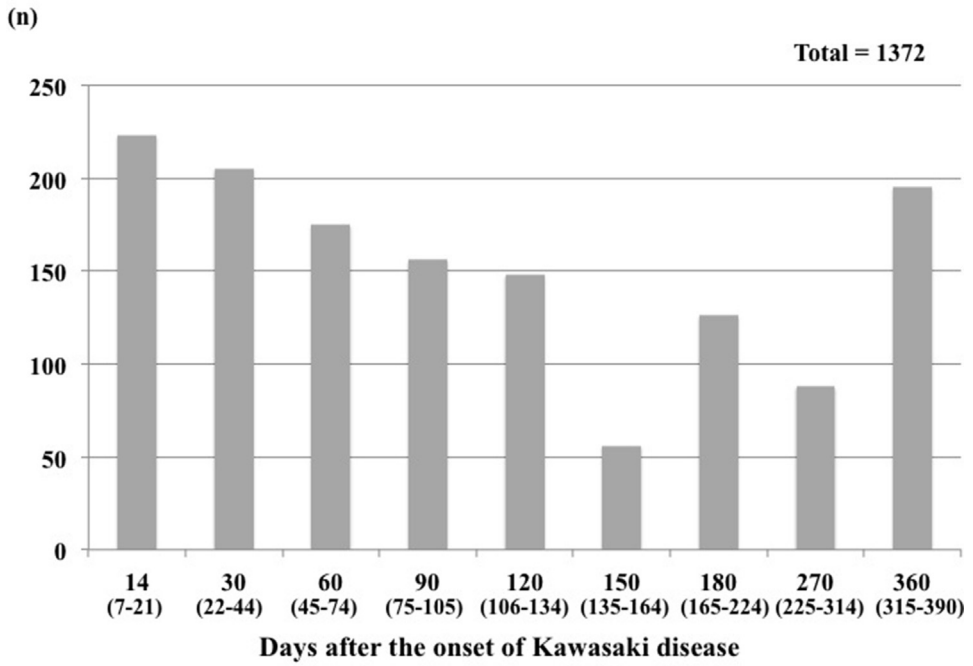

Figure 1. The number of the branches measured by 2DE in each time after the onset of Kawasaki disease.

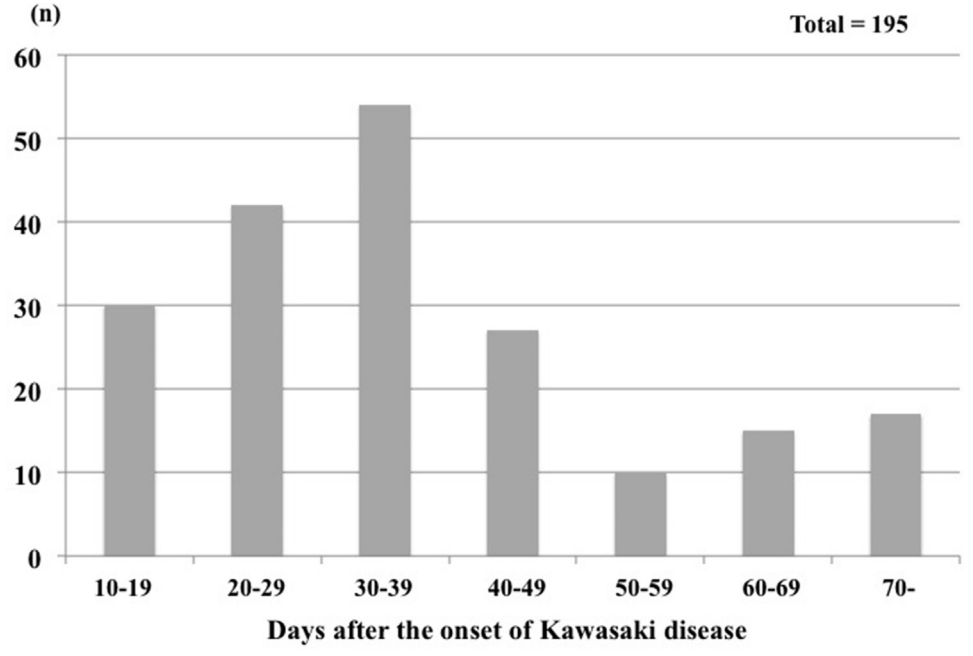

Figure 2. The detection of the largest CAA within 100 days after Kawasaki disease. The number by the interval from the onset of Kawasaki disease to the detection of the largest CAA is shown.

Table I. Patient characteristics

Diagnosis and treatment	No. (%)
No. of patients	84
Sex	
Male	60 (71%)
Female	24 (29%)
Age at the onset of Kawasaki disease	
Median	26 months
Range	2 months to 13 years
Diagnosis of Kawasaki disease	
Typical Kawasaki disease	80 (95%)
Incomplete Kawasaki disease	4 (5%)
IVIG	
≤2 g/kg	26 (31%)
>2 g/kg but ≤4 g/kg	42 (50%)
>4 g/kg	10 (12%)
None	5 (6%)
Adjunctive therapy	38 (45%)
Steroids	14
Ulinastatin	14
Steroids and ulinastatin	10
Steroids and cyclosporine	3
Cyclosporine	1
Plasmapheresis	1
Initial day of IVIG treatment	
Median	5
Range	2-20
Duration of fever (days)	
Median	10
Range	3-25
Site of CAAs	
Total	195
RCA	72
LAD	73
LCA	50
Antithrombotic therapy	
Antiplatelets and coumadin	29 (35%)
Antiplatelets alone	55 (65%)